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GENETIC KNOWLEDGE, OPINIONS AND PRACTICES AMONGST GENERAL PRACTITIONERS

Kelly Lea Margaret Trenton

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of
Master of Science in Medicine

Johannesburg 2003

DECLARATION

I, Kelly Lea Margaret Trenton declare that this research report is my own work. It is being submitted in partial fulfilment for the degree of Master of Science in Medicine to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any other degree or examination at this or any other University.



Kelly Lea Margaret Trenton

10th day of May 2003

DEDICATION

To my family who never cease to inspire and support me.

ABSTRACT

Medical Genetics is playing a greater role in healthcare than ever before. The question arises though, as to whether these scientific advances are moving swiftly enough from the field of science to the practices of general practitioners (GPs) of medicine. In general, since the introduction of genetic services in South Africa (SA) in 1971 (Jenkins, 1990), knowledge and attitudes regarding the utilization of these services have often been confused. Medical institutions and practicing doctors are sometimes unaware of the important intricacies of genetics that may impact on their patients. Genetic counselling is underutilized and many genetic conditions are neither recognised nor diagnosed. Medical Genetics is an important part of complete patient care, but in SA it has lagged far behind in areas such as health service and education. The aims of this study were to assess and analyze the current genetic knowledge and attitudes that are in place amongst GPs in the Gauteng province of SA, and to obtain a clearer understanding of their opinions towards genetic counselling. A researcher-designed questionnaire was posted to 1091 GPs in the Gauteng area. Approximately 6.7% of this target group replied. Fifty-one face-to-face interviews using the same questionnaire were also conducted by the researcher so that first hand responses could be recorded. The findings from all data collected show that there are many areas where knowledge could be improved. Whilst genetics and genetic counselling is held in high regard, and deemed important in the primary care context by GPs, it is generally viewed to be out of their area of expertise. Genetic education programs aimed at improving GP awareness and knowledge are thus recommended to enhance the quality of patient care.

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CHAPTER 1

INTRODUCTION

In this chapter motivation is given for the study undertaken, and the aims are outlined. A literature review is included to introduce topics which are relevant to this project. Medical genetics is rapidly expanding, and it is discussed in both a worldwide and a South African context. New developments such as the Human Genome Project and gene therapy and their potential impact on the practice of medical practitioners are also discussed. A questionnaire was used to assess the knowledge of general practitioners (doctors working in a frontline, primary care service to patients). Many topics including single gene disorders, multifactorial disorders, prenatal diagnosis, dynamic mutations and genetic counselling were covered in this questionnaire and are thus discussed in the literature review. Common South African disorders and current genetic services are discussed and information relevant to the background of this study is mentioned.

1.1 Motivation for the study

Medical genetics is playing an increasing role in primary health care. There is little doubt that the way in which medicine is practiced will be influenced as genetic technology continues to grow. According to Wertz *et al* (1995) approximately one in ten people will

have a genetic disorder in their lifetime and it has been estimated that every person carries approximately three or four recessive mutations.

In a country such as South Africa, the need for genetic services is often greatly underestimated. Often, more prevalent health conditions (such as HIV and TB) have been targeted for research and development, and medical genetics is perhaps not seen as a priority (Kromberg and Jenkins, 1997). When the benefits that an established medical genetic service can provide are examined, it is clear that where medical genetic testing is considered a great cost, the prevention of the birth of an infant with a genetic disorder or birth defect renders these costs insignificant. The costs of providing medical attention for a handicapped child throughout its lifetime are an enormous burden on the health budget (Viljoen and Beighton, 1995). As genetic knowledge improves, minimising disease risks through preventative medicine and identifying potential genetic disorders in patients is becoming vital (Karanjawala and Collins, 1998). The introduction of screening programs to high-risk populations has been, and will continue to be invaluable in genetic disease prevention (Sachs and Korf, 1993).

Human genetics in South Africa has lagged far behind in areas such as health service and education – aspects, which are clearly of benefit. Although South African medical genetic services have been in place for nearly three decades, they are based mainly in cities and academic centres and are thus not accessible to the vast majority of the population (Jenkins, 1990). These services are provided primarily by academic staff who also have teaching and research commitments and thus it has become pertinent for other health care

professionals to become involved to extend the service to a larger proportion of the population. South Africa is a developing country with many health care issues. At present the public health care system is not felt to be adequately meeting the needs of patients and there has been a noted need for reform (Volmink *et al*, 1993). The patient-doctor ratio is extremely high (Rajendra, 1995), this means that there is extreme pressure on doctors and less and less patients have access to specialists should they need them. It is becoming more obvious that general practitioners need to incorporate elements of genetic medicine into their role to cope with the demand arising from the needs of patients (Emery and Hayflick, 2001).

Emery and Hayflick (2001) have identified the following potential roles of primary care practitioners in genetic medicine:

- Identification of individuals who may benefit from genetic services, including those with a genetic and those at risk for having or transmitting a genetic disorder
- Recognition of historical and physical features of genetic conditions
- Monitoring the health of individuals with a genetic disorder, in conjunction with specialists in genetics
- Provision of basic genetic information to patients and families to help understanding and informed decision making
- Coordination of care for individuals with complex genetics service needs
- Recognition of the special psychological issues for a family in which one or more members are affected with a genctic disorder or susceptibility

- Knowledge of how to access the full range of genetics services from which patients might benefit
- Appropriate referral of patients with additional genetics services needs
- Facilitation of use of genetic services

This study aimed to assess the knowledge of primary medical caregivers such as general practitioners (GPs) so as to ascertain how able they were to provide these aspects of genetic medicine. GPs come into contact with a large number of patients and, according to Walpole *et al* (1997), are considered the most common health professional to be asked questions regarding hereditary diseases by patients.

1.2 The aims of the study

The aims of this study were to:

1. Assess the level of knowledge that GPs have in various areas of the field of medical genetics (knowledge of Mendelian inheritance, chromosomal abnormalities, prenatal diagnosis, epidemiology of the more common genetic disorders in South Africa and potential teratogens, were examined).
2. Explore the current views, practices and understanding of genetic counselling of GPs in Gauteng.
3. Obtain information that may influence the way in which future genetic education programs are implemented for GPs.

4. Gain experience as a trainee genetic counsellor in interacting with medical professionals and to improve my interpersonal skills by conducting interviews with GPs
5. Obtain additional information that postal questionnaires alone may not yield by being present and encouraging participation during interviews with GPs

This study represents the first of its kind in many years and aimed to get a general idea of the level of genetic knowledge so as to aid the design of educational programmes and to pave the way for further, larger studies of its kind. The setting and scope of this study are described in Section 2.1

1.3 Literature Review

1.3.1 Medical genetic development

Recent advances in the field of genetics have been revolutionary. We need look no further than daily newspaper headlines to see how such modern technological advances have infiltrated every part of our lives. Our understanding of human genetics has changed substantially in recent years and our knowledge has increased exponentially (Williamson and Robertson, 1999).

The knowledge of hereditary disease has existed since biblical times in one form or another but was truly only elucidated from the theories of "bad blood" and diseases "running in families" since the time of Gregor Mendel (Bains, 1993). Mendel, in the nineteenth century, produced the first scientific explanation for inherited traits and

established the laws of inheritance. Since then, the field of genetics has developed rapidly. More and more genetic traits are becoming known to us and since the 1960s, investigations have moved from clinical elucidation, to understanding such traits at the molecular and biochemical levels (Bains, 1993). DNA-based technologies have uncovered a new research tool for studying disease aetiology and successful identification of genes that cause disease is under way (Kaprio, 2000).

Genetic disorders and birth defects occur in approximately 3-5 % of all live births and are responsible for neonatal deaths and stillbirths (Wertz *et al*, 1995). A mere twenty years ago only about twelve human genes had been sequenced and roughly one hundred located chromosomally (Williamson and Roberston, 1999). Today, our knowledge in this area has improved and with the Human Genome Project practically now, is soon to be revolutionised. Genetic prediction of an individual's risk of disease and their respective responsiveness to certain drugs will become a part of medical practice and will influence the way in which disorders are diagnosed and managed (Collins and McKusick, 2001).

1.3.1.1 The Human Genome Project

The Human Genome Project (HGP) began formally in 1990 (Guyer and Collins, 1993). The HGP is an international effort to ascertain a working draft of the entire genetic sequence of the human genome. The human genome sequence will represent a description of all genes and will inevitably allow us to establish associations between

specific genes and disease presentations (Bentley, 2000). It is thus expected to have a greater impact on medical practice than any other previous contribution.

According to Sachs and Korf (1993), the human genome is estimated to consist of 50 000 to 100 000 genes encoded in 3 billion base pairs of DNA. The isolation and description of genes will provide the medical community with more information, which may have an impact on patient care. Disease detection, diagnosis, screening, prevention and counselling will become more advanced and more complex as we are able to offer patients more and more. Prenatal diagnosis will also become more advanced as techniques improve and revolutionary concepts such as gene therapy gain momentum (Sachs and Korf, 1993).

The year 2000 marked the announcement that the vast majority of the human genome had been sequenced and in 2001 the results of both the private-funded (Venter *et al*, 2001) and public-funded (The International Human Genome Sequencing Consortium) projects were published (Patrinos and Drell, 2002). All public-funded results are required to be made available to everyone and although this doesn't strictly apply to private-funded ventures, suggestions have been made that policies be drafted to enforce this (Patrinos and Drell, 2002). At present, the identification of the sequence of the human genome has little immediate impact on medical practice. Work needs to be done to match a gene sequence to a gene function so that identification of specific disease causing alleles can be orchestrated (Cardon and Watkins, 2000). This is where the challenge now lies and it is estimated that each gene will require 40 years of study (Cohen, 2000). Once sense has

been made of the human genome however, its importance in a medical setting will be insurmountable.

In the future, it is believed that knowledge of the human genome sequence will lead to a shift towards preventative medicine. If we know what genes do, we can potentially predict problems before they occur. This kind of information will lead to novel therapies and means of preventing genetic illnesses (Guyer and Collins, 1993). Understanding our genetic make-up will be not only be helpful in understanding how the human body functions, but may explain the role of genetic factors in many diseases. Approaches to treatment and prevention may alter and new effective treatment strategies may be implemented (Collins and Mansoura, 2001).

1.3.1.2 Gene therapy

Gene therapy can be described as the replacement of a deficient gene product or correction of an abnormal gene (Meuller and Young, 1998). This technology is still in its infancy and according to Lin (1998), it is a proactive measure stemming from the inspirations of the HGP. Gene therapy can be performed *in vitro*, or *in vivo* depending on whether cells can be cultured and replaced in the affected individual. Much controversy surrounds gene therapy, as although it may represent a promising form of treatment for some disorders, it may also lead to many ethical dilemmas as we face the challenge of

deciding whether gene therapy can be used on an unborn baby (fetal gene therapy) (Sachs and Korf, 1993).

A seemingly simple and obvious prerequisite for gene therapy is that the gene in question must have been cloned and the sequence elucidated. Early attempts at gene therapy proceeded without this knowledge and failed. A clear path towards the more frequent use of this technique is thus visible in light of the HGP and the many more genes that will be available to use in this type of therapy. As the realm of medicine becomes more and more orientated towards the field of genetics, the use of gene therapies will be more common (Karnes, 1992). Although technological advances are paving the way for new treatment options such as gene therapy, there are many obstacles to still overcome. The process is indeed complex and we are still in the early stages of developing proper research strategies (Nevin, 2000).

1.3.1.3 Single gene disorders

Single gene disorders are disorders which are caused by a gene fault in a single gene. In some disorders, both copies of a gene need to be faulty in an individual for the disease to occur (autosomal recessive) whilst other disorders require that only one of the copies of a gene in an individual have a mutation for disease presentation (autosomal dominant). Other disorders are sex linked, as the gene involved is present on either the X or Y chromosome. This group of disorders are also termed "Mendelian" disorders as their inheritance modes follow the patterns that were first elucidated by Mendel.

The first single gene trait to be discovered was for the rare disorder called alkaptonuria. This disorder was first characterised by William Bateson and Archibald Garrod and together they proposed that this condition had a recessive pattern of inheritance (Meuller and Young, 1998).

Over 10 000 single gene traits and disorders have been identified. Many of these are quite rare on an individual scale but together affect between 1 and 2% of the general population (Meuller and Young, 1998). Some of the most common single gene disorders are Huntington disease, myotonic dystrophy, albinism, cystic fibrosis, neurofibromatosis, Haemophilia A, Duchenne muscular dystrophy, spinal muscular atrophy and sickle cell anaemia.

The HGP has great implications for single gene disorders. For many, the mutations have been identified and this allows for the molecular diagnosis of the disorder and the potential for carrier testing and prenatal diagnosis (Williamson and Robertson, 1999).

As research continues, computer technology is able to assist GPs in learning more about genetic advances and keeping track of newly elucidated disorders (Emery, 1999). "Online Mendelian Inheritance in Man" is an Internet site that represents an up-to-date reference source where anyone can access information regarding single gene disorders. It allows one to gather information about all disorders caused by mutations in single genes.

1.3.1.4 Multifactorial disorders

The importance of new genetic advances is that they are leading to a greater understanding of the inheritance of complex or multifactorial traits (Williamson and Robertson, 1999). Multifactorial disorders may be defined as disorders, which have a genetic component, but do not follow a simple mode of inheritance (Wolpert *et al*, 1999). In other words, there is an interaction between different genes in an individual and the environment that the individual is exposed to (Bains, 1993). Multifactorial disorders are responsible for a major contribution to human morbidity and mortality (Meuller and Young, 1998).

Two sub-classes of alleles termed "causative" and "susceptibility" need to be distinguished whilst comparing Mendelian and complex disorders: (Wolpert *et al*, 1999). The first pertains to the fact that presence of the allele confers significant risk for disease presentation. The influence of other genetic factors may reduce or increase penetrance, but on the whole, the presence of the causative allele is enough to allow the disease phenotype. "Susceptibility" alleles pertain more to complex disorders in that the allele itself is usually not sufficient to cause disease but may predispose the individual to the disorder.

Research involving multifactorial disorders has increased, as success has been achieved in the realm of single gene disorders (Kaprio, 2000). As our knowledge increases, we will have a greater understanding of the genetic and environmental influences that affect a person. Knowledge of a person's predisposition to a certain illness is extremely valuable,

as avoiding certain activities such as smoking for example in someone found to have a genetic predisposition to cancer, may be life saving (Williamson and Robertson, 1999). Testing for multifactorial diseases such as cancer, diabetes, cardiovascular diseases and Alzheimer disease may not at this stage predict certainties about developing the condition. Rather, a mechanism for generating a set of risks and possibilities is represented and this may help to guide a patient's life-style and medical regime (Williamson and Robertson, 1999).

1.3.1.5 Dynamic mutations

A relatively recent discovery has been a class of mutations involving triplet DNA sequences (trinucleotides). Since 1991, the mechanism behind this new class of disease mutation has become clearer (Rosenberg, 1996). We now know of 14 trinucleotide repeat diseases, all of which affect normal neurological function (Cummings and Zoghbi, 2000). Triplet repeat sequences are found in many genes, but it is when these expand, that a gene may be interrupted or compromised (Singer, 1996). This class of dynamic mutations does not conform to classic Mendelian inheritance patterns. The repeat sequences are unstable and usually expand from generation to generation. This may increase the severity of the disease from generation and may also cause an earlier age of onset in the offspring than in the parents (Singer, 1996).

In this study, three DNA triplet repeat disorders were assessed. The first, Huntington disease, is an adult-onset disorder, which is inherited in an autosomal dominant manner (Harper, 1998). In South Africa, Huntington disease in the white population is believed to

have been introduced by a Dutch settler in the 1600's (Hayden *et al*, 1982). Although rarer in the South African black population, it has also been shown to occur (Silber *et al*, 1998). Predictive, prenatal and diagnostic testing for Huntington disease exists in South Africa and those who enter the testing procedure for the predictive testing must adhere to international guidelines that are in place (Kromberg *et al*, 1999). The second triplet repeat disorder discussed is myotonic dystrophy. This is found to have a relatively high prevalence in the Afrikaans-speaking community of South Africa, possible due to founder effect (Goldman *et al*, 1996). Myotonic dystrophy is autosomal dominant with a severity that may range from mild to severe. A congenital form may occur with maternal transmission (Harper, 1998). The third and last dynamic disorder dealt with in this study is fragile X syndrome. This disease occurs in all ethnic groups and has been shown to be present in the South African black population (Goldman *et al*, 1998). This disorder is one of the commonest causes of mental retardation in boys (Heitz *et al*, 1992).

1.3.1.6 Prenatal diagnosis

Prenatal diagnosis is the detection of congenital or hereditary abnormalities in the unborn child. Approximately 7-8% of all pregnancies have an indication for prenatal diagnosis in South Africa annually (Viljoen, 1996). Chromosome abnormalities may be the cause of up to 50% of spontaneous miscarriages, and may be present at a level of 0.5-1% of live births (Meuller and Young, 1998). The most common aneuploid condition found is Down syndrome with an incidence of approximately 1 in 700.

Two main categories of prenatal diagnosis exist: screening and diagnostic. The questionnaire used in this study examined knowledge amongst GPs regarding three prenatal diagnosis procedures: the maternal serum triple test (screening), and amniocentesis and chorionic villus sampling (CVS) (diagnostic).

The maternal serum triple test may identify pregnancies at high risk for Down syndrome. The test has a sensitivity of approximately 60-65% in women under 35 years with false positives averaging 5-6% (Ormond, 1997). Three biochemical markers (alpha fetoprotein, human chorionic gonadotrophin and oestriol) are measured, and together with gestational age a risk is calculated (Harper, 1998). Amniocentesis and CVS are invasive tests, which carry risks of miscarriage. Studies performed in South Africa report these risks to be approximately 0.7% for amniocentesis (Kromberg *et al*, 1989a) and 4.2% for CVS (Rosendorff *et al*, 1989). Both CVS and amniocentesis may be used for cytogenetic, molecular genetic and in some cases biochemical studies.

1.3.2 Medical Genetics in South Africa

Since the late 1960's the majority of developed countries have had some form of structured genetic services in place. South Africa first began to conceptualise such genetic programs in 1971 (Op't Hof and Roux, 1983). Community-based genetic services were initially promoted by nursing staff that had received genetic training and were assisted by other key health personnel and diagnostic laboratories. Training has been of a high standard, but has only been available to those directly involved in the field of human

genetics. Medical genetics has only recently become recognised as a subspeciality in South Africa. Previously, medical geneticists had to specialise in other fields such as paediatrics, pathology or internal medicine and then subsequently undergo further training in genetics (Jenkins, 1990).

Currently not enough peripheral and referral institutions such as hospitals, clinics and most importantly practicing doctors, are aware of the important intricacies of genetics that may impact on their patients. South Africa has seven medical schools, but only three have Human Genetics Departments. Genetic counselling is underutilised and many genetic conditions are neither recognised nor diagnosed (Jenkins, 1990). This poses potential problems not only for the patient whose condition could be confirmed by genetic testing and appropriately managed, but also for future generations that may be at high risk for inheriting the same condition.

South Africa has yet to fully appreciate the benefits that an established genetic service can provide. Costs to care for handicapped children throughout their lifetime are a substantial financial drain. The prevention of births of infants with genetic disorders or birth defects will increase the availability of funds within the health budget for other medical problems such as HIV and TB. At present, in South Africa, a final draft of "Guidelines for the Management and Prevention of Genetic Disorders, Birth Defects and Disabilities" is awaiting endorsement (Department of Health Annual Report, 1999/2000).

1.3.3 Medical Genetics and Education

1.3.3.1 Medical Professional's Domain

As technology advances rapidly, it needs to just as rapidly be integrated into medical school curricula. The lay public and secondary schools also need to be made aware of what science can now offer them. It is the general feeling, that genetics is not receiving the attention it deserves in the medical curriculum (Childs, 1993). Childs (1993) also believes that some medical courses do not reach the heart of the matter and that facts are pushed at the expense of understanding.

Educating medical practitioners about genetics has become an important priority (Kolb *et al*, 1999) and it has been recognised that community based medical genetic services need to be incorporated into primary care (Christianson, 2000). When it comes to education it can be said that two groups of practitioners exist. The first represent those who have yet to graduate. They are still closely tied with their medical fraternity and may be more likely to absorb and receive genetic information. The second group represents those doctors who have already qualified. These doctors are harder to target as they are spread out geographically and usually have little time to devote to studying whilst they practice medicine on a daily basis. The Health Professions Council of South Africa has instituted a Continuing Professional Development (CPD) program. To an extent, this has made doctors more open to ongoing education attempts as each doctor has to obtain at least 50 CPD points a year by participating in medical education programs.

Many attempts have been made to target GPs to improve their genetic knowledge. In the United States Guttmacher and Allen (1993) designed an information newsletter on teratology aimed at educating a broad spectrum of health care givers. This method was successful, as access to knowledge presented in this format is available long after it was first imparted and can be used as a source material. A single copy of such a newsletter can also be read by more than one person, making this cost-effective. Registered welfare organisations also strive to educate and inform both the lay public and medical professionals. One such organisation is the Genetic Interest Group (GIG) of the United Kingdom. This group recently sponsored a student research project aimed at examining current educational initiative for genetics in the United Kingdom (Gamache *et al*, 1999). This study assessed relative successes and failures of education campaigns and also identified GPs as being the primary target of education for many support groups. In the age of computer technology, computers could help to supplement genetic services and information. In South Africa, many support groups target GPs and try to educate them about particular disorders. The Southern African Inherited Disorders Association (SAIDA) is an organisation, which strives to help support groups in achieving such goals.

1.3.3.2 Public Domain

In 1993, Griffiths conducted surveys in North America and Britain that revealed that on the whole, the public is grossly unaware of the discoveries of science. Many feel that this is something to worry about as it represents a failure on the part of educators. Although

recently, the public has become more exposed to the discoveries of science as the press has become more involved, it is felt that this is not enough (Griffiths, 1993). A more recent study conducted in Finland by Jallinoja and Aro (2000) showed that better knowledge in the field of genetics led to a greater awareness and an improved process of decision-making when it came to facing ethical and social problems that were presented by the potential of being affected by a genetic disorder.

Griffiths (1993) stresses five reasons why it is important for the public to understand genetics: 1) Genetics affects one's worldview, 2) Genetics can give insights on crucial societal issues, 3) Society depends on genetics, 4) A large proportion of human ill health has a genetic basis and 5) Genetics provides classic examples of logical reasoning.

How do we rectify this situation? Griffiths (1993) believes that the onus is on the scientific community to extend beyond their laboratory environments and reach out to the public more often. Grinell (1993) believes that this can be aided by employing certain tools in science education such as choosing communicators who can match and expand on the audience's pre-existing notions and desires regarding the information being conveyed.

It is also felt that school children should be taught the intricacies of human genetics as high school students of today will be affected throughout their lives by the developments of genetics and in particular the Human Genome Project (McInerney, 1993).

1.3.4 GPs and medical genetics

In a South African context, GPs have to work in a medical environment that has been affected by the countries ongoing political and social change. This has resulted in a health care system that in some respects can be compared to the best in the world, but in others is characterised by lack of access to the most fundamental of medical services in rural areas (de Villiers and de Villiers, 1999).

As the HGP continues and as the application of new technology increases, an increased responsibility will be placed on the shoulders of the GPs (Hunter *et al*, 1998). In a setting such as South Africa and indeed in many other countries, the GP is a patient's first and perhaps only contact with the medical fraternity. GPs come into contact with a large number of patients and, according to Walpole *et al* (1997), are considered the most common health professional to be asked questions regarding hereditary diseases by patients.

The incorporation of genetics into a medical practice is becoming vital and the role of the GP is thus central. According to Williamson and Robertson (1999), GPs deal with families and thus live with genetics all the time. They should thus be responsible for prevention and treatment of genetic disorders. The GP is also regarded as the best person to take a family history – an invaluable tool in identifying any genetic disorder. GPs are in an extremely valuable position to advise patients about lifestyle choices and preventative measures, especially in the case of multifactorial disorders that are commonly encountered by GPs. It is envisaged that the role of the GP is not necessarily

to be involved in personally offering gene tests at this stage, but more importantly to identify patients at high risk for genetic disorders and to refer those who require testing to the appropriate specialists (Williamson and Robertson, 1999). The GP is also expected to be knowledgeable about the risks to other family members should a result indicate an abnormality.

In the future, GPs will be expected to participate more and more in the area of genetics as there will be insufficient geneticists and genetic counsellors to cope with the demand made by patients once the full benefits of the HGP are available (Fetters *et al*, 1999). Studies investigating the preparedness of GPs to take on this role need to be performed so that gaps in genetic knowledge and protocol can be rectified. As medical genetics moves from the domains of the geneticists and statisticians to the domains of GPs, there is a potentially huge benefit to patients in disease prevention and management. On the other hand, if not used with precision, confusion and misunderstanding may arise (Collins and Bochm, 1999).

A study by Walpole *et al* (1997) attempted to elucidate the reasons why genetic services are not fully utilised and investigated potential strategies for reversing this scenario. Although developments in molecular genetics have revolutionised clinical genetic practice, offering many opportunities for choice in the prevention of hereditary disease, the use of such technologies has been relatively slow. According to Walpole *et al* (1997), the reasons could be:

1. Health professionals have failed to fully accept that genetic health issues are part of total health care
2. The elucidation of family histories and presence of genetic disease may require biological and social knowledge which some health professionals do not possess
3. Misinformation regarding genetic disease is commonly encountered
4. The lack of accurate information and therefore a poor understanding regarding the principles and uses of available DNA technology

The use of educational and health promotion strategies directed at both the public and health professionals clearly improves knowledge and awareness but requires constant monitoring and improvement to remain effective and current (Walpole *et al*, 1997).

It has been shown that preclinical training within tertiary education institutions and postclinical follow up courses concentrating on genetic issues are invaluable. Kershner *et al* (1993) examined the genetic knowledge of two groups of obstetrics and gynaecology residents. One group of residents had undertaken a course that included a genetic component whilst the other had not. The former group scored significantly higher in a questionnaire that examined clinical genetic knowledge, implying that such training programs were of immense importance.

1.3.5 Genetic counselling

The term "genetic counselling" refers to the process whereby an individual or family obtains information about a real or possible genetic problem (Hsia *et al*, 1979). Harper (1998, p. 3) gives a more expanded definition:

"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 or transmitting it and the ways in which this may be prevented, avoided or ameliorated."

A workshop on genetic counselling sponsored by the National Genetics Foundation, Inc. based in the US, developed a set of guidelines that would ensure optimal genetic counselling in the future. This resulted in a thorough definition for genetic counselling as follows (Fraser, 1974, p. 637):

"Genetic counselling is a communication process which deals with the human problems associated with the occurrence, or the risk of recurrence, 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) comprehend the medical facts, including the diagnosis, the probable course of the disorder, and the available management; (2) appreciate the way heredity contributes to the disorder, and the risk of recurrence in specified relatives; (3) understand the options for dealing with the risk of recurrence; (4) choose the course of action which seems appropriate to them in view of their risk and their family goals and

act in accordance with that decision; and (5) make the best possible adjustment to the disorder in an affected family member and or to the risk of the recurrence of that disorder"

Genetic counselling is a facet of medical care, which has, in the past, largely been perceived as the imparting of medical facts and risks rather than emotional support as well (Check, 1980). Dealing with emotional as well as intellectual issues are functions that genetic counsellors are encouraged to deal with today. Dealing with issues such as stress, coping and empowerment must be at the forefront of a genetic counselling session (McConkie-Rosell and Sullivan, 1999).

Ideally, genetic counselling interventions should (1) reduce anxiety; (2) enhance control and mastery and (3) increase understanding, thus providing the individual and family with greater control over their lives and decisions they need to make (Kessler, 1997). Genetic counselling should promote the autonomy of individuals by supporting their decisions and helping them by providing emotional tools to make these decisions (McConkie-Rosell and Sullivan, 1999). Non-directiveness is based on the aspiration to preserve the personal nature that reproductive decision-making involves and it represents the avoidance of passing judgement on the worthiness of the life of a person who may be affected with a genetic condition (Biesecker and Marteau, 1999).

Genetic counselling offers many benefits to the individuals and families who receive it. The way in which genetic knowledge is imparted however is essential to the success of a

counselling session. Maintenance of the individual's integrity and autonomy is vital and thus non-directive methods coupled with the introduction of useful emotional tools such as those mentioned above are employed. As genetics develops however, we see that in order to cope with increasing demands it is moving from the hands of the specialists to the hands of primary care givers such as GPs. It is essential that the integrity of genetic counselling be maintained through this shift so those patients are still offered high quality and complete service (Biesecker and Marteau, 1999).

1.3.6 GPs and Genetic Counselling

Genetic knowledge may be a field that GPs need to improve, but it is important to note that genetic counselling is a specialised realm of genetics. Geller *et al* (1993) sought to establish whether or not GPs are willing to do the counselling and if so, would their counselling be directive or not. The results showed that approximately half of the GPs felt they would counsel themselves whereas the other half would rather refer to a genetic counsellor. It was noted that GPs were more likely to express their own opinions about prenatal diagnosis and abortion than professionals in genetics thus indicating that their method of counselling would be of a more directive nature.

Weitz (1981) discusses that patients' emotional needs are often neglected at the expense of medical facts and interventions. Although the primary physician may have the best intentions, the patient in this kind of scenario is not having all of his/her needs met. GPs need to be made aware that genetic counselling is a facet of medicine whereby non-directive counselling is aspired to (McConkie-Rosell and Sullivan, 1999) and counselling

methods, as well as genetic knowledge need to be taught. GPs need to be made aware that their value systems and their method of presenting risks and options, have an impact on patients' choices (Weitz, 1981).

1.3.7 Common genetic disorders in South Africa

South Africa has a diverse population. According to the census in 1996 published on the internet (http://www.odci.gov/cia/publications/factbook/sf), it was reported that 75.2% of the population was black, 13.6% white, 8.6% 'coloured' or of mixed ancestry and 2.6% Indian.

White people first settled in South Africa in 1652 when the Cape of Good Hope became a rest station for passing ships (Jenkins, 1990). These European settlers grew quickly in number and were joined in 1688 by Huguenot immigrants. The descendants of the Dutch, German and French immigrants evolved rapidly into a large population of people who today are known as Afrikaners. The Afrikaans people possess a number of disease-causing genes in relatively high frequency – a result of founder effect. Porphyria variegata was the first of such disorders to be described and the molecular basis has now been established (Jenkins, 1997). Familial hypercholesterolaemia and Huntington disease (Botha and Beighton, 1983) and myotonic dystrophy (Lotz and van der Meyden, 1985) are also found in higher frequencies in this population. Fanconi anemia has also been shown to have a high prevalence in the Afrikaans population (Rosendorff *et al*, 1987).

Among all Caucasoids in South Africa, the carrier frequency of cystic fibrosis is approximately 1 in 23 (Goldman *et al*, 1994).

Amongst the indigenous black population, a gene for albinism is particularly frequent with a carrier frequency of approximately 1 in 32 individuals (Kromberg and Jenkins, 1982). Greek and Indian people living in South Africa are at higher risk for carrying mutations causing thalassaemia (Bonafede *et al*, 1983) and Jewish people similarly are at a higher risk for carrying mutations that cause Tay-Sachs disease (Lane *et al*, 1985; DeMarchi *et al*, 1996).

1.3.8 Genetic screening, testing and prenatal diagnosis in South Africa

Genetic services have proven to be cost-effective and may potentially prevent many genetic disorders (Kromberg and Jenkins, 1997). Well-orchestrated population screening has been shown to reduce the incidence of those affected by genetic disease considerably (Meuller and Young, 1998). Prenatal screening tests for neural tube defects and chromosomal abnormalities are available, and neonatal screening for treatable disorders such as phenylketonuria is possible. In South Africa however, although such tools are present, they are not offered to the population at large. At present, no broad newborn screening is performed for the abovementioned disorders (except on a research basis) thus leading to morbidity in children affected by such disorders (Kromberg and Jenkins, 1997).

Prenatal diagnosis is offered in South Africa and many genetic disorders can be diagnosed and detected, but once again these opportunities are not being offered widely. Since the early seventies, amniocentesis, and later chorionic villus sampling and cordocentesis, have been performed in South Africa. Most private laboratories also offer the maternal serum triple test, but it is not routinely offered by the state health services. Genetic counselling is recommended with all prenatal testing to ensure the individual's autonomy and right to free choice (Kromberg and Jenkins, 1997).

1.3.9 Background to the study

Studies investigating various aspects of the new technology at our disposal and how GPs make use of it have been undertaken. Each study is adding to our volume of knowledge and aiding our understanding of how improvements may be made so that patients may reap the full benefits of having more control over their health and reproductive decisions. Patients in need of genetic services are often not managed appropriately as it is generally felt that genetic knowledge amongst GPs is poor (Kolb *et al*, 1999). Concerns have been raised as to how prepared GPs are to offer genetic advice (Hayflick and Eiff, 1998). Investigations in this area and suggestions regarding possible solutions are thus invaluable.

1.3.9.1 GPs' knowledge of genetics

A review article by Emery *et al* (1999) collated information from numerous studies that investigated the issue and demonstrated that in general GPs have a limited knowledge

about genetics. GPs have difficulty assigning risks and often convey an overestimated rather than an underestimated risk. A large number of GPs did not know the carrier frequency for cystic fibrosis (Julian *et al*, 1996) or the haemoglobinopathies (Shickle and May, 1989), nor were they aware of when or how to offer prenatal diagnosis. A study examining knowledge of Mendelian disorders such as cystic fibrosis, Huntington disease and Duchenne muscular dystrophy was conducted by Firth and Lindenbaum (1992). Replies to this postal questionnaire study showed that 95% of respondents believed that offering prenatal diagnosis for these disorders was appropriate yet less than 50% knew the correct details pertaining to the availability of such tests.

In Mendelian and multifactorial disorders, the majority of GPs support screening and testing and see themselves as being a part of this process. When it comes to multifactorial disorders however, they believed their role was in tracking the family history and performing a "gatekeeping" function, but they expressed difficulty in communicating the risks such disorders may represent (Emery *et al*, 1999).

Studies comparing other health care professionals such as paediatricians and obstetricians with GPs, show that in general they are found to be more knowledgeable in the realm of genetics and they had more interaction with genetic services (Hunter *et al*, 1998). Hunter *et al* (1998) also showed that whilst GPs relied on their undergraduate medical school courses for information, specialists were more likely to seek further information from other sources. Many GPs in this study felt that their knowledge was inadequate although a few felt that they could provide genetic counselling for simple genetic situations.

Hofman *et al* (1993) sent out a questionnaire in the United States, which was targeted at both the non-genetic (GPs, obstetricians and gynaecologists, paediatricians etc,) and genetic professionals (genetic counsellors and genetic clinicians). The latter scored an average of 94.6% whilst the non-genetic professionals averaged 73.9%. Knowledge of genetics was also found to be associated with younger age (<40 years) and previous training, involvement in obstetrics and participating in continuing medical education were all factors, which influence knowledge positively. According to previously established data, this confirmed that genetic knowledge has indeed increased over the years although deficits still occur. These authors also felt that although courses in genetics at medical school may improve genetic knowledge, it is not sufficient. Greater emphasis is required in all tiers of education.

1.3.9.2 GP's attitudes towards genetics

Watson *et al* (1999) used qualitative methods to conduct four focus groups and 15 individual interviews in their study to explore attitudes towards new genetic developments, the role GPs envisage for themselves and to clearly define the education, information and training they might need in support of their chosen roles. The results revealed that although GPs feel genetics is important, views are varied as to what their level of involvement should be. Current knowledge about genetic issues and management skills of genetic patients is lacking. Time, costs as well as ethical and legal issues are also areas of concern for GPs.

Suchard *et al* (1999) conducted a study in the United Kingdom to ascertain information about GP's willingness to provide genetic services for common diseases. The results indicated that although the majority of GPs felt they had a role to play in the genetic services, only 29% felt sufficiently prepared to take family histories and only 15% felt confident enough to counsel about genetic test results. A large proportion (69%) however felt that after proper training they could possibly offer these services.

Fetters *et al* (1999) performed a qualitative study to ascertain the perceived impact of the HGP on GPs' practices. The general trend of responses indicated that the GPs in this study did not perceive genetics as having a substantial impact on their medical practices at present but expected major changes to take place in the future. GPs also felt that there had been inadequate educational opportunities, and felt reluctant to invest in self-education themselves until they felt that genetics was more relevant.

A study by Fry *et al* (1999) to investigate GPs' roles in cancer genetic services demonstrated that there is a lack of understanding and confidence regarding the knowledge of hereditary cancers. GPs felt that their function would be to take family histories and make appropriate referrals to specialist services. A need for referral guidelines and community genetics clinics was identified.

Family history taking appears to be a role that GPs are willing to take on. Summerton and Garrood (1997) report however that although it is agreed upon that family information is a valuable tool, opportunistic family history taking is not occurring in general practice.

CHAPTER 2

METHODOLOGY

This study represents the first of its kind in many years and aimed to get a general idea of the level of genetic knowledge so as to aid the design of educational programmes and to pave the way for further, larger studies of its kind. The materials used in this study and the manner in which they were administered will be discussed in this chapter. A description of the scope and settings of the research and the manner in which the subjects were selected and ascertained will be included. The questionnaire used in this study will be explained in detail including general aims, design and content. The pilot study will be discussed and the collection and analysis of the data pertaining to this study will be described.

2.1 Setting and scope of the study

The research project was based in the Department of Human Genetics, South African Institute for Medical Research (SAIMR) and the University of the Witwatersrand where the researcher was a student and where the appropriate and necessary research facilities were available.

In this study, a General Practitioner (GP) was taken to mean a doctor working in a frontline primary care scenario. In some studies, the term 'primary care/family physician' was used and those included in this report were ascertained to have the same meaning as the term GP in this study. Subjects were selected from the 5500 doctors on the database

of the South African Medical Association (SAMA) in the Gauteng region of South Africa. These 5500 doctors were all registered with SAMA and within this database were classed as general practitioners. As was discovered however, many were no longer working as primary care givers. Some were working in administration, the pharmaceutical industry, laboratories, occupational health, insurance etc. These doctors were not included in the study. A list of names was chosen for the postal component of the study and a separate list was constructed to obtain subjects for face-to-face interviews. The same questionnaire was utilized for both groups. Those subjects residing or practicing within a close enough geographical region (within a maximum of 1 hours travel by car from the South African Institute for Medical Research (SAIMR), Johannesburg) were chosen for interviews as limited time (12 months) and funding were available. Initially it was hoped that at least one hundred postal replies would be obtained and fifty face-to-face interviews would be conducted. Both postal responses and interviews were assessed as it was felt that postal questionnaires may yield a greater number of responses than could be achieved by interview alone, yet interviews were conducted to give the researcher experience with interacting with medical professionals and enhancing communication skills. The questionnaire was administered with no aid from the researcher during the face-to-face interviews. If the questionnaire was discussed at all, it was only after the questionnaire was handed back to the researcher after completion. It was felt that face-to-face interviews would help with obtaining general opinions and for allowing GPs to voice their questions and/or concerns. These were recorded utilizing a 'GP Interview Sheet' (see Appendix C). With postal questionnaires, the researcher is not present for such discussion after the questionnaire is answered and

subsequent questions or matters arising would not be recorded. In this study, interviews were conducted in conjunction with postal responses to try and gather additional information and to encourage GPs to discuss issues that may have arisen after the questionnaire was completed.

As the questionnaire was self-administered for both the postal and face-to-face interviews (although here the researcher was present), it was decided that the data arising from the questionnaire would be pooled and analysed. Although this is not ideal (it could be possible that in some way, the presence of the researcher may have had an impact on responses even though interaction was not encouraged until the questionnaire was complete), it was felt that as there was a relatively small number of subjects in this study, the data would be best presented in this way. Comparisons between the postal and interview groups have additionally been made.

2.2 Ascertainment and selection of subjects

2.2.1. Subjects approached by post

In order to ensure that a broad range of GPs were targeted (different universities, different years of graduation, and different locations of medical practice etc.) every fifth name was chosen from the alphebetised (by surname) SAMA list. Questionnaires were posted to 1091 GPs and of these, 73 responded.

2.2.2. Subjects approached for face-to-face interviews

Every ninth name was chosen from the alphabetized (by surname) SAMA list to obtain the names of GPs for this section of the study. This resulted in a list of approximately 550 GPs as potential subjects for interviewing. Where names appeared on both the lists, it was established whether these doctors were suitable candidates to be approached for a face-to-face interview (i.e. whether they were within a maximum distance of 1 hours drive from the SAIMR). If not, these names were left on the postal list.

Difficulty was experienced in contacting many GPs as telephone numbers supplied by SAMA were incorrect (an additional search for their correct number in each case was performed by consulting the telephone book). If a GP was unable to be contacted, declined to participate in an interview, or was too far away, the next ninth name generated on the SAMA list was consulted. In some instances, towards the end of the study doctors not on this list but in the local area were also approached for interviews (the telephone book was used). Face-to-face interviews were held in conjunction with the postal survey so that the researcher could develop interpersonal skills and experience and so that more lasting impressions could be made with the doctors approached. These interviews also aimed to yield more information regarding a GP's thoughts, opinions and issues that the postal component of the study may not have ascertained. During the interviews, a 'GP Interview Sheet' was completed (Appendix C). This was used so that issues raised by the GPs during the interviews could be recorded. The total number of interviews conducted was 51.

It is important to note that the GPs who participated in this component of the study were not randomly selected. As noted above, many GPs were chosen based on proximity and convenience. Another factor was personal safety. Some areas were not felt to be suitable to drive to on one's own. This is not ideal, however it was hoped that by consulting as many GPs as possible, some useful data may be obtained.

2.3 Research Tool: the questionnaire

The primary research tool utilised was a questionnaire specifically designed for this study. A questionnaire was used, as it can yield a large amount of useful details in a relatively short period of time, and can be administered on a large scale with relative ease. This questionnaire was designed so that it could be used for both the postal (self administered) and interview (self administered but with the researcher present) subject groups.

2.3.1 The aims of the questionnaire

The questionnaire aimed to obtain information about GPs located in the Gauteng area regarding facets of their practice, the genetic disorders that they have encountered, their current genetic knowledge and their views and opinions of genetic counselling. The GPs targeted by post, each received the questionnaire accompanied by a letter of introduction and consent form (Appendix A). An envelope with the researcher's address on it was also enclosed for easy return of the questionnaire.

2.3.2 The questionnaire design

The questionnaire (Appendix B) was designed to be as clear and unambiguous as possible. Where applicable, tick boxes were used to facilitate the completion of the questionnaire in as little time as possible. This structure was also used to simplify analysis of the data. Subheadings and explanations preceded each main section of the questionnaire so that the subject was well informed as to the intent and the potential uses for the data collected. The questionnaire was printed in an A5 booklet format to aid the continuity of the questions and to ensure that no pages were lost or skipped.

Whilst constructing the genetic knowledge section of the questionnaire, the questionnaire used in a study conducted by Kershner *et al* (1993) was consulted. In their study, Obstetricians and Gynaecologists in the Philadelphia area of the United States were examined as to their level of genetic knowledge. The option of "unsure of the correct answer" was included for each question in their questionnaire so as to eliminate correct responses made by chance rather than by actual knowledge of the topic. The same method and style of scoring was used in the questionnaire for this study.

2.3.3 The questionnaire content

The questionnaire contained four main sections annotated A to D:

2.3.3.1 Section A: Personal details

The purpose of this section was to obtain personal information about the participant. The participants' gender and date of birth; in addition basic information such as telephonic, residential, postal and e-mail contact details were asked. Each GP was also asked to supply their Health Profession's Council of South Africa (HPCSA) membership number so that a CPD point (see 2.7) could be awarded to them for completing the questionnaire. Participants were assured of confidentiality and discretion.

2.3.3.2 Section B: You and your practice (information regarding the medical practice)

This section was designed to give the researcher an idea of the type of environment the GPs were working in and to establish information regarding the patients with whom they came into contact.

The first part of this section questioned the participants' educational background and qualifications, including information regarding the university attended, year of graduation and degrees completed. The participants were also asked whether or not they had been exposed to the teaching of Human Genetics in their training. If they had received training,

they were requested to specify the degree in which this took place, the approximate duration of the course, whether this course was of a formal or informal nature and whether they felt that this training had been adequate.

Detailed information on the participants' medical practice was requested including the type of practice, number and ethnicity of patients and the nature of the services that GPs provided (particularly regarding antenatal care). Participants were also asked to indicate whether any of their patients had any genetic disorders such as those listed in the questionnaire as well as any others not listed.

2.3.3.3 Section C: Genetic Knowledge Assessment

This section asked questions regarding genetic facts that members of the Department of Human Genetics regarded as core knowledge to get an idea of the current level of knowledge amongst GPs. The Genetic Knowledge Assessment section was broadly grouped into five main categories:

1. **"Mendelian"**- this section consisted of eight main questions about Mendelian modes of inheritance. Understanding of risk assessment and inheritance patterns amongst autosomal recessive, dominant and X-linked recessive inheritance were investigated (two questions for each inheritance mode). An additional two questions pertaining to atypical or unusual Mendelian patterns of inheritance such as multifactorial disorders and those

disorders involving dynamic/unstable mutations such as triplet repeat expansions, were also included in this section.

2. **"Aneuploidy"** - the four main questions in this section dealt with knowledge regarding variations in chromosome number. The first three of these questions dealt with Down syndrome and asked facts such as incidence, the nature of the chromosome abnormality and common clinical features. The fourth question dealt with frequently observed features amongst individuals with Turner syndrome.

3. **"Prenatal Diagnosis"** - the purpose of this section was to investigate the level of knowledge regarding the various techniques used to detect abnormalities prenatally. This section consisted of six questions, three examining aspects of the maternal serum triple test, one on chorionic villus sampling, and one on amniocentesis. The last question dealt with situations in which the risk of having a child with a chromosomal abnormality increases.

4. **"Genetic Epidemiology"** - these seven questions examined the GPs' level of knowledge of the carrier frequencies of certain disorders and the population groups in which these disorders would be found more frequently, knowledge of the incidence of live born babies with major anomalies and disorders that were caused by triplet repeat expansions. The last question examined whether GPs could identify the mode of inheritance responsible for 12 relatively common genetic disorders found in South Africa.

5. **"Teratogens"** - this category consisted of three questions. The first and second dealt with the possibility of teratogenesis in the presence of certain infectious agents and drugs respectively. The third question requested GPs to identify characteristic physical features of Fetal Alcohol Syndrome (FAS) from a list provided.

2.3.3.4 Section D: Genetic Counselling Investigation

This section aimed to assess current opinions and practices in the field of Genetic Counselling. GPs were asked to furnish details about how and when they had first heard of genetic counselling and whether or not they had ever referred a patient to such a service. Opinions regarding the importance of genetic counselling in general practice were investigated and GPs were questioned as to whether they felt patients who received genetic counselling had benefited from this. The GPs were also asked whether or not they felt that all genetic disorders should be dealt with by a genetic counselling facility. Knowledge of the nearest genetic counselling facility was enquired about. GPs' perceived abilities to participate in the various aspects of a genetic counselling session were also questioned. The GPs were also asked if they were interested in attending courses on medical genetics, and if they responded positively to this, information regarding preferred events and times was requested.

2.4 The pilot study

A pilot study was undertaken to determine whether there were any problems or ambiguities in the questionnaire and the subsequent data collation and analysis. It was also important to establish how long the questionnaire took to answer so that GPs

participating in the study could be informed of this and an appropriate amount of time could be set aside to complete the questionnaire.

The pilot study was conducted by approaching ten GPs (some known personally to the researcher and some in the local area surrounding both the SAIMR and the researcher's residence) for face-to-face interviews. The GPs were asked if any ambiguities were present or if clarification of any of the questions asked was required.

As stated above, some of the GPs in the pilot study were known to the researcher and others were targeted based on proximity. The pilot group then was not randomly selected. One thus has to consider that responses to this questionnaire may potentially have differed and have there would have been less potential for bias if a random sample had been used. The pilot study group chosen however responded as follows:

The questionnaire, although quite lengthy was found to be of an acceptable length by the GPs in the pilot study (it took an average of approximately 40 minutes to complete). The GPs that were approached thought that the questions were generally clear and unambiguous and covered a good selection of genetic topics. Upon analysis of the responses however it was felt that a few questions should be altered to ensure that the meanings of the questions were clearer and that the data obtained from the responses could be analysed appropriately. The questionnaire was therefore revised in the following way:

In Section A, a question asking GPs to fill in their date of birth was included. It was felt that the age of the GP might be relevant to his/her current level of knowledge and opinions in the field of medical genetics. Previous studies have shown that age seems to be an influencing factor regarding level of knowledge (Hofman *et al*, 1993; Julian *et al*, 1996). In Section D a question was asked, " Do you feel that you have adequate information and resources to counsel patients with the most common genetic disorders?" This question was replaced with three questions (Questions 8, 9 and 10 of Section D of the questionnaire) to aid the analysis of specific aspects of the possible answers to this question namely taking of a family history and pedigree, counselling about risks and counselling about test results.

The question whether the GPs would be interested in attending courses or seminars dealing with current genetic issues was expanded by asking GPs to specify the genetic topics that would interest them most.

2.5 Collection of data

2.5.1 The postal participants

The questionnaire was posted to the selected GPs (Section 2.2.1). Each doctor received an envelope containing a letter of introduction and consent form (Appendix A), the questionnaire (Appendix B) and a return envelope.

As too many GPs (1091) were targeted by post to all be contacted telephonically, approximately every tenth GP on the mailing list (approximately 100) was phoned one

month after the questionnaire had been posted. If the GP on the list was unobtainable by phone the next consecutive GP was tried. The GPs were asked if they had received the questionnaire and were requested to post their responses back as soon as possible (if they wished to participate in the study). If those GPs contacted could not find their questionnaire, had not received it or had lost it I send out another copy. These telephone calls resulted in an extra four responses being received.

2.5.2 The face-to-face interviews

The questionnaire was administered face-to-face to GPs practicing or living in the Johannesburg area. An appointment was made with the GP beforehand and the interview generally took place at their medical rooms except for four cases where it was done in their homes. The interview schedule (questionnaire) was given to the GP by the researcher for him/her to complete. Discussion was also usually held after the questionnaire was completed to explore opinions and feelings more thoroughly. Following each interview, the researcher completed a brief interview assessment form at which time relevant issues and comments made by the GPs during this discussion were recorded (see Appendix C).

2.6 The Genetic Information Sheet

An information sheet with core genetic knowledge was compiled by the researcher (see Appendix D). This sheet was handed out to GPs as soon as the face-to-face interview was completed and also sent to GPs who had returned completed questionnaires by post together with their CPD certificates. The aim of this information sheet was to answer

many of the questions posed in the original questionnaire, and to refresh basic genetic knowledge in a manner that the information could be used as a reference sheet and would be quickly and easily absorbed. The genetic information contained in the sheet covered broad topics including Mendelian patterns of inheritance, non-Mendelian patterns of inheritance, aneuploidy, prenatal diagnosis and screening, teratogens and genetic counselling. Also included were some recommended readings and contact phone numbers, should referrals need to be made. The sheet was designed to be brief and easy to read and thus comprised only one A4 double-sided piece of paper folded in half to form an A5 booklet.

2.7 CPD point allocation

The Continuing Professional Development (CPD) representative of the Department of Human Genetics applied, at the request of the researcher, for CPD accreditation to the CPD committee of the Faculty of Health Sciences of the University of the Witwatersrand. It was decided by this committee that one CPD point could be awarded for participating in the study (completing the questionnaire) and reading the Genetic Information Sheet (see 2.6). Upon the return of a completed questionnaire by post or by completion of the face-to-face interview, a CPD certificate was issued and sent to participating GPs by post. Each CPD certificate (awarding one point) was accompanied by a letter of thanks (see Appendix E and F for the postal and interview thank you letters respectively).

2.8 Data analysis

The responses from the completed questionnaires were entered into a Microsoft Access computer database. Quantitative data obtained from the questionnaire were entered and analysed using Microsoft Access so that analyses of data could be made easier. Microsoft Excel was also used to aid statistical analysis. Qualitative data were analysed by examining all responses and categorising the data by using an organised set of categories into which certain responses would belong. In both data sets, various comparisons were made between the interviewed and postal participants using Microsoft Access to establish whether there were any significant differences.

Where quantitative data required statistical analysis, the Chi-Square Goodness-of-fit test was used to ascertain whether the sub-sets of data differed significantly in various areas (Clarke and Cooke, 1983).

2.9 Discretion and confidentiality

This study made use of a questionnaire that required participants to disclose personal biographical information (such as name and address) about them. The primary requirement for this was so that in the case of the postal group, the 'Genetic Information Sheet' (Appendix D) could be sent to them and also so that they could be accredited with a CPD point for participating (See Appendix E). In the letter of introduction (Appendix A), which was sent with the questionnaire to each postal recipient, 'discretion and confidentiality' was assured. All of these participants were also asked to sign a consent form, indicating they agreed for their information to be used in this study. Those who

were interviewed by the researcher were also assured that all information would be treated with the utmost confidentiality and discretion. At no time has any personal information pertaining to any participants been disclosed to any other party. All documentation and paperwork has also always been kept in a secure location. The issue of maintaining privacy is always important (Coy, 2001). It is also important (and vital from an ethical viewpoint) that participants feel reassured and confident that their responses are going to be used in a way that will benefit a research field without their individual privacy being compromised. By carefully securing data at all times and by not disclosing any personal details or using them in any kind of data analysis the issues of confidentiality and discretion were ensured for the participants of this study.

2.10 Research approval

The questionnaire, the letter of introduction and consent form, and the Genetics Information Sheet were submitted to the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand for approval. The project was approved by the committee and an approval number (M991115) was assigned (Appendix G). The protocol of the study was submitted to the Postgraduate Committee of the University of the Witwatersrand and was approved (Appendix H).

CHAPTER 3

RESULTS & DISCUSSION

In this chapter the results of the analyses of the data collected will be presented and discussed. The data were collected using the questionnaire designed by the researcher (Appendix B).

This chapter has five main sections. The first contains a detailed description of the GPs who participated in the study including their biographical data and their working environment, as well as a profile of their patients. The second section presents the results of the questions aimed at assessing basic genetic knowledge. The third section deals with the responses obtained regarding genetic counselling issues. Where necessary, content analysis techniques have been used so that responses could be stratified and analysed. The fourth section deals with GPs' willingness and availability to participate in educational programs and the last chapter discusses the results of the face-to-face interviews.

3.1 GP Details (Section A and B)

3.1.1 GP participation

The total subject group consisted of 124 GPs. Of these, 51 (41%) were interviewed face-to-face by the researcher, 73 (59%) completed the postal questionnaires. A pilot study group consisting of 10 doctors was performed (see section 2.4).

3.1.2 Response rate

3.1.2.1 Postal Replies

A response rate of approximately 6.7% was achieved within the postal reply section as 73 out of the 1091 questionnaires posted were returned completed. Response rates in other studies examining genetic knowledge range from 34% (Julian *et al*, 1996) to as high as 81% (Shickle *et al*, 1989). Although both these studies were targeted at GPs, they were performed in other countries (South of France and Wales respectively). It is important to realize that direct comparisons cannot be made with GPs in other countries as they may have a totally different work environment, which may affect their response rates and attitudes. The questionnaire in each case, the incentives and the manner of its administration were also different and this may also have affected the response rate.

The study of Lemkus *et al* (1978), although undertaken many years ago, is the only other one known by the researcher in which GPs in South Africa were targeted with the aim of assessing their knowledge of genetics. In that study GPs were also targeted by post and a response rate of 37% was obtained. This value is similar to that of Julian *et al* (1996) but is still considerably higher than the value found in this current study.

In a survey by Emery *et al* (1999), studies examining GPs' attitudes towards genetics yield response rates averaging approximately 66% (with a range of 29% to 100%). It is important to consider though that these studies were all performed in first world countries and thus not directly comparable to this one. The only other study that examined GPs'

attitudes towards genetics that came close to receiving as poor a response rate was that of Friedman *et al* (1997). This study investigated GPs' attitudes towards cancer genetics in the US state of Texas and only 29% of the questionnaires were returned.

Possible reasons for the low response rate obtained in the current study, could be that GPs have little time to participate and the questionnaire was too long. The incentive offered in this study of one CPD point (see section 2.7) might not have been sufficient to encourage GPs to participate. A study by Tambor *et al* (1993) in the US used a monetary incentive ($25 per doctor) scheme to increase participation and found that when they did so, their response rate increased from 19.6% to 64.8%. Although this kind of incentive may prove beneficial in other areas, in a country such as South Africa it is probably not practical.

Another potential reason for the poor response is that many of the contact details for the doctors held by South African Medical Association were incorrect. Many GPs may thus have not received the questionnaire and so then did not have the option of responding.

This questionnaire required GPs to disclose their names and other biographical details. Although they were assured of confidentiality and discretion, this may have contributed to some doctors not wanting to participate. In a study by Campbell and Waters (1990) however, it was demonstrated that anonymity had no significance with regards to response rate of a postal questionnaire, even if a sensitive subject (AIDS in this case) was asked about. It may however still be a factor for this study.

3.1.2.2. Interviews

For the interviews, doctors were approached telephonically from the SAMA list as described in Section 2.2.2. It was hoped that 50 GPs could be interviewed for this study. Of the doctors who were on the list and in the Johannesburg area and who could be contacted (within a maximum of 1 hour's drive from the researcher), approximately 1 in 4 were willing and available to be interviewed. This value was obtained by consulting the SAMA list kept by the researcher which was annotated accordingly when doctors were contacted. It is important to note however that this list is merely an approximation however because as mentioned in Section 2.2.2, some doctors that were not on this list were approached.

The interviews took place in the following suburbs (alphabetical order): Blackheath, Blairgowrie, Bordeaux, Braamfontein, Bromhof, Buccleuch, Edenvale, Fairlands, Fellside, Fourways, Fontainbleau, Glenhazel, Greenside, Houghton, Hyde Park, Kempton Park, Kensington, Killarney, Linden, Linksfield, Lyndhurst, Morningside, Montgomery Park, Northcliff, Olivedale, Parktown, Randburg, Randpark Ridge, Rynfield, Sandringham, Sandton, Sunninghill, Victory Park and Witkoppen. It's important to note here that bearing in mind traveling distance and personal safety the above sample is not representative of all areas within a 1 hour drive of the SAIMR. All are within the Northern suburbs. This thus represents a convenient sample rather than a random one and may introduce an area of bias to the study.

the most recent to have graduated from medical school, responses may have been greater as GPs may feel more confident towards the subject of genetics and more knowledgeable of current genetic trends.

3.1.4 Professional qualifications (Question B1)

Of the 124 GPs who participated in the study, 50 (40%) had studied further than their basic medical school degree. Additional studies included both undergraduate degrees such as the BSc and BSc (Hons) degrees and postgraduate studies such as diplomas in aviation medicine, diving medicine, obstetrics and gynaecology, midwifery and tropical medicine. Four GPs had undertaken a Masters in Family Medicine or the equivalent thereof. Two GPs were busy completing their M. Phil in Sports Medicine.

3.1.5 Universities attended (Question B2)

The majority of the GPs (113, 91%) in the study had obtained their medical degree in South Africa. Table 3.3 illustrates the South African universities that the GPs in this study had attended. Doctors who had studied overseas came from Italy, Ireland, Uganda, India, Holland, Argentina, Zambia, Zimbabwe and the United Kingdom.

Table 3.3. The universities attended by the GPs

UNIVERSITY	NO. OF GPs	% OF GPs
University of the Witwatersrand	63	51
University of Pretoria	30	24
University of Cape Town	6	5
University of Natal	3	2.5
University of Stellenbosch	6	5
University of the Orange Free State	3	2.5
MEDUNSA	2	1
Others (International)	11	9
TOTAL	**124**	**100%**

The majority of South African GPs in this study attended the University of the Witwatersrand or the University of Pretoria (both situated in Gauteng where this study was conducted).

3.1.6 Year of graduation (Question B3)

The GPs who responded had all graduated from medical school and were practicing medicine or working in a related field. The year of graduation of the participants ranged from 1949 to 1998 and were distributed as shown in Table 3.4:

Table 3.4 Year of graduation from medical school

GRADUATION YEARS	NO. OF GPs	% OF GPS
1941-1950	0	0
1951-1960	4	3
1961-1970	7	6
1971-1980	24	20
1981-1990	44	35
1991-1998	45	36
TOTAL	**124**	**100%**

Table 3.4 shows the majority of the doctors who participated in the study were those that had graduated in the last 20 years.

In the questionnaire, GPs were asked to state how long they had been in practice. The responses ranged from six months to 50 years with a mean of approximately **9.8** years.

3.1.7 Exposure to the teaching of Human Genetics (Question B4-B7)

GPs who had received some form of exposure to the teaching of medical genetics in their medical training numbered 104 out of 124 (84%). Thus 20 (16%) of the GPs who participated had had no such exposure.

Of those 104 GPs who had been exposed to the teachings of medical genetics, 65 (62.5%) felt it was adequately taught at the time. When questioned about their current perceptions, 50 of the 65 (77%) GPs felt in retrospect that the training was insufficient, 10 (15%) felt that their training was still adequate and two (3%) did not comment. Four (5%) GPs felt that their training was adequate, as they had come into little or no contact with genetics whilst practicing and therefore had not had much opportunity to put this knowledge into practice. One GP commented, "I need superficial knowledge of genetic inherited diseases only".

Of the 20 doctors who had received no form of medical genetics training, most did not comment on how they felt about this.

3.1.8 Working environment (Question B9)

Each GP was asked to state the environment in which they were working. The majority of them (92, 74%) were in private practice, whilst the rest worked in private hospitals and/or hospitals and clinics as shown in Table 3.5.

Table 3.5. Work environments of the GPs

WORK ENVIRONMENT	NO. OF GPs	% OF GPS
Private practice	92	74
Hospital/Clinic	17	14
Private practice and Hospital/Clinic	15	11
Total	124	100%

3.1.9 Details of GPs' patient base

3.1.9.1 Approximate number of patients (Question B10)

Each doctor was asked to estimate how many patients they were responsible for within their practice, per day and annually. Most doctors had difficulty estimating how many patients they saw annually. Many were also unsure how many patients were within their practice (and indeed this may not apply to hospital or clinic GPs). All GPs however could give a rough estimate of how many patients they saw on average in a day. Thus, this information was used for analyses. The approximate numbers of patients seen by each GP per day were used to calculate a mean average. The result revealed that GPs in this study saw approximately 27 patients per day.

As it was known these values were only approximate estimates the question was asked mainly to give a general idea of how many patients the GPs in this study came into contact with.

3.1.9. 2 Consultation time (Question B11)

Five time allocations for average consultation time were provided for GPs to indicate the time spent per patient. The results obtained are as shown in Table 3.6:

Table 3.6. Average time allowed for each GP consultation

Average time for each consultation	No. of GP responses	% of GPs responses
<5 minutes	1	1
5-10 minutes	20	16
10-15 minutes	42	34
15-20 minutes	48	39
>20 minutes	13	10
Total	**124**	**100%**

For this question, it should be noted that an error was made in the values stated from which GPs could choose a response. The values overlap (e.g. 5-10 minutes; 10-15 minutes), thus potentially not giving doctors clear options for answering this question. The following responses however were obtained:

The options of 15-20 minutes and 10-15 minutes were chosen by the largest group of GPs (48 (39%) and 42 (34%) respectively). In South Africa, the doctor to patient ratio is high

in most areas (Kale, 1995). This may mean that consultation times may be shorter than would be preferred. Providing genetic information and counseling can be complex and time consuming (Agan and Gregg, 2002). Although in practice, GPs may take more time with patients with more complex issues than with other patients whose issues are simpler, the aim of asking this question was to try and get a sense of how much time GPs felt they had on average for each patient. In reality however the issue is far more complex than this and one must also take into consideration the relationship, familiarity and knowledge that is built up between a GP and his/her patients over time.

3.1.9.3 Antenatal Care (Question B12)

Antenatal care is provided by 69 (56%) of the 124 GPs working in medical practice. Although most GPs said they referred patients to gynaecologists when they became pregnant, many GPs manage patients through the first and second trimester. Eight (6%) GPs provided antenatal care in the first trimester, forty-six (37%) GPs provided antenatal care in the second trimester. Fifteen (12%) GPs that participated in the study managed pregnant mothers to term.

3.1.9.4 Administration and fees of patient care (Question B 13-17)

The purpose of these questions was to try and obtain information about how the medical practice worked was also gathered. These questions asked about fees charged, whether or

not appointments were scheduled and approximately how many of their patients were on medical aid schemes.

Medical aid rates were charged by 76 (61%) of the 124 GPs in practice. Of the remaining 48, 11 worked in state hospitals where rates are charged well below medical aid tariffs whilst 37 charged rates exceeding the medical aid tariff guidelines.

The GPs were asked to estimate the approximate proportion of patients within their practice who had medical aid. 121 of the participants answered and the results are shown in Table 3.7.

Table 3.7. Proportion of patients on medical aid

Percentage of patients with medical aid	No. of GPs with this percentage of patients	% of GPs with this percentage of patients
0-5%	11	9.3
5-10%	7	5.7
10-25%	2	1.7
25-50%	7	5.7
50-75%	51	42.1
75-100%	43	35.5
Total	**121**	**100%**

For this question , it should be noted that an error was made in the values stated from which GPs could choose a response. The values overlap (e.g. 5-10 %; 10-15 %), thus

potentially not giving doctors clear options for answering this question. The following responses however were obtained:

Up front payment (meaning cash payment at time of consultation) for services to patients with medical aid was required in 30 (24%) of the medical practices whilst the remaining 94 (76%) submitted the bill directly to the medical aid. Where patients did not belong to a medical aid, the majority (88, 71%) were required to pay cash at the time of the consultation whereas the rest had an account-based system.

Altogether, 80 (65%) of GP practices required patients to make appointments for consultations; the remaining 44 (35%) did not have a formal appointment procedure.

3.1.9.5 Age and ethnicity of patients (Question B18 and B19)

Question 18 asked GPs to estimate the percentage of patients they had within their practice which belonged to certain age groups. There were five age groupings provided and all respondents entered percentages to total 100%. It should be taken into however account that the age groups shown (e.g. 0-10 years; 10-20 years etc) overlapped, so values may have been influenced by this. Additionally, the groupings are not evenly divided. The data obtained however was aggregated and GPs in the study were found to have the following average percentage of patients in each age group: 18% (0-10 years), 15% (10-20 years), 31% (20-40 years), 22% (40-60 years) and 14% (>60 years).

Question 19 aimed to gain more information about the ethnic composition of patients. In all cases, either white or black patients constituted the majority of patients seen at any one GP practice, and in all cases, Indian and 'Coloured' individuals featured as minority groups. Here, 72 GPs (58%) stated that over 50% of their patients were white with the remaining fifty-two (42%) stated that over 50% of their patients were black. Of these 52 GPs, 7 indicated that they saw black patients only. Eleven GPs stated that other minority groups in South Africa such as Chinese, Taiwanese and 'oriental' patients visited their practice (although always in small numbers).

GPs were asked to state the percentage of patients in that belonged to their practice in each ethnicity group. These were then aggregated and averaged. The following average percentages were obtained: 51% (White), 35% (Black), 7% (Indian), 6% (Coloured). An average of one percent of patients were stated under the category 'Other' and these were, as stated above, specified as being either Chinese, Taiwanese or 'oriental' in origin.

Based on the information gathered, the majority of GPs who participated in this study had a working environment where there were formal procedures in place such as booking of appointments and where a large proportion of patients had some form of medical aid. As the setting of this study was predominantly urban, this is perhaps not surprising. In more rural settings, the patient to doctor ratio may be far higher (Lovenstein, 1981; Rajendra, 1995) access to genetic clinics may be more difficult and there may be fewer people on medical aids. Access to tertiary education institutions and facilities where educational

programs may be held would also be more difficult. It would also be more difficult to refer patients to specialised facilities if needed.

3.1.9.6 Patients with genetic disorders seen by GPs (Question B20)

GPs were asked to specify if any of their patients had any genetic disorders (and if so the approximate number) from a list of the more common disorders that was provided. The results are displayed in Table 3.8.

Table 3.8 GPs' patients with genetic disorders

Genetic disorder	No. GPs with patients with the disorder	Average number of patients with the disorder/respondents*
Albinism	30	2
Cystic fibrosis	25	2
Haemophilia	35	2
Cleft palate/cleft lip	53	3
Neural tube defects	21	2
Porphyria variegata	63	4
Familial Hypercholesterolaemia	78	31
Down syndrome	67	3
Myotonic dystrophy	10	1
Duchenne muscular dystrophy	11	2
Genetic or congenital deafness	40	2
Genetic or congenital blindness	12	3
Genetic mental retardation	45	3
Others	10	1

* The calculated average was rounded off so as to represent actual individuals with the disorder

It was noted that 83% (103) of the 124 GPs that participated in this study indicated that they had at least one patient with one of the above disorders. Based on the number of patients stated to have a known genetic disorder and the number of GPs who encountered them, it was calculated that each GP could potentially have an average of 33 patients with a genetic disorder within their patient base. Under the category of 'Other', disorders mentioned by GPs included Turner syndrome, Friedreichs ataxia, limb girdle dystrophy, xeroderma pigmentosum, Charcot-Marie Tooth disease, Fanconi anaemia, alpha and beta thalassaemia, haemochromatosis and haemophilia B.

These results are important and indicate that GPs do come into contact with patients who have genetic issues. It is thus important that they be aware of how to handle them. As previously mentioned, it was calculated that each GP could in theory be presented with approximately 33 patients who could have some kind of genetic disorder within their practice patient base. It should be noted however that this value however could be influenced by other factors. Of the GPs who participated in this study, ten belonged to a practice in which a partner GP also participated in the study. There is thus potential for some doctors to be seeing each others patients and therefore when they stated the number of patients with genetic disorders that they see, this number may be overrepresented. Their partners may have also mentioned these same patients. Another factor to consider is that not all genetic disorders may be diagnosed or recognised. Thus it is possible that this value may be underestimated in some scenarios.

3.1.10 Differences between postal and interview GP responses in Sections A and B

In this section, I will briefly comment on any significant differences that were noted in the results of Section A and B between the two groups. The chi-squared test was utilized with p values less that 0.05 denoting significance. As there was one degree of freedom, Yates correction was implemented to increase accuracy.

Upon analysis, there were only a two areas where there was a significant difference found between the two groups. The first significant difference pertained to antenatal care. The difference between the number of GPs who offered antenatal care in the postal component (50 GPs) and the number of GPs in the interview component (19 GPs) was significant (p=0.025).

Secondly, there was a significant difference between the number of GPs in the postal component who indicated that patients needed to schedule appointments (33 GPs) and the number of GPs in the interview component (11). Here, p=0.045.

Another point worthy of note is that GPs who were part of the postal component may have come from areas farther a field than those who were chosen for interviews (as a criterion for this was locality). Postal replies were received from GPs from areas such as Vereeniging, Brakpan, Lenasia, Industria, Germiston, Krugersdorp, Centurion, Moreleta Park, Brooklyn, Arcadia, Dainfern, Benoni, Meyerton, Bronkhorstspruit, Kibler Park, Laudium, Glenstantia, Boksburg, Maraisburg, Pyramid, Orchards, Springs, Fordsburg,

Erasmusrand, Heidelburg, Sinoville, Paardekraal, Lynnwoodridge, Lyttleton, Queenswood, Edleem, Actonville, Marshaltown and Kyalami which perhaps may not have been targeted by the researcher for interviews.

3.2 Assessment of genetic knowledge (Section C)

In Section C multiple-choice questions were used to assess genetic knowledge. Participants were asked to choose from multiple answers or to specify whether certain statements were True or False. For all the questions, an option of "Unsure" or "Uncertain of the correct answer" was included so that there was a greater chance of the answers being a reflection of true knowledge rather than a guess. In this section the results of the questions asked were grouped according to subject rather than analysing each question of the questionnaire consecutively in some instances.

3.2.1 Mendelian Inheritance

In genetics, understanding of the modes of inheritance is extremely important so that genetic problems can be dealt with properly. Even if a disorder is looked up in a book, the pattern of inheritance is normally stated, but not explained. An understanding of the modes of inheritance is important in order to be able to explain recurrence risks.

3.2.1.1 Autosomal dominant (AD) inheritance (Questions C1 and C2)

Table 3.9 shows that when one parent has a genetic disorder that is AD, 73 (60%) GPs knew the risks involved to offspring.

Table 3.9 Responses to autosomal dominant risk assessment

Risk Options	No. of GP responses	% of GP Responses
Close to 0%	0	0
25%	22	15
50% (Correct)	**73**	**60**
100%	19	15
Uncertain of the correct answer	13	10
Total	**124**	**100%**

The fact that AD disorders are frequently varied in their clinical presentation (Meuller and Young, 1998) was known by 52 (42%) of GPs. A further 52 (42%) believed this statement to be false and 20 (16%) were unsure.

In a large proportion of cases, new mutations are the cause of such disorders, as only one of the two homologous genes needs to be faulty for disease presentation. This fact was considered true by 36% (45) of GPs. Unsure answers totaled 28% (35) and 36% (44) of GPs disagreed with this statement.

In AD inheritance, males and females are affected with the same frequency. This fact was chosen as correct by the majority (90, 73%) of GPs whilst 17% (21) disagreed. Ten percent (13) of GPs were unsure.

3.2.1.2 X-linked recessive inheritance (Questions C3 and C4)

A pedigree of a family with an X-linked recessive condition was shown and GPs were asked to choose the correct mode of inheritance. The results are shown in Table 3.10:

Table 3.10 Interpretations of a pedigree showing X-linked recessive inheritance

Inheritance pattern	No. GP responses*	GPs Responses (%)*
X-linked dominant	5	4
X-linked recessive	**69**	**56**
Autosomal dominant	20	16
Autosomal recessive	5	4
Uncertain of the correct answer	24	20

*The numbers in bold indicate the correct answers

As shown above, 69 (56%) GPs chose 'X-linked recessive' which correctly identified the pattern of inheritance in this pedigree.. A further 24(20%) were 'uncertain of the correct answer' and 30 (34%) chose other patterns of inheritance. Family histories and the means of documenting them with a pedigree, are important in ascertaining whether or not individuals are at risk or have genetic disorders in their families (Summerton and Garrood, 1997).

Certain facts about X-linked inheritance were also examined. Five statements were presented in Question C4. The statement and the percentage of responses selected are displayed in Table 3.11.

The majority of doctors had good knowledge and chose correctly in each case except statement (a) pertaining to new mutations. For statement (a), 40 (32%) GPs felt that this

was false, 52 (42%) were unsure and 32 (26%) chose the option of 'true' (correct answer). This level of knowledge may be significant as many new cases of X-linked conditions may be disregarded in the absence of a family history, yet a new mutation may be the cause and the history would not be present (Ballo *et al*, 1994). It is important that such a fact be understood in order for such disorders to be recognised and the correct recurrence risks given (Harper, 1998).

Table 3.11. Responses to statements about X-linked recessive disorders

Statement	True*	False*	Unsure
a)The disorder may often arise owing to a new mutation	**32 (26%)**	40 (32%)	52 (42%)
b) The disorder usually only manifests in males	**92 (74%)**	25 (20%)	7(6%)
c) An affected male may pass on the disorder to his sons	33 (27%)	**78 (63%)**	13 (10%)
d) All daughters of an affected male are carriers of the disorder	**89 (72%)**	25 (20%)	10 (8%)
e) Carrier females have a 50% chance of passing on the disorder to their sons	**93 (75%)**	15 (12%)	16 (13%)

*The numbers in bold indicate the percentage of correct answers

3.2.1.3 Autosomal recessive (AR) inheritance (Questions C5 and C6)

When GPs were asked to comment on the percentage risk present to children of a couple who both carried a mutation for the same AR disorder, 56% (70) chose the correct risk percentage as shown in Table 3.12.

Table 3.12 Responses to autosomal recessive risk assessment (Question C5)

Risk Options	No. of GP responses	% of GP responses
0%	0	0
25% (Correct)	**70**	**56**
50%	29	23
100%	11	9
Uncertain of the correct answer	13	12
Total	**124**	**100%**

Question C6 required GPs to comment on certain statements about AR inheritance. The results are displayed in Table 3.13. Knowledge in this area was good with 84% (104) identifying that AR disorders may occur more often with consanguineous parents and 73% (90) correctly recognised that both males and females are equally affected.

Table 3.13. Responses to statements regarding autosomal recessive inheritance

Statement	True*	False*	Unsure
1) A positive family history is almost always present	37 (30%)	**71 (57%)**	16 (13%)
2) They are more common in the children of consanguineous (related) parents	**104 (84%)**	5 (4%)	15 (12%)
3) Males and females are equally affected	**90 (73%)**	15 (12%)	19 (15%)

*The numbers in bold indicate the correct answers

Mendelian genetic knowledge:

Knowledge of the autosomal recessive mode of inheritance may be important if GPs are to be able to determine accurate risks for patients. Knowledge within this section was quite good with all but one question (C4 statement (a)) being answered correctly by the majority of GPs. A good knowledge of this topic is important as mistakes involving risk assessment on the part of a GP can significantly alter couples' life plans and choices. If

one does not understand the intricacies of genetic diseases and how they present, prevention will be made difficult (Rose *et al*, 1999).

3.2.2 Non-Mendelian Inheritance

3.2.2.1 Multifactorial inheritance (Question C7)

This question attempted to elucidate whether GPs understood that multifactorial disorders have both a genetic and an environmental component. The majority (95 or 77%) chose this option whilst 2 (1%) attributed the cause to abnormal genes only. 'Uncertain of the correct answer' was chosen by the remaining 27 (22%) of the participants. Many disorders that GPs see routinely follow a multifactorial inheritance pattern (Williamson and Robertson, 1999). Diabetes, cancer, hypertension, cardiovascular disease and Alzheimer disease all have genetic and environmental components and we are quickly developing tools to elucidate and understand the heritability of such complex diseases (Wolpert *et al*, 1999). A study by Fry *et al* (1999) conducted in the United Kingdom, investigated the role that GPs feel they should play in dealing with a multifactorial disorder such as cancer. In general, GPs felt that although they identify a role for themselves in the process of cancer genetic services, they felt that this role only involved taking a family history and making referrals. The level of understanding of cancer genetics was felt to be low and GPs required the knowledge of specialists in this area.

It is clear that many conditions have a strong genetic component but are not transmitted in clearly defined inheritance modes. Progress in understanding how these atypical inheritance patterns is advancing and improvements are being made in diagnosis, genetic counselling and how treatment regimes and lifestyle changes can sometimes reduce the risks of such disorders from presenting themselves (Wagstaff, 2000). It is becoming increasingly important that medical practitioners become aware of both the genetic and environmental components that such disorders may have so that they can advise patients correctly about these issues (Emery and Hayflick, 2001).

3.2.2.2 Dynamic mutations (Question C8 and C24)

Since 1991, a number of diseases have been identified as being caused by the amplification of simple triplet repeat expansions (Usdin and Grabczyk, 2000). These DNA sequences are unstable and the number of repeats present may increase from generation to generation. Three specific triplet repeat disorders were dealt with in this questionnaire: Fragile X syndrome, Huntington disease and myotonic dystrophy. These three were chosen as they are found in relatively high frequencies in South African populations (Venter *et al*, 1986; Hyden *et al*, 1982; Goldman *et al*, 1996) and thus may be pertinent to GPs in this country.

Four statements were presented and GPs had to answer whether each was True or False. The statements and the responses chosen are shown in Table 3.14.

Table 3.14. Responses to DNA triplet repeat expansion statements

Statement	True*	False*	Unsure
a) May display marked variability in the clinical severity between individuals	**67 (54%)**	1 (1%)	56 (44%)
b) May show an earlier disease onset in the offspring than in the parents	**47 (38%)**	7 (6%)	70 (56%)
c) All display autosomal dominant inheritance	6 (5%)	**42 (34%)**	76 (61%)
d) Show a disease severity that may be influenced by the sex of the transmitting parent	**28 (23%)**	14 (11%)	82 (66%)

*The numbers in bold indicate the correct answers

For this question, the number of "unsure" responses was amongst the highest in the study. This is not surprising as this area of genetics is relatively new, and this may reflect how slowly new information infiltrates into general medical practice and knowledge. Hofman (1994) conducted a study to ascertain whether new developments in genetics penetrate the medical community and their patients. This study dealt with new testing for neurofibromatosis type 1 (NF1). Two years after testing for this disorder was instituted, a survey was conducted to ascertain what proportion of GPs and patients knew about this and how many had informed their NF1 patients about this. This paper suggested that new technological developments are only very slowly made use of in medical practice. Only 65% of individuals with NF1 had been alerted by their doctors of the availability of testing. Thus, new advances take time to be absorbed by the medical community. Triplet repeat expansions represent the cause of 14 human genetic diseases (Cummings and Zoghbi, 2000) and thus knowledge regarding mechanisms of inheritance and disease presentation may become increasingly important in the management of patients with these disorders.

In Question 24, GPs were asked to identify which disorders were caused by DNA triplet repeat expansions. Three such disorders, Fragile X syndrome, Huntington disease and Myotonic dystrophy were listed and correctly identified as such by 22 (18%), 16 (13%) and 11 (9%) respectively. GP knowledge of the inheritance pattern of Huntington disease and myotonic dystrophy can be seen in Section 3.2.2.3.

3.2.2.3 Inheritance patterns of common genetic disorders (Question C25)

Question 25 aimed to assess whether GPs knew how commonly-encountered genetic disorders are inherited. This knowledge is thought to be important if patients are to be advised properly about risks and to be assessed as to whether they require referrals for genetic counselling. DNA analysis and testing is expensive and thus it is essential that GPs utilise these properly and do not send samples of individuals who are clearly not at risk for a disorder (e.g. sons of fathers who have an X-linked disorder).

Table 3.15 Knowledge of inheritance patterns of genetic disorders

Genetic disorder	AD[1]*	AR[2]*	X-L[3]*	Multifactorial*	Uncertain of answer
Cystic fibrosis	10 (8%)	**81 (65%)**	1 (1%)	3 (2%)	29 (24%)
Huntington disease	**53 (43%)**	9 (7%)	8 (6%)	9 (6%)	46 (36%)
Familial Hypercholesterolaemia	**53 (43%)**	24 (19%)	1 (1%)	13 (10%)	33 (24%)
Albinism	11 (9%)	**61 (49%)**	6 (5%)	4 (3%)	42 (33%)
Myotonic dystrophy	**15 (12%)**	21 (17%)	15 (9%)	8 (6%)	65 (52%)
Haemophilia A	7 (6%)	12 (10%)	**74 (60%)**	1 (1%)	29 (23%)
Neural tube defects	1 (1%)	11 (9%)	1 (1%)	**73 (59%)**	38 (30%)
Cleft lip and/or palate	1 (1%)	11 (9%)	1 (1%)	**69 (56%)**	41 (33%)
Porphyria variegata	**31 (25%)**	35 (28%)	0	6 (5%)	51 (42%)
Duchenne muscular dystrophy	10 (8%)	20 (16%)	**40 (32%)**	3 (2%)	51 (42%)
Spinal muscular atrophy	3 (2%)	**20 (16%)**	4 (3%)	10 (8%)	87 (71%)
Tay-Sachs disease	11 (9%)	**61 (49%)**	2 (2%)	3 (2%)	47 (38%)

*The numbers in bold indicate the correct answers
[1]AD- Autosomal dominant, [2]AR-Autosomal recessive, [3]X-L-X-linked

The average percentage of certain correct answers for this set of 12 disorders was 42.46%. As all these disorders are considered to be fairly common in South Africa, this average could represent an area where knowledge about genetic disease, how it occurs and how it manifests may need improving. The inheritance mode of cystic fibrosis was known by most GPs (81 (65%)) whilst myotonic dystrophy and spinal muscular atrophy were known by the least (15 (12%) ;and 20 (16%) respectively). This may be significant as both myotonic dystrophy (Goldman *et al*, 1996) and spinal muscular atrophy (Stevens *et al*, 1999) have been shown to be prevalent causes of genetic disorders in South Africa.

As mentioned, albinism is probably the most commonly found genetic disease in black patients. The results of the responses revealed that 61 (49%) GPs chose the correct pattern of inheritance (AR), 42 (33%) GPs were 'uncertain of the answer' and 21 GPs (18%) chose one of the other inheritance patterns which were not correct. The correct inheritance mode of Familial Hypercholesterolaemia, the most commonly cited genetic disease of GPs who participated in this study was chosen by 43% (53) of GPs. In the case of Duchenne muscular dystrophy and porphyria variegata the correct inheritance mode was chosen by 40 (32%) and 31 (25%) GPs respectively.

3.2.3 Aneuploidy

3.2.3.1 Down syndrome (Question C9, 10 and 11)

GPs were asked to identify the correct karyotype of a female child with Down syndrome in Question 9, see Table 3.16.

Table 3.16 Interpretation of female Down syndrome karyotype

Karyotypes	No. of GP responses	% of GP responses (%) (n=124)
a) 47 chromosomes, XY, +21	8	6
b) 47 chromosomes, XX, +13	4	3
c) 47 chromosomes, XX, +21*	76	61
d) 21 chromosomes, XX	9	7
e) Uncertain of the correct answer	16	13
Total	**113** (remaining 11 chose (a) & (c) together)	**91%** (remaining 9% chose (a) & (c) together)

* Correct option

The correct Karyotype (Option C) was chosen by 71 GPs (61%). Some (11, 9%) chose both karyotypes "a" and "c" together. This could perhaps indicate that GPs knew Down syndrome was caused by the presence of an extra copy of chromosome 21 but either did not know the difference between male and female sex chromosomes or they did not notice the difference in the question.

Down syndrome occurs with an incidence of 1 in 700 live births (Meuller and Young, 1998) and this fact was investigated in Question 11. Misconceptions about the frequency of Down syndrome exist. A few of these misconceptions were stated and GPs were invited to choose between them. Table 3.17 displays results.

Table 3.17 Choice of statements regarding frequency of Down syndrome in SA

a) Is approximately 1 in 700 (Correct)
b) Is greater in the white population
c) Varies greatly from area to area
d) Is lower in South Africa than First World Countries
e) Uncertain of the correct answer(s)

Options chosen	Percentage of GPs (Total 100%)
a*	40%
a*,b	7%
a*,c	2%
a*,b,c	1%
a*,b,d	2%
b	12%
b,c	2%
b,c,d	1%
c	1%
c,d	1%
d	1%
e	30%

*** Correct response**

It is important to note that for this question (and as demonstrated above) more than one answer could have been chosen. It was stated at the beginning of Section C of the questionnaire more than one answer could be correct so that GPs could answer more than once for a question if they wished. In retrospect however, this question may have been confusing to a GP as although this was stated at the beginning of the section, it was not reiterated when this question was presented on page 7 of the questionnaire. Additionally, the option of 'e' (uncertain of the correct answer(s)) may have been chosen in relation to any of the statements 'a','b','c','d' regarding the frequency of Down syndrome. It is thus difficult to establish whether those that chose 'e' were uncertain regarding the frequency as such or whether they were uncertain about one of the statements presented. Some GPs however did choose from options besides 'e', giving results, which although must be

looked at with the above in mind, may help recognize misconceptions surrounding the frequency of Down syndrome.

From the above table one can see that 40% chose the correct answer, 30% were 'uncertain of the correct answer' and 30% chose one of the misconceptions known to exist. The most commonly chosen misconception was 'b', i.e. that Down syndrome is more commonly found in white populations. This correlates with a study by Christianson *et al* (1995) in which it is revealed that Down syndrome has only recently been shown to have a high incidence in black neonates. This study also makes mention of the fact that difficulty has been noted in recognising and diagnosing this disorder in this population group. This may explain why such misconceptions still persist, but it is important that such misconceptions be identified so that they can be addressed.

Knowledge of the typical clinical features of Down syndrome was also investigated and the results are shown in Table 3.18.

Table 3.18 Responses regarding typical features of Down syndrome

Physical feature	True*	False*	Unsure
a) cleft lip and palate	27 (21%)	**80 (65%)**	17 (14%)
b) epicanthic folds	**120 (97%)**	3 (2%)	1 (1%)
c) polydactyly	40 (32%)	**70 (56%)**	14 (12%)
d) mental retardation	**121 (98%)**	1 (1%)	1 (1%)
e) cardiac defect	**112 (90%)**	4 (4%)	8 (6%)

*The numbers in bold indicate the correct answers

As stated in Meuller and Young (1998), epicanthic folds, mental retardation and cardiac defect are amongst the common clinical features in Down syndrome. Polydactyly and cleft lip and palate however are not classified as common features of Down syndrome. These arc found more commonly in cases of trisomy 13 and 18. Recognition of the typical physical features of individuals with Down syndrome is important in order to diagnose this disorder (Christianson, 1997).

In this question the word 'typical' was used. In retrospect perhaps another term should have been used as it was thought perhaps that this may potentially have been confusing for GPs when answering this question. Additionally it may influence the interpretation of data. The following results however were noted:

Knowledge in the section was very good with 121 (98%) GPs recognizing mental retardation as a common feature of Down syndrome and 112 (90%) GPs indicating that cardiac defects may often be present. Additionally 120 (97%) knew epicanthic folds to be a common feature. Polydactyly and cleft lip and palate were believed to be typical features by 32% (40) and 21% (27) respectively. As stated these are found more commonly in cases of trisomy 13 and 18.

As mentioned, knowledge regarding common disorders like Down syndrome is important so that the condition can be diagnosed. Early intervention and medical treatment may then be offered, and the ability of the individual to reach full emotional and intellectual potential may be enhanced (Christanson, 1997). In this study, questions pertaining to Down syndrome revealed that knowledge surrounding the identification of features of

Down syndrome was very good (see above) and that 61% of GPs chose the correct karyotype for a female patient with Down syndrome (Table 3.19). Although misconceptions about the incidence of Down syndrome may exist (Table 3.20), 40% of GPs recognized the correct frequency of the syndrome.

3.2.3.2 Turner syndrome (Question C12)

Knowledge of Turner syndrome was investigated. Table 3.19 shows the responses to these statements.

Table 3.19 Responses to statements about Turner syndrome

Statement	True*	False*	Unsure
a) Mental retardation	72 (58%)	**38 (31%)**	14 (11%)
b) A missing X chromosome	**85 (69%)**	22 (18%)	17 (13%)
c) Normal stature	6 (5%)	**110 (89%)**	8 (6%)
d) Normal secondary sexual characteristics	9 (8%)	**107 (86%)**	8 (6%)
e) Oedema at birth	**39 (31%)**	32 (26%)	53 (43%)
f) Cardiac defect	**60 (48%)**	31 (25%)	33 (27%)

*The numbers in bold indicate the correct answers

A common misconception appears to be that individuals with Turner syndrome are mentally retarded. Although many have learning problems, mental retardation is found only in a very small percentage of individuals with Turner syndrome (Meuller and Young, 1998). This fact is important as it may affect the way in which GPs may counsel parents and affected individuals. The cause of Turner syndrome was known by 69% (85) of GPs.

In general, knowledge about Turner syndrome is good. Facts however pertaining to 'oedema at birth' and 'mental retardation' seemed less well known. This could be

significant in light if diagnosing the disorder and understanding the condition. Over half (52%, 64) of GPs did not know about the potential of cardiac defects in such patients – a potentially significant fact in light of a patients potential management.

3.2.4 Prenatal diagnosis

The results of this section were analysed in the following way: The level of knowledge was looked at for the entire group of respondents (sections 3.2.4.1-3.2.4.3). Then, the knowledge was looked at with reference to doctors who provided antenatal care within their practice (section 3.2.4.4). This part of the analysis was performed to see whether GPs in this study who probably encounter this field more often (as they provided antenatal care), had a higher level of knowledge.

3.2.4.1 Maternal Serum Triple Test (Question C13, 14 and 15)

This test has been in use since 1988 (Wald *et al*, 1997) and is also useful in detecting the presence of open neural tube defects (by monitoring the maternal AFP level), as well as other chromosome abnormalities (Ormond, 1997). This test detects only approximately 60% of fetuses with Down syndrome. This fact was correctly chosen by 21 (17%) of GPs (Q. 13). Forty-six (37%) thought that the sensitivity of this test was 80% and three (2%) thought it was 100% (higher than it actually is). Twelve GPs (10%) thought the sensitivity was 20% (lower than it is) and 42 GPs (34%) were 'uncertain of the correct answer'. Although normal range values and sensitivities of a test may be stated as part of a laboratory report displaying the results, it may be of interest to note what GPs may think the answer is without this. Although not offered throughout the country, is widely

used among the private sectors of medical practice and in small-scale screening programs in specific areas of South Africa (Kromberg and Jenkins, 1997).

This test is a screening test only and it is felt that it is best discussed fully with mothers before being performed so that the limitations of the test are understood (Ormond, 1997). Table 3.20 illustrates the GPs' responses to question 14.

Table 3.20. Responses regarding the MSTT

Statement	True*	False*	Unsure
a) Has a false positive rate of 5%	**68 (55%)**	5 (4%)	51 (41%)
b) Is a diagnostic lab test	58 (47%)	**48 (39%)**	18 (14%)
c) May identify high risk fetuses with other congenital abnormalities	**95 (77%)**	9 (7%)	20 (16%)
d) When positive, identifies fetuses with a higher risk of having DS	**104 (84%)**	6 (5%)	14 (11%)
e) Is administered at 10 weeks of pregnancy	33 (27%)	**56 (45%)**	35 (28%)

*The numbers in bold indicate the correct answers

In this question, it should be noted that there are two areas which could have influenced the response a GP made. For statement 'a', a fixed value of 5% was stated. If a GP thought that it was perhaps slightly higher or lower than this could potentially have made him/her choose 'unsure' or 'false' even though they were close to the correct value. The same applies to statement 'e' regarding '10 weeks'. This should be borne in mind for these questions. As can be seen from Table 3.23 knowledge regarding statements 'c' and 'd' was good (77% and 84% correct respectively). For statement 'b', 58 GPs (47%) believe this test to be a diagnostic test rather than a screening test. This is potentially significant as it may lead to patients being misinformed. This could cause considerable

anxiety for patients who have positive results and may lead to choices such as termination of pregnancy being made by patients who do not have all the correct facts.

As mentioned, the MSTT can detect anomalies such as open neural tube defects. A test revealing a significantly raised AFP level could point to such anomalies in 80% of cases (see Q. 15). The aim of this question was to assess knowledge of this information. Unfortunately however, it was felt that the question may have been ambiguous. One interpretation of the question could be that the value that had to be indicated pertained to the number of pregnancies in which AFP levels were raised and neural tube defects occur. In fact what was meant was that GPs should indicate what percentage of raised AFP levels which were associated with neural tube defects. As there was such potential for misinterpretation in this question, it was thought best to not include it in the results of this study as it would be difficult to gain any significant knowledge from the responses.

3.2.4.2 Chorionic villus sampling (CVS) (Question C16)

CVS offers a means for early detection of a genetic disorder and therefore an option of earlier termination of pregnancy (should this be the patient's choice) which may thus be less emotionally and physically traumatic for patients.

Question 16 attempted to see how GPs would handle a situation where a pregnant woman approached them and informed them that there was a genetic disorder running in her family for which she required testing by DNA analysis. Various options for prenatal

diagnosis were presented. Criteria such as a request for the earliest possible diagnostic intervention and for testing of a disorder that required DNA analysis were stressed so that the only correct answer was "c" for chorionic villus sampling.

It was stated at the beginning of Section C of the questionnaire more than one answer could be correct so that GPs could answer more than once for a question if they wished. This was however not reiterated when this question was presented on page nine of the questionnaire. In this particular instance, only option 'c' was correct, however as can be seen below some doctors decided to chose more than one answer.

Table 3.21 Choice of statements regarding the earliest prenatal genetic testing

a) Maternal serum triple test
b) Amniocentesis
c) Chorionic villus sampling
d) High level ultrasound scan
e) Uncertain of the correct answer

Options chosen	Percentage of GPs (Total 100%)
a	17%
a,b	3%
a,c*	2%
a,b,c*	1%
a,b,c*,d	2%
a,b,d	2%
b	16%
c*	36%
c*,d	5%
d	2%
e	14%

*** Correct response**

As shown above, 36% of GPs chose the correct option. A further 10% chose "c" in conjunction with another option. The MSTT ("a") was chosen by 17% of GPs and 2% would offer "d", high-level ultrasound. These tests are not appropriate for diagnosing genetic disorders by DNA analysis. Only "b" and "c" (amniocentesis and CVS) can be used for this. Amniocentesis was chosen by 16% of GPs and although it was not the correct answer asked for in this question, it would still benefit patients to be offered such a test in similar scenarios (where a diagnosis could possibly be made later). Option 'e' for 'uncertain of the correct answer' was chosen by 14%

The above perhaps represents that knowledge regarding CVS sampling as a current technique could be improved on so that it is well known that it may be a means of establishing early prenatal diagnosis using DNA analysis. CVS has been offered in South Africa since the 1980s and it would be beneficial if GPs were aware of its use and value in such scenarios (Rosendorff *et al*, 1989).

3.2.4.3 Amniocentesis (Question C17)

Amniocentesis is a useful method for the diagnosis of many genetic defects. This procedure has become a safer and more successful technique in expert hands over time and a study performed in Johannesburg revealed that it has a spontaneous abortion risk of 0.7% (Kromberg *et al*, 1989a). Chromosomal, biochemical and DNA testing can be performed using amniocentesis. The responses regarding amniocentesis are shown in Table 3.22.

Table 3.22. Responses regarding amniocentesis

Statements about amniocentesis	True*	False*	Unsure
a) Is best performed at 12 weeks	44 (35%)	**62 (50%)**	18 (15%)
b) Has a miscarriage risk of less that 1%	**98 (80%)**	12 (10%)	14 (10%)
c) Allows the examination of chromosomes only	12 (10%)	**100 (81%)**	12 (9%)
d) Takes 3-4 weeks for a complete result	**72 (58%)**	22 (18%)	30 (24%)
e) Can be used for biochemical and/or DNA studies	**106 (85%)**	6 (5%)	12 (10%)
f) Is an indication for the administration of Anti-D gammaglobulin if the mother is Rh-	**58 (47%)**	42 (34%)	24 (19%)

*The numbers in bold indicate the correct answers

For statements 'b', 'c', 'd' and 'e' the majority of GPs chose the correct answer. Of potential significance however is that for statement 'f', 34% (42) of GPs did not think that an invasive procedure such as an amniocentesis, might be an indication for an Anti-D gammaglobulin injection to avoid maternal sensitisation. A further 24 (19%) were unsure. Statement 'a' examined the optimum time to perform the test. Here, 35% (44) agreed with the incorrect date given of 12 weeks and 15% (18) were 'unsure' of the answer leaving 62 (50%) choosing the correct answer. Amniocentesis usually takes 3-4 weeks for a complete result. Here, 72 (58%) GPs correctly chose this fact to be true with 22 (18%) choosing incorrectly and 30 (24%) being unsure.

Prenatal tests such as the MSTT, amniocentesis and CVS are important parts of patient care. Since 56% (69) of GPs in this study provide some degree of antenatal care especially in the first and second trimester when these tests would be performed (section

3.1.9.2), a correlation was made as to whether such GPs had a higher knowledge of prenatal diagnosis techniques. Section 3.2.4.4 takes a further look into this.

3.2.4.4 Comparison of Prenatal Diagnosis knowledge amongst GPs providing Antenatal Care vs. those who do not

To get an idea whether GPs who offered antenatal care as part of their practice had a better knowledge of the some aspects of prenatal diagnosis, the percentage of the entire sample group who got correct answers for each question in this section were compared with the percentage of correct answers from GPs who provide antenatal care. The results follow in Table 3.23.

As can be seen from the table, differences in the level of knowledge between the two groups did exist but most of which were small. The differences in scores ranged from 0% to 13% with a mean overall difference of 4.4%. Using the chi-squared test however, there were no significant differences found ($p < 0.05$) between the two groups. It is interesting to note however that more often than not the group not providing antenatal care often scored a little higher than those that did offer this care. The question with the highest difference in score pertained to the time taken for a full amniocentesis result. Surprisingly, GPs who did not offer antenatal care seemed more aware of the answer to this.

Table 3.23 Prenatal diagnosis knowledge of GPs offering antenatal care versus those that do not

Prenatal Diagnosis Questions/Statements	Percentage Correct answers of respondents not offering antenatal care (n=55)	Percentage Correct answers of respondents offering antenatal care (n=69)
Maternal Serum Triple Screen		
Question C13	11 (20%)	10 (14%)
Question C14		
a) Has a false positive rate of 5%	31 (56%)	37 (53%)
b) Is a diagnostic lab test	23 (42%)	25 (36%)
c) May identify high risk fetuses with other congenital abnormalities	43 (78%)	52 (75%)
d) When positive, identifies fetuses with a higher risk of having DS	46 (84%)	58 (84%)
e) Is administered at 10 weeks of pregnancy	25 (45%)	31 (45%)
QuestionC15	19 (35%)	22 (32%)
Chorionic Villus Sampling		
Question C16	22 (40%)	23 (33%)
Amniocentesis		
Question C17		
a) Is best performed at 12 weeks	26 (47%)	36 (52%)
b) Has a miscarriage risk of less that 1%	43 (78%)	55 (80%)
c) Allows the examination of chromosomes only	45 (82%)	55 (80%)
d) Takes 3-4 weeks for a complete result	36 (65%)	36 (52%)
e) Can be used for biochemical and/or DNA studies	48 (87%)	58 (84%)
f) Is an indication for the administration of Anti-D gammaglobulin if the mother is Rh-	24 (44%)	34 (49%)

3.2.4.5 Chromosome abnormalities (Question C18)

Certain situations may be present where there is a higher risk for having a child with a chromosomal abnormality. Five such situations were presented to the GPs and their comments are shown in Table 3.24.

Table 3.24 Responses to situations about risks of chromosomal abnormalities

Statement	True*	False*	Unsure
a) If a mother already has a child with a chromosomal disorder	**111 (90%)**	0	13 (10%)
b) In mothers over 35 years of age	**123 (99%)**	0	1 (1%)
c) In fathers over 35 years of age	20 (16%)	**91 (73%)**	13 (11%)
d) In parents with balanced translocations	**49 (40%)**	16 (13%)	59 (47%)

*The numbers in bold indicate the correct answers

Pregnancy in women 35 years and older is known to present a scenario of increased risk for chromosomal abnormalities as are situations where a couple already have a child with such a disorder. These facts were correctly recognised by 99% (123) and 90% (111) of GPs indicating that knowledge in this area was good. Chromosomal abnormalities are not associated with increasing paternal age, a fact recognised by 91 (73%) GPs. More uncertainty was seen about the statement regarding "balanced translocations". Here, 59 (47%) were unsure of the answer and 16 (13%) chose the statement to be false.

3.2.5. Genetic Epidemiology

3.2.5.1 Cystic fibrosis (Question C19)

Cystic fibrosis is a severe disorder, which has an autosomal recessive mode of inheritance. It has a high prevalence amongst the Caucasoid population of South Africa with a carrier frequency of approximately 1 in 23 (Goldman *et al*, 1994). A number of studies investigating GPs' knowledge regarding cystic fibrosis have been done. Firth and Lindenbaum (1992) sent postal questionnaires to clinicians in the UK to research knowledge and attitudes towards prenatal diagnosis of single gene disorders. They found that only 41% of GPs were aware that prenatal diagnosis was available for cystic fibrosis. Julian *et al* (1996) showed that approximately 20% of GPs were unaware that carrier status for cystic fibrosis in both parents was an indication for prenatal diagnosis. Patients affected by such a disorder need to be made aware of carrier testing and options for prenatal diagnosis. A study by Rona *et al* (1994) indicates that most patients intended to make use of such options once they were made aware of them.

Question 19 of the questionnaire aimed to assess whether GPs knew the carrier frequency of cystic fibrosis amongst Caucasoid individuals. The results are shown in Figure 3.1

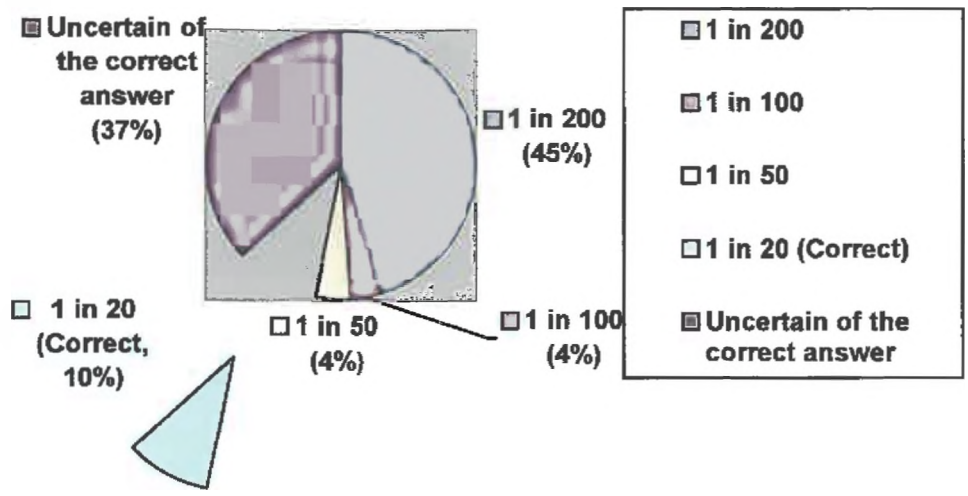

Figure 3.1 Responses regarding the carrier frequency of cystic fibrosis in white South Africans (n=124)

Here, 13 (10%) of GPs knew the correct carrier frequency. Other carrier frequencies were chosen by 65 (53%) and 46 (37%) GPs were uncertain of the correct answer. Boulton and Williamson (1995) posed a similar question amongst GPs in London and found that 44% did not know the carrier frequency.

In Section 3.1.9.4, the ethnicity of patients that GPs in this study encountered was discussed. Seventy-two GPs (58%) stated that over 50% of their patients were white. Of these 72 GPs, 7 (10%) identified the correct carrier frequency of cystic fibrosis.

As shown above, knowledge of the cystic fibrosis carrier frequency could potentially be relevant to a number of GPs. Although it may not be imperative than an exact figure is known (for a carrier frequency of a disorder) in order to be able to offer assistance, it is perhaps important that they be aware of a range within which the frequency might be. It

is also important to bear in mind that as exact frequencies were offered for GPs to chose from, some may have opted for 'uncertain of the correct answer' if the value they thought of did not exactly match one of the options provided (even if their answer could have been close to one of these). This could potentially affect the results obtained and this should be taken into account.

3.2.5.2 Albinism (Question C20)

The black population of South Africa has a relatively high frequency of oculocutaneous albinism (Kromberg and Jenkins, 1982). This disorder has an autosomal recessive pattern of inheritance and has a prevalence of approximately 1 in 3900 births and a carrier frequency of approximately 1 in 33 (Kromberg and Jenkins, 1982; Stevens *et al*, 1997). Question 20 attempted to ascertain if GPs knew this. Carrier frequencies were shown and GPs had to choose the correct value. The results of this question are illustrated in Figure 3.2 and show that 58% of GPs were 'unsure of the correct answer', 1% chose the correct option of '1 in 30' and 41% chose one of the other frequencies shown.

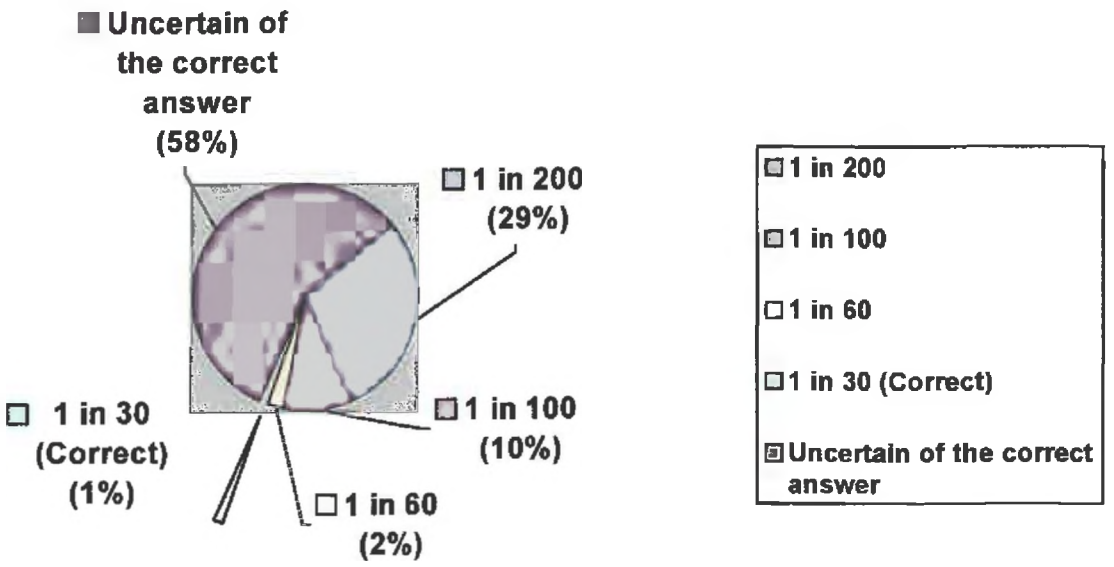

Figure 3.2 Responses regarding the carrier frequency of albinism in black South Africans (n=124)

These results may be of potential significance. The majority of the South African population is black and albinism is a serious disorder that can cause visual impairment and an extreme sensitivity to the sun, which predisposes affected individuals to skin cancer (Kromberg *et al*, 1989b). It also has major emotional ramifications for both the individuals and families involved, as there is much stigmatisation of individuals with albinism amongst communities (Kromberg *et al*, 1987; Kromberg, 1992). In this study, 52 (48%) GPs stated that over 50% of their patients were black. Of these 52 GPs, 5 (9.6%) chose the correct carrier frequency.

As stated earlier regarding the carrier frequency of albinism, although it may not be imperative than an exact figure is known (for a carrier frequency of a disorder) in order to be able to offer assistance, it is perhaps important that they be aware of a range within which the frequency might be. It is also important to bear in mind that as exact frequencies were offered for GPs to chose from, some may have opted for 'uncertain of

the correct answer' if the value they thought of did not exactly match one of the options provided (even if their answer could have been close to one of these). This could potentially affect the results obtained and this should be taken into account.

As with most autosomal recessive disorders there is usually no positive family history, so it may be important that GPs be aware of the fact that carrier frequencies may be high in certain population groups. As there is as yet no cure for either cystic fibrosis or albinism, there is a need for these disorders be prevented where possible. In the South African situation, it may not be possible to offer screening and referrals in many cases. This would be extremely costly and time consuming. However, in the future this situation could change. Primary health care practitioners would then need to become aware of the risks of these common disorders amongst the populations they treat so that appropriate tests and referrals could be made if necessary. Intervention such as genetic counseling, carrier testing, prenatal testing and selective abortion if chosen may assist in the prevention of these disorders (Kromberg and Jenkins, 1995).

3.2.5.3 Tay-Sachs disease (Question C21)

Tay-Sachs disease is characterised by a deficiency in hexosaminidase isoenzyme A. The Ashkenazi Jewish population is at increased risk for this disease with an incidence of 1 in 2000 births expected in South Africa (Lane *et al*, 1985). The fact that this population group was at high risk for Tay-Sachs was known by 81% (100) of GPs. One individual

believed it to be common in individuals originating from Greece and Cyprus (0.8%) and the rest (18.2%) were 'uncertain of the correct answer'.

3.2.5.4 Thalassaemia in the Greek population (Question C22)

Question 22 aimed to determine whether GPs knew that Greek individuals are at higher risk for haemoglobinopathies such as alpha and beta thalassaemia. The results are shown in Table 3.25.

Table 3.25 Responses regarding screening advice to a Greek couple

Genetic disorder	Yes*	No*	Unsure
Alpha thalassaemia	**70 (56%)**	24 (20%)	30 (24%)
Beta thalassaemia	**99 (79%)**	2 (2%)	23 (19%)
Porphyria variegata	8 (6%)	**78 (63%)**	38 (31%)
Albinism	0	**92 (74%)**	32 (26%)
Fanconi anaemia	28 (23%)	**39 (31%)**	57 (46%)
Myotonic dystrophy	5 (4%)	**63 (51%)**	56 (45%)

*The numbers in bold indicate the correct answers

As can be seen, 79% (99) of GPs correctly chose beta thalassaemia and a further 56% (70) felt that alpha thalassaemia screening should also be offered. The rest of the conditions presented are not more commonly found in the Greek population. An interesting result observed however is that whilst the majority of GPs correctly chose not to screen for these disorders, 23% (28) believed that such a Greek couple should be screened for Fanconi anaemia. This disorder is more prevalent amongst the Ashkenazi

Jewish (Auerbach, 1997) and Afrikaner community (Rosendorff *et al*, 1987) and it is uncertain as to why this perception is present.

3.2.5.5 Birth defects (Question C23)

It is also important for GPs to be aware of how often birth defects occur amongst the general population, as patients need to be advised of possible risks and may need to receive counselling. Certain defects can be detected early in pregnancy and sometimes even prevented (periconceptual folic acid may reduce neural tube defects (Hall and Solehdin, 1998). Congenital birth defects, mild and severe, are present in about 4-5% of all live births in South Africa (Kromberg and Jenkins, 1995). Major congenital defects are present in approximately 3% of neonates (Meuller and Young, 1998). A study by Delport *et al* (1995) showed that the incidence of congenital anomalies in black neonates is as high as in other countries, with some individual congenital anomalies being higher. Knowledge of the frequency of such anomalies may aid doctors (who are often seen to be primary source of medical information) in offering advice to patients and make them more aware of certain risks (Tan *et al*, 1994).

As shown in Figure 3.3, 45% (56) of GPs were aware of this statistic. About 23% (29) underestimated this risk, 4% (5) overestimated this risk and 28% (34) chose the option 'uncertain of the correct answer'.

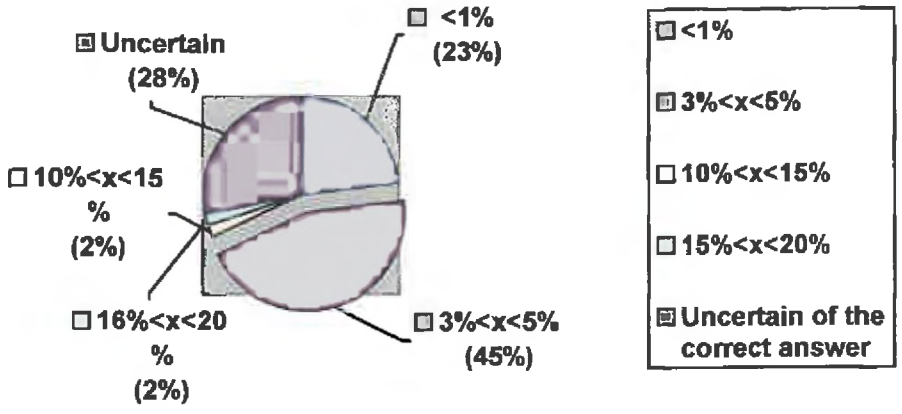

Figure 3.3 Responses regarding the frequency of major birth defects in South Africa (n=124)

It is important to bear in mind that in this question, as exact frequencies were offered for GPs to chose from, some may have opted for 'uncertain of the correct answer' if the value they thought of did not exactly match one of the options provided (even if their answer could have been close to one of these). This could potentially affect the results obtained and this should be taken into account.

3.2.6 Teratogens

3.2.6.1 Infectious agents and drugs (Questions C26 and C27)

Both infectious agents and drugs, which act as teratogens, were examined. The responses were as follows (Table 3.26):

Table 3.26 Knowledge regarding agents that pose risks of teratogenesis

Teratogenic agent	Yes*	No*	Unsure
Infectious Agent			
Syphilis	**98 (79%)**	20 (16%)	6 (5%)
Rubella	**123 (99%)**	1 (1%)	0
Cytomegalovirus	**108 (87%)**	10 (8%)	6 (5%)
Toxoplasmosis	**108 (87%)**	6 (5%)	10 (8%)
Influenza	7 (6%)	**105 (85%)**	12 (9%)
Adenovirus	9 (7%)	**92 (74%)**	23 (19%)
Drug			
Warfarin	**81 (65%)**	32 (26%)	11 (9%)
Valproic acid	**64 (52%)**	23 (19%)	40 (29%)
Retinoids	**122 (98%)**	0 (0%)	2 (2%)
Paracetamol	0	**122 (98%)**	2 (2%)
Tricyclic antidepressants	26 (21%)	**56 (45%)**	42 (34%)
Antimalarials e.g. chloroquine	**73 (59%)**	35 (28%)	16 (13%)
Lithium	**77 (62%)**	11 (9%)	36 (29%)

*The numbers in bold indicate the correct answers

Overall, knowledge in this section of the questionnaire was higher than in other sections. Syphilis, Rubella, cytomegalovirus and toxoplasmosis were correctly identified as teratogenic by 79%, 99%, 87%, and 87% respectively. Influenza and adenovirus were correctly identified as not being teratogenic by 85% and 74% of GPs respectively. Of the drugs listed, 65% (81) of GPs were correct about the threat of warfarin. The remaining 26% (32) were incorrect and 9% (11) were unsure. For valproic acid, 52% (64) correctly identified that it may be teratogenic (valproic acid which is known to increase the risks of neural tube defects and other abnormalities if taken during pregnancy (Aulthouse and Hitt, 1994)). The remaining 19% (23) felt it was not teratogenic and 29% (40) were unsure.

All but two GPs (98%) recognized retinoids as a teratogen. The same was found regarding paracetomol in that 98% correctly chose it not to be teratogenic. More doubt seemed to exist however regarding the teratogenicity of tricyclic antidepressants and

lithium. Here, 45% (56) of GPs got the question correct, 21% (26) chose the incorrect option and 34% (42) were unsure. For antimalarial drugs such as chloroquine, 59% (73) correctly agreed that these drugs may be teratogenic, but 28% (35) were incorrect and 13% (16) were unsure. In fact, these drugs may cause chorioretinitis and deafness in the child if administered in therapeutic doses during pregnancy (Meuller and Young, 1998). In retrospect though, this statement was ambiguous as it was not specified whether these antimalarial drugs were in therapeutic or prophylactic doses. This may have influenced the way in which this statement was responded to.

This area is one where GPs' knowledge is important to ensure proper medical care. Knowledge about drugs in pregnancy and of the risks certain infections may pose, are part of the everyday care of patients. A lack of knowledge in this area threatens the quality of this care. Doctors often prescribe antimalarials, antidepressants and anti-epileptics. It is thus important that they are aware of the effects such drugs can have on a developing fetus so that patients are not put at increased risk during pregnancy. It is vital that patients are advised correctly and referred for specialist help should a potentially teratogenic infection develop during pregnancy.

3.2.6.2 Fetal Alcohol Syndrome (FAS) (Question C28)

Fetal Alcohol Syndrome is caused by mothers who consume alcohol during pregnancy. Children with FAS have a distinctive facial appearance (which includes a long smooth philtrum and short palpebral fissures). Developmental delay, microcephaly and growth retardation are also common findings (Smith and Jones, 1997). In South Africa, the

frequency of FAS is one of the highest in the world, especially amongst those who live in the Western Cape (Croxford and Viljoen, 1999). Question 28 asked GPs to identify the correct physical findings that one would see in a child with FAS and Table 3.27 shows their responses.

Table 3.27 Responses to identifying features of FAS

Physical feature	Yes*	No*	Unsure
Short palpebral fissures	**91 (73%)**	5 (4%)	28 (23%)
Long smooth philtrum	**80 (65%)**	8 (6%)	36 (29%)
Developmental delay	**119 (96%)**	0%	5 (4%)
Normal growth parameters	14 (12%)	**96 (76%)**	14 (12%)
Polydactyly	21 (17%)	**70 (56%)**	33 (27%)

*The numbers in bold indicate the correct answers

For each statement, the majority of GPs chose the correct one indicating that most GPs know about FAS. An interesting finding was that polydactyly was thought to occur by 17% (21) of GPs and 27% (33) of them were unsure.

A syndrome such as FAS is completely preventable if mothers refrain from consuming alcohol whilst they are pregnant and this fact needs to be well known amongst the public and medical communities. GPs need to be able to recognise children who have FAS so that they can be managed properly and perhaps FAS can be prevented in subsequent pregnancies by educating the mother.

3.2.7 Differences between postal and interview GP responses in Sections C

In this section, any significant statistical differences found in the responses between the postal and interview group are listed. To make this section clearer, I have tabulated the results. Within the table I have stated the question number, which part of the question is involved (for example if the option was for 100% or 'true' etc), listed the number of postal or interview responses and stated the 'p' value if a significant difference was found. The chi-squared test was utilized with p values less that 0.05 denoting significance. Where there was one degree of freedom, Yates correction was implemented to increase accuracy. It is important to note that 51 GPs were interviewed and 73 returned the questionnaire by post. All these factors were considered when calculating significance.

Table 3.28 Significant differences between postal and interview responses

Question Number and option	Number of responses by those interviewed n=51	Number of responses by those who responded by post n=73	Total No. of responses n=124	X^2	Probability (p)
Question 5, option of '100%'	1	10	11	4.02	0.055
Question 12E option of 'true'	7	32	39	7.64	0.005
Question 14B, option of 'true'	12	6	18	6.02	0.014
Question 26E, option of 'no'	8	4	12	4.41	0.036

As can be seen there were relatively few significant differences found between the two groups. A point to note is that as shown above, significance occurred if the total number

of GPs who chose an option was low. In other words the sample size was very small. Here, differences found then between the 'interview' and 'postal' GPs who chose these options had greater impact although in reality this must be considered when considering the difference.

This was highlighted even further as in some questions there was a total of just one response for an option of a question. This meant that, for example, if that response was from a GP in the 'interview' group, there was no (or zero) corresponding value for the 'postal' group. As there are more GPs in the 'postal' group than the 'interview' group, a total of '1' for the interview group and '0' for the postal group for an option of a question is significantly different (it is not so for the reverse scenario however). In reality, as this is based on just one GP response, there is little value in a result from such a small sample. The situation in which an option of a question had just one response (and this was chosen by a GP in the 'interview' group) occurred in only two scenarios and I have mentioned them for completeness:

In Question 20, one 'interview' GP chose the option of '1 in 30' and in Question 25 one 'interview' GP chose 'Multifactorial' as an inheritance mode for Haemophila A.

3.3 Results of Genetic Counselling Investigation (Section D)

Genetic counselling (see section 1.3.5.) and the knowledge and opinions GPs have of the process (as a general part of medical care and in a formal capacity at Genetic Counselling Clinics), were investigated in Section D of the questionnaire. The aim (by means of a

series of multiple choice and open-ended questions) was to assess how GPs perceive genetic counselling fitting into the realm of general medical care and how frequently it is utilized or deemed necessary by GPs. Formal genetic counselling has been available to small numbers of patients in South Africa since the 1950's (Jenkins, 1990) but began to be more broadly offered in the 1980's by which time approximately 2000 families were being seen annually (Kromberg and Jenkins, 1995).

3.3.1 Previous knowledge of genetic counselling (Question D1)

When GPs were asked if they had heard of genetic counselling before all but one GP had. The majority 84% (103) had first heard of it at least five years ago, 12% (15) within the last two to five years and the remaining 4%(5) had heard of it between one and two years ago. The majority of GPs had heard of genetic counselling whilst at medical school (66%, 82), some heard of it from their colleagues (21%, 26), a few from conferences and/or seminars (3%, 4), or read about it in pamphlets (2%, 2). The remaining 8% (10) had read about genetic counselling in various medical journals.

3.3.2 Understanding of genetic counselling (Question D2)

An open-ended question was asked to ascertain whether GPs understood what genetic counselling was. It is important to note that respondents only had a short space (two and a half lines) to comment regarding this. This then means that we are perhaps only getting a

limited perspective of their comments regarding this question. The results of the responses obtained however were grouped according to common themes that arose when the answers were looked at. Each GP's answer was carefully looked at and analysed to see which themes were present in their responses. They were then assigned and listed accordingly (some answers contained more than one theme). The results are displayed in the table below:

Table 3.29 Interpretation of GPs' understanding of genetic counselling (n=124)

Response categories	**No. of GPs who mentioned this category**	**% of GPs who mentioned this category**
1) Discussing and ascertaining risks of genetic disorders	90	73
2) Discussing risks of recurrence	24	19
2) Screening and offering of tests	51	41
3) Explaining of medical facts – educating about genetic facts	26	21
4) Discussing the prognosis of the disorder and the potential management	9	7
6) Discussing options available to patients	12	10
7) Assistance with emotional adjustment	6	5
8) Discussing genetic matters (and potentially investigating these) with parents before they plan a family	19	15

As the above table shows, the most commonly mentioned response-based theme pertained to assessing risk. Risk themes pertaining to ascertaining risks in a general sense and also to ascertaining in scenarios where a family may have already had a child or relative with a disorder (recurrence) were mentioned. Other themes that came up related to offering testing and screening; discussing and educating patients about genetic

situations; discussing prognosis and the potential management of genetic disorders and discussing options that may be available to patients. Six GPs mentioned that genetic counselling might be a source of emotional support. This is relevant as genetic counselling has become recognised for its psychological and psychosocial component (Borreani and Gangeri, 1996). Nineteen (15%) of GPs mentioned that genetic counselling should ideally be performed before couples start a family. As there was limited space, responses which included this theme were often not put into context however counselling before starting a family may be beneficial if a genetic disorder was known to exist in the family, or if a pregnancy would be at potential risk (for example if the mother was taking medication). This may assist and educate parents so that they are aware of certain potential scenarios and risks.

3.3.3 Referrals for genetic counselling (Question D3)

Of the 124 GPs participating in this study, 53 (43%) had previously referred a patient for genetic counselling. The most common reason for referring a patient was Down syndrome. Amongst the other referrals were Turner syndrome (3), Tay-Sachs disease (7), albinism or thalassaemia carrier testing (8). The number of GPs who made the appointment on behalf of the patient was 23 (43%), whilst 11 (21%) provided the patient with the relevant telephone numbers for them to make their own appointment, 4 (8%) referred them to the nearest provincial hospital for genetic counselling and the remaining 3 (6%) asked their secretaries to make the appointment.

3.3.4 Opinions regarding genetic counselling (Question D4, D5, D6)

GPs were asked questions about their opinions regarding aspects of genetic counselling in the context of general practice.

3.3.4.1 The importance of genetic counselling in general practice (Question D4)

This first question asked whether GPs felt that genetic counselling was an important facet of health care in general practice. The majority (115 or 93%) answered "yes". They were then asked to comment about this and these comments were grouped into eight response-based categories/themes in order to analyse them. Table 3.30 shows these categories and the number of GPs who commented in these ways.

Table 3.30 Comments made by GPs who agreed that genetic counselling is an important facet of health care in general practice (n=124)

Response categories	No. of GPs who mentioned this	% of GPs who mentioned this
1) It is important for prevention, screening and detection & management	35	30
2) It is important for patient information	11	10
3) It is an essential part of complete patient care	19	17
4) It is important for emotional support and preparedness	5	4
5) It aids parents in making informed decisions	5	4
6) Is important in primary care, but mostly dealt with by specialists	6	5
7) It is important but rarely used	10	9
8) No comment	31	23

The largest group of GPs (35 or 30%) felt that genetic counselling was important for prevention, screening and management (1). One GP said "We deal directly with families and are thus in an ideal position to identify and prevent problems". Another GP said, "A GP has an ideal position to pick up a family history and prevent repeat occurrences of

genetic abnormalities". This indicates this GP's willingness to be an integral part of the genetic counselling process. Another quote frequently given was "prevention is better than cure"

In category (6), 5% of GPs who felt that it was important in general practice but mainly referred to specialists. Some comments like "It is important, but GPs don't know enough to make this a reality" and "GPs don't know enough about genetics" potentially reveal areas where GPs feel they need to be further educated in genetic matters.

Of the nine GPs who did not think that genetic counselling was an important facet of general care, five did not comment further. Two said that they did not see enough patients who required genetic information to warrant it being an important issue, one said it belonged in the realm of specialists like obstetricians and gynaecologists only and the last commented that genetic counselling should be important, but felt that in reality it was not.

It is reassuring to see that 93% of GPs feel that genetic counseling has a place in general practice. As genetic research continues, technological advances have altered the manner in which certain patients are to be managed and it is important that doctors feel inadequately prepared to deal with such cases when confronted with them. In light of the high percentage of GPs who feel genetic counselling is important, educational programs that will both demonstrate the importance of medical genetics and genetic counselling in a primary health care setting will potentially be well received.

3.3.4.2 Do you think that patients with hereditary disorders would benefit from genetic counselling? (Questions D5)

This question was answered "yes" by all 124 participants. All GPs felt that patients with hereditary disorders would benefit from genetic counselling. Once again, GPs were invited to comment on their choice of answer and these comments were assessed by GPs' responses. These themes and the number of GPs who mentioned them are listed in Table 3.31.

Table 3.31 Comments made by GPs who agreed that genetic counselling is beneficial to patients who have hereditary disorders (n=124)

Response categories	No. of GPs who mentioned this	% of GPs who mentioned this
1) To improve understanding (information regarding management, prognosis & inheritance)	27	22
2) To allow better coping and to deal with emotional issues	11	9
3) For screening, prevention and awareness	16	13
4) To aid informed decision making	19	15
5) No comment	50	41

Although fifty (41%) of GPs did not comment on this question (it was not obligatory), a large number of GPs mentioned opinions, which fell into category (1). Comments such as "forewarned is forearmed" were among many which stressed the benefits of being informed and thus leading to educated decision making (4). Although, the emotional side was not stressed as frequently as the educational side, 11 (9%) indicated that emotional distress surrounding genetic issues may be assisted with. Phrases such as "alleviate guilt", "cope better", "massive emotional impact" and "put their mind at ease" all reflect this. Two GPs stated that although genetic counselling is indeed beneficial, GPs are not experienced enough or knowledgeable enough to provide this

3.3.4.3 Should all hereditary disorders be dealt with at a genetic counselling facility? (Questions D6)

This question was aimed at getting an idea of how GPs perceived genetic counselling as fitting into general practice. Of 124 GPs, 83 (67%) chose "yes" whilst 41 (33%) chose "no" to the question posed.

In reality, matters may not be as 'black and white' regarding the management and care of patients. It may not be as simple as a 'yes' or a 'no'. For instance, many doctors use a team approach when managing patients, yet this may not have come across since this question requested that they choose either one or the other. Thus, the design of this question with a 'yes/no' choice followed by a request for comments may not allow us to get an accurate reflection of the real situation. The various comments that were made however were analysed and grouped together based on respondent-based common themes (Table 3.32).

Table 3.32 Comments made by GPs who think hereditary disorders should be dealt with at a genetic counselling facility (n=83)

Response categories	No. of GPs who mentioned this	% of GPs who mentioned this
1) Genetic counselling benefits patients (includes reasons as for Table 3.21)	14	17
2) GPs are not knowledgeable enough in this area	13	16
3) Specialised facilities could serve such patients better	24	28
4) Teamwork-GP and genetic counselling facility should interact	2	3
5) No comment	30	36

Twenty-four GPs (28%) felt that specialists who had specific knowledge and facilities necessary for genetic testing would be the best resource for a patient (3). Comments such as "to provide accurate and precise measurement of all risk factors" and "this is a specialised field which needs knowledgeable people" reflect this. Another comment indicating that GPs would prefer to refer was "This takes the pressure off GPs". When it came to category (2), comments were made such as "GPs are not adequately trained to inform patients", "GPs need to be better skilled to do this", "Most of us know too little to give accurate advice" and "GPs don't know enough about medical genetics in general practice". It seems perhaps that some GPs may not feel comfortable giving genetic advice. GPs, who indicated that this should be a team effort (4), indicated that the genetic counselling facility should deal with the diagnosis and testing, but that GPs could be involved in the patient follow-up. It is thus important to offer further genetic education to GPs who may want to take a more active role in the genetic counselling process.

As seen for question D6, 33% of GPs did not feel that all disorders should be dealt with at a genetic counselling facility. All these respondents commented that GPs should handle the "simpler" disorders whilst only refer the more complex matters. Multifactorial disorders such as diabetes and hypertension were often mentioned as being within the GPs' capabilities. This may be true in some aspects of treatment, but from a genetic point of view, multifactorial disorders are one of the most complex and least understood (Wagstaff, 2000). As we begin to understand more about the genetic components of such

multifactorial disorders however, treatment approaches and management may alter based on new technologies. Therefore geneticists, genetic counselors and GPs may have to incorporate a team approach when dealing with patients with these disorders so as to optimize care.

3.3.5 Knowledge of the nearest genetic counselling facility (Question D7)

Just over half 68 (55%) of GPs knew where the nearest genetic counselling facility was. Of those, 23 (34%) stated that it was at the Transvaal Memorial Institute, indicating that they have not had contact with it for a while as it moved to the South African Institute for Medical Research (SAIMR) in 1998. The remaining 45 (66%) correctly identified the SAIMR, Johannesburg Hospital and Pretoria Academic Hospital. These kind of data are important as they indicate that genetic counselling facilities should perhaps make more effort to advertise themselves so that GPs be made more aware of them and thus make use of them more often. The information sheet distributed after completion of the questionnaire had contact details for the nearest genetic counselling facilities in an attempt to do just this.

3.3.6 Preparedness to participate in the genetic counselling process (Question D8, 9 and 10)

GPs were asked about whether they felt were sufficiently prepared to perform certain tasks which form the basis of the genetic counselling process. A point worthy of note is that there was potential for misinterpretation with the term 'prepared' in the question. Although the intended meaning for this word was 'felt ability' or 'competence' it may have been misinterpreted. For instance some GPs may have thought it meant 'willingness'. This misinterpretation was not encountered during the pilot study, nor was it ever brought up during any of the face-to-face interviews, it must nonetheless be considered. The results are displayed in Table 3.33:

Table 3.33 GPs' preparedness to be able to offer aspects of genetic counselling

Genetic counselling task	Yes	No
1)Take family histories and draw pedigrees	23 (19%)	101 (81%)
2) Counsel patients about genetic risks	9 (8%)	113 (91%)
3) Counsel patients about genetic test results	13 (10%)	111 (90%)

Although there is potential for misinterpretation in the question, the findings here could point to a possibility that the GPs in this study potentially do not feel adequately prepared to provide these activities. Should GPs have felt that the meaning of 'prepared' meant 'willing' then another possibility could be that some GPs felt unwilling to provide these activities. The taking of a family history taking is an invaluable tool in the genetic

counselling process (Rose *et al*, 1999). It allows for inheritance modes to be elucidated and makes clear which individuals may be at risk. A family history may also allow genetic disorders to be prevented or detected (by subsequent testing) before they occur i.e. hereditary cancers (Summerton and Garrood, 1997). Suchard *et al* (1999) performed a study in the United Kingdom, which also investigated GPs' ability to take family histories. They found that only 29% felt prepared enough to do this and 15% of GPs felt prepared enough to counsel patients about genetic test results. Although we cannot directly compare their results to those of this study (the questions were not asked in the same way) we can see that the trend is similar.

3.3.7 GP's responses as to how they would to deal with the emotional consequences of patients (Question D11)

In Question 11 of Section D, a question was posed to GPs enquiring as to how they would deal with the emotional reactions of patients who were either at risk or affected by a genetic disorder. The aim of this question was to get an idea of how GPs would deal with the psychosocial aspects of the genetic counselling process or if they would rather refer to specialists. Answers were varied and included details about how they would counsel the patients themselves or how they would prefer to refer such cases. A few GPs answered this question with adjectives or phrases like "poorly" or "with difficulty", which demonstrated that they perhaps felt poorly equipped to manage patients' emotional needs. Table 3.34 shows the five main response categories that arose from the responses and the number of GPs who responded in these ways.

Table 3.34 GPs' responses to dealing with the emotional consequences of genetic issues (n=124)

GP responses	No of GPs who responded in this way	% of GPs who responded in this way
1) Would refer for psychological assistance	48	39
2) Would counsel themselves	41	33
3) Would counsel themselves but refer if necessary	19	15
4) Would be unable to handle this adequately	7	6
5) No comment	9	7
Total	**124**	**100%**

As shown above, just over one third of GPs (39%) would refer these patients rather than deal with them themselves. Comments such as "Would not feel competent or confident to do this" and "Do not feel qualified to do this" were mentioned. Referrals to psychologists, social workers and genetic counsellors were mentioned.

A further 33% indicated that they would counsel the patients themselves. This group of GPs was very positive about dealing with genetic issues, but indicated that if they did not know all the genetic facts, they would look them up in order to be of more help to the patient. Many GPs also indicated they would respond with empathy and would hold in-depth discussions if necessary.

The third class of responses accounted for 15% and indicated that GPs were willing to start the emotional counselling but would refer if the problem became too complicated or the patients required more qualified emotional support from a social worker or psychologist.

The last group of responses account for 6% and represent GPs who felt inadequately prepared to deal with the emotional consequences. The remaining 7% chose not to comment on this question.

3.4 GPs' interest in attending educational courses (Question D12)

Question 12a dealt with whether or not GPs would be interested in improving their genetic knowledge. Here, approximately 85% (106) of GPs indicated they would be interested in doing so. Question 12b asked about the types of topics these doctors would be interested in. The majority, 56% (69) of GPs, requested basic courses on the most common disorders affecting South Africans. Fifteen (12%) also felt they needed a basic general overview that dealt with basic facts such as that of inheritance modes. The following disorders were specificically mentioned regarding topics that would be of interest: Down syndrome (10 GPs (8%)) and cystic fibrosis (3 GPs (2%)). For thalassaemia, Tay-Sachs disease and hypercholesterolaemia mention was made once for each. Seven (6%) GPs indicated that they would like information regarding a general approach to the management of genetic cases and four (3%) were interested in learning more about counselling.

Question 12c asked which type of event GPs (who were interested in improving their education) preferred. Some GPs chose more than just one option. The table below (Table 3.35) shows the results:

Table 3.35 GPs' response to Question 12c regarding appropriate event to deal n=106

Type of event	No of GPs who chose this option	% of GPs who chose this option (of those that answered 'yes' to Q. 12a) n=106
Lecture	49	46
Seminar	38	36
Individual hands-on instruction	11	10
Distance education course	26	25
Other	3	3

Lectures and seminars were the chosen the most. The next preferred choice was distance education. Twenty-six GPs indicated that they would do a distance education course. Of the three GPs that chose the option of 'other', all stated that they thought and workshop would be appropriate.

For 12d, the most commonly chose day was Wednesday. Here, 36 (34%) GPs chose this day. Saturday (28%, 27 GPs) and Thursday (25%, 30 GPs) were chosen second and third respectively. When asked for the preferred time of day for such a course, most GPs chose the evening (53%, 56 GPs).

Approximately 60% of the GPs interested in a medical genetics course would be willing to pay for it, but many indicated on the questionnaire that the fee would have to be reasonable. Four GPs also suggested by writing on the questionnaire that sponsorship should be obtained to reduce costs.

3.5 Additional data from the face-to-face interviews

Face-to-face interviews were conducted with 51 of the 124 GPs in this study. The aim of these was for me, as a trainee genetic counsellor, to gain experience in interacting with medical professionals and to improve my interpersonal interviewing skills. It was also hoped that by dealing with GPs personally, in-depth comments to questions could be recorded and an awareness of the presence of genetic counselling facilities would be emphasised. The GPs interviewed were asked to complete the questionnaire in my presence. After the questionnaire was given back, there was a discussion about topics raised by the questionnaire.

All but four of the GPs interviewed commented in one form or another about how infrequently a genetic issue arises in their daily practice. All of them were shocked at the high carrier frequencies of common disorders such as cystic fibrosis and albinism. One doctor commented that although she rarely saw genetic cases, it did not mean they were not there and that if one knew what to look for, they would be encountered more frequently. Indeed, as shown in section 3.1.9.5, each GP may encounter at least 33 patients with genetic disorders within their practice. This, in my view, could represent one of the main problems regarding medical genetics in general practice. GPs are perhaps unaware of how prevalent common disorders are and they may thus consider them to be obscure and rare and not often considered as potential causes for illness.

Certain common trends became apparent during these face-to-face interviews. GPs seemed uncomfortable analysing the pedigree in Question C3. Although not explained until after the questionnaire was returned, GPs often asked which symbol represented male and female. Understanding and interpretation of a pedigree is often essential to GPs being able to understand genetic literature and to giving patients accurate information about inheritance modes and risks. Regarding dynamic/unstable mutations, only one GP that the researcher interviewed had heard of them before and this was in the United Kingdom whilst training in paediatrics. Other GPs, whilst expressing that they had not heard of this type of genetic finding before, either stated that they were unsure or took educated guesses. This perhaps emphasises a delay in information reaching GPs. Another poorly understood concept was that of balanced translocations mentioned in Question C18(d). The majority of GPs did not understand this concept whilst completing the questionnaire and it was thus explained to them afterwards. Translocations need to be understood as they play a role in multiple miscarriages and patients need to be aware of the high risks of recurrence and of fetal anomalies should a balanced translocation exist in a parent.

Most GPs I encountered were extremely interested in medical genetics but voiced their feelings of not being well equipped with genetic knowledge. All GPs seemed extremely interested in reading the genetic information sheet I handed to them at the end of each interview. Five GPs requested additional information on triplet repeat expansions; one requested information on Poland's syndrome and one on Williams's syndrome. Since

completing these interviews, at least two referrals have been made by GPs I interviewed to the Genetic Counselling Clinic at the SAIMR. The first involved a case of suspected Down syndrome and the second dealt with carrier status for X-linked agammaglobulinaemia.

3.6 Differences between postal and interview GP responses in Section D

All questions and options were looked at, including responses categorized into respondent-based themes to see if there was any significant difference between the number of responses in the postal and interview groups. The chi-squared test was utilized with p values less that 0.05 denoting significance. As there was one degree of freedom, Yates correction was implemented to increase accuracy. It is important to note that 51 GPs were interviewed and 73 returned the questionnaire by post. All these factors were considered when calculating significance.

Only one area of significant difference was noted. This involved the last question of the questionnaire, Question 12f. Here, there was a significant difference noted between the postal and interview groups when asked if they would be prepared to pay for a course. Here, out of a total of 70 GPs who chose 'Yes' for this option, 40 GPs were in the interview group and 30 were in the postal group. The difference between these groups for this option was significant ($p=0.004$). There could be a number of reasons for this. One could be that the sample could perhaps be biased in that by agreeing to participate in an interview and give up their time for a face-to-face interview, a GP in this group may have

had an existing interest in genetic concepts and thus be more willing to spend money to improve on their knowledge in this area. Another could be that as there was interaction and discussion with the GPs in the interview group after the questionnaire was answered this could also have encouraged a GP to be interested in the subject matter and this could potentially make them feel more likely to spend money on a course. Yet another possibility is that as interviews were conducted in areas which would have been convenient to the researcher (mainly the Northern suburbs which may be considered more affluent), such GPs may potentially be more able to afford to pay for a course.

APPENDIX A

Letter of Introduction

The South African Institute for Medical Research
University of the Witwatersrand, Johannesburg

SCHOOL OF PATHOLOGY
Department of Human Genetics

Hospital Street, Johannesburg 2001. PO Box 1038, Johannesburg 2000.
Telephone: +27-11-489-9000. Telefax: +27-11-489-9226 or +27-11-489-9209

Professor D Viljoen	489-9239	Dr TJL de Ravel	489-9212	Dr H Soodyall	489-9208
Professor M Ramsay	489-9214	Dr A Krause	489-9219	Dr AB Lane	489-9221

Dear Doctor

My name is Kelly Trenton and I am a postgraduate student currently undertaking a Masters degree course in Genetic Counselling. This degree is offered by the Human Genetics Department of the University of the Witwatersrand at the South African Institute for Medical Research. I am conducting a research project for my second year of study to investigate the knowledge and opinions of general practitioners (GPs) in the field of Human Genetics and Genetic Counselling. I would appreciate it if you could fill in a questionnaire, which addresses these issues and return it to me as soon as possible.

It is hoped that this study will provide a clearer picture regarding the level of genetic knowledge of GPs so that more effective genetic training programs and services may be implemented. Little research data are currently available in this area of study and your participation would be greatly appreciated. Upon completion of the questionnaire (which will take about 45 minutes) and its return, model answers of the study will be forwarded to you. **If you complete this questionnaire you will be eligible for 1 CPD point in the self-study category.** The CPD certificate will be sent to you along with the model answers after the completed questionnaire has been received. **Please use the self-addressed envelope provided to return the questionnaire.**

Participation is entirely voluntary and you are under no obligation to complete the questionnaire. Should you choose to participate however, I would request that your answers be as candid as possible to ensure that the results represent a true reflection of the current standard of genetic understanding and practice. Your participation in this study will be treated with the utmost **discretion and confidentiality**. The first section containing your personal details is for the purpose of CPD accreditation only and will be analysed separately from the rest of your answer sheet. If you are willing to take part, please sign the attached consent form and return it with the completed questionnaire.

Should you have any questions regarding this study please contact Kelly Trenton, (011) 489-9236. Should you wish to refer a patient for Genetic Counselling please contact (011) 489-9223/4.

Your help in this study is most appreciated.

Thank you

KTrenton

Kelly Trenton (Miss)
MSc (Med) student

This organisation rejects racism and racial segregation. It is committed to non-discrimination, particularly in the constitution of its student body, in the selection and promotion of its staff, and in its administration.

The South African Institute for Medical Research
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rofessor D Viljoen	489-9239	Dr TJL de Ravel	489-9212	Dr H Soodyall	489-9208
Professor M Ramsay	489-9214	Dr A Krause	489-9219	Dr AB Lane	489-9221

Informed Consent Form

Questionnaire No..... (for official use only)

I, ...(name) hereby give consent to participate in this study which involves the completion of a questionnaire that will investigate my attitudes and knowledge in the field of Human Genetics and Genetic Counselling.

Signature.....
Date.....

tion rejects racism and racial segregation. It is committed to non-discrimination, particularly in the constitution of its student body, in the selection and promotion of its staff, and in its administration.

APPENDIX B

Questionnaire

Questionnaire No._____

Genetic Knowledge, Opinions and Practices amongst General Practitioners

A. PERSONAL DETAILS (please tick where appropriate)

This questionnaire is for research purposes only and will be treated confidentially and analysed anonymously. In order for us to allocate a CPD point to you however, we require that certain details be provided.

1) Title: _____

2) Surname: _____

3) First Name (s): _____

4) Sex: ☐ **Male** ☐ **Female**

5) Date of Birth: ____/____/____ **(YYYY/MM/DD)**

6) Postal Address: _____

_____

_____

7) Physical Address: _____

_____

8) TELEPHONE NUMBER: (W): (___)_____

(H): (___)_____

(FAX): (___)_____

9) E-Mail address: _____

10) Health Profession's Council of South Africa No: _____

Questionnaire No._____

B) YOU AND YOUR PRACTICE

The following section will give us an idea as to the type of environment you are working in and the patients with whom you come into contact. Please complete the following, using ticks where necessary.

1) What are your professional qualifications?

_____

2) Which university did you attend? _____

3) When did you complete your studies? _____

4) During your medical training were you exposed to the teachings of Human Genetics?
☐ Yes ☐ No

5) If answered Yes to the previous question, please specify the year of your study in which this took place, how many years ago this was and the duration of the course(s). Please also state whether this course was of a formal or an informal nature.

Degree	Year of medical training e.g. 3rd year	Year course took place e.g. 1992	Duration of the course in hours e.g. 1 hour a day for 6 weeks	Formal (F)or informal (I) training

6) If answered Yes to question 4, did you feel that this training was adequate at the time? ☐ Yes ☐ No

7) How do you feel now? Please comment on your answer

_____

_____

_____

_____

_____

8) How long have you been practicing as a General Practitioner? _____years

Q. No._____

9) Are you currently working in:

☐ Private practice
☐ Hospital/clinic practice
☐ Both
☐ Other (specify) _____

10) Approximately how many patients are you responsible for?
At your practice: _____
Per day: _____
Annually: _____

11) What is the average time allowed for each consultation?

☐ <5 mins ☐ 5-10mins ☐ 10-15mins
☐ 15-20mins ☐ >20mins

12a) Is antenatal care provided within your practice? ☐ Yes ☐ No

12b) If Yes, until what stage of pregnancy is this care usually provided? _____

13a) Do you charge medical aid rates? ☐ Yes ☐ No

13b) If No, what rates apply? _____

14) Do patients need to schedule appointments to see you? ☐ Yes ☐ No

15) What proportion of your patients have medical aid?

☐ 0-5% ☐ 5-10% ☐ 10-25%
☐ 25-50% ☐ 50-75% ☐ 75-100%

16) Do your medical aid patients need to pay cash and claim back? ☐ Yes ☐ No

17)If a patient has no medical aid are they required to pay cash up front or can an account be sent?

☐ Up front payment ☐ Account basis payment

Q. No._____

18)What age group do the majority of your patients belong to? Please state the approximate percentage in each case.

- 0-10 years _____%
- 10-20 years _____%
- 20-40 years _____%
- 40-60 years _____%
- >60 years _____%

19) What is the approximate ethnic composition of the patients belonging to your practice?

White _____%
Black _____%
Indian _____%
Coloured _____%
Other (specify) _____ _____%

20) Do any of your patients have the following genetic disorders? If the answer is yes, please specify the approximate number of these patients in the column provided.

GENETIC DISORDER	NUMBER OF PATIENTS
☐ Albinism	_____
☐ Cystic fibrosis	_____
☐ Haemophilia	_____
☐ Cleft palate /cleft lip and palate	_____
☐ Neural tube defects	_____
☐ Porphyria variegata	_____
☐ Familial hypercholesterolaemia	_____
☐ Down syndrome	_____
☐ Myotonic dystrophy	_____
☐ Duchenne muscular dystrophy	_____
☐ Genetic or congenital deafness	_____
☐ Genetic or congenital blindness	_____
☐ Genetic mental retardation	_____
☐ Other (specify)	_____

Q. No._____

C. GENETIC KNOWLEDGE ASSESSMENT

This section asks questions regarding certain genetic facts. Please answer the questions by ticking the correct answers or answering in written form where appropriate. More than one answer may be correct.

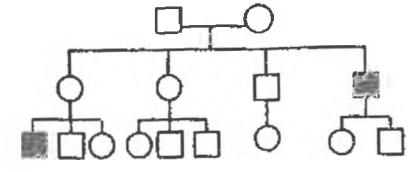
MENDELIAN

1) In autosomal dominant inheritance if either parent is affected by a genetic disorder the chance of one of the offspring also having this disorder is:
   - ☐ Close to 0%
   - ☐ 25%
   - ☐ 50%
   - ☐ 100%
   - ☐ Uncertain of the correct answer

2) In autosomal dominant disorders:

a) Different individuals vary greatly in their clinical symptoms	True ____ False____ Unsure ___
b) New mutations may be the cause	True ____ False____ Unsure ___
c) Males and females are affected equally	True ____ False____ Unsure ___

3) The pedigree below, best illustrates which mode of inheritance?



- ☐ X-linked dominant
- ☐ X-linked recessive
- ☐ Autosomal dominant
- ☐ Autosomal recessive
- ☐ Uncertain of the correct answer

Q. No._____

4) In X-linked recessive disorders:

a) The disorder may often arise owing to a new mutation (30-50% of the time)	True ____ False____ Unsure ___
b) The disorder usually only manifests in males	True ____ False____ Unsure ___
c) An affected male may pass on the disorder to his sons	True ____ False____ Unsure ___
d) All daughters of an affected male are carriers of the disorder	True ____ False____ Unsure ___
e) Carrier females have a 50% chance of passing the disorder on to their sons	True ____ False____ Unsure ___

5) If both parents carry a mutation for a gene that has an autosomal recessive pattern of inheritance, their offspring has the following risk of inheriting the disorder:

- ☐ 0%
- ☐ 25%
- ☐ 50%
- ☐ 100%
- ☐ Uncertain of the correct answer

6) Autosomal recessive disorders display the following characteristics:

a) A positive family history is almost always present	True ____ False____ Unsure ___
b) They are more common in children of consanguineous (related) parents	True ____ False____ Unsure ___
c) Males and females are equally affected	True ____ False____ Unsure ___

7) Multifactorial disorders are:

- ☐ Usually single gene disorders
- ☐ Caused by abnormal genes only
- ☐ Caused by teratogens only
- ☐ Caused by both genetic and environmental factors
- ☐ Uncertain of the correct answer

Q. No._____

8) Disorders characterised by dynamic/unstable mutations such as those involving triplet repeat expansions:

a) May display marked variability in the clinical severity between individuals	True ____ False____ Unsure ___
b) May show an earlier onset of the disease in the offspring than in the parents	True ____ False____ Unsure ___
c) All display autosomal dominant inheritance	True ____ False____ Unsure ___
d) Show a disease severity that may be influenced by the sex of the transmitting parent	True ____ False____ Unsure ___

<u>ANEUPLOIDY (Numerical chromosome abnormalities)</u>

9) A typical laboratory report of a female child with Down syndrome would be summarised as follows:

- ☐ 47 chromosomes, XY, + 21
- ☐ 47 chromosomes, XX, + 13
- ☐ 47 chromosomes, XX, + 21
- ☐ 21 chromosomes, XX
- ☐ Uncertain of the correct answer

10) A child with Down syndrome may typically present with the following:

a) cleft lip and palate	True ____ False____ Unsure ___
b) epicanthic folds	True ____ False____ Unsure ___
c) polydactyly	True ____ False____ Unsure ___
d) mental retardation	True ____ False____ Unsure ___
e) cardiac defect	True ____ False____ Unsure ___

11) The frequency of liveborn babies with Down syndrome in South Africa :

- ☐ Is approximately 1 in 700
- ☐ Is greater in white populations
- ☐ Varies greatly from area to area
- ☐ Is lower in South Africa than First World countries
- ☐ Uncertain of the correct answer(s)

Q. No._____

12) Frequent observations in individuals with Turner Syndrome include:

a) Mental retardation	True ____ False____ Unsure ___
b) A missing X chromosome	True ____ False____ Unsure ___
c) Normal stature	True ____ False____ Unsure ___
d) Normal secondary sexual characteristics	True ____ False_ __ Unsure ___
e) Oedema at birth	True ____ False____ Unsure ___
f) Cardiac defect	True ____ False____ Unsure ___

PRENATAL DIAGNOSIS

13) The maternal serum triple test (maternal serum alpha-fetoprotein (AFP), hCG and oestriol) will detect the following percentage of pregnancies in which the fetus has Down syndrome:

- ☐ 20%
- ☐ 60%
- ☐ 80%
- ☐ 100%
- ☐ Uncertain of the correct answer

14) The maternal serum triple screen test:

a) Has a false positive rate of 5%	True ____ False____ Unsure ___
b) Is a diagnostic laboratory test	True ____ False____ Unsure ___
c) May identify high risk fetuses with other congenital abnormalities	True ____ False____ Unsure ___
d) When positive, identifies fetuses which have a higher risk of having Down syndrome	True ____ False____ Unsure ___
e) Is administered at 10 weeks of pregnancy	True ____ False____ Unsure ___

Q. No._____

15) Significantly increased maternal serum alpha-fetoprotein (AFP) levels are associated with open neural tube defects in the following percentage of pregnancies:

- ☐ 20%
- ☐ 60%
- ☐ 80%
- ☐ 100%
- ☐ Uncertain of the correct answer

16) A 22 year old woman who is 10 weeks pregnant has requested prenatal genetic testing as soon as possible as she has just discovered that a genetic disorder (for which genetic testing is possible by DNA analysis) is being transmitted in her family. For religious reasons, the sooner a diagnosis can be made and action taken, the better. You offer her:

- ☐ Maternal serum triple screen test
- ☐ Amniocentesis
- ☐ Chorionic villus sampling
- ☐ High level ultrasound scan
- ☐ Uncertain of the correct answer

17) Amniocentesis:

a) Is best performed at 12 weeks	True ____ False____ Unsure ___
b) Has a miscarriage risk of less than 1 %	True ____ False____ Unsure ___
c) Allows the examination of chromosomes only	True ____ False____ Unsure ___
d) Takes 3 – 4 weeks for a complete result	True ____ False____ Unsure ___
e) Can be used for biochemical and/or DNA studies	True ____ False____ Unsure ___
f) Is an indication for the administration of Anti-D gammaglobulin if the mother is Rh negative	True ____ False____ Unsure ___

Q. No._____

18) The risk of having a child with chromosomal abnormalities increases:

a) If a mother has already had a child with a chromosomal aberration	True ____ False____ Unsure ___
b) In mothers over 35 years of age	True ____ False____ Unsure ___
c) In fathers over 35 years of age	True ____ False____ Unsure ___
d) In parents with balanced translocations	True ____ False____ Unsure ___

GENETIC EPIDEMIOLOGY

19) The carrier frequency of cystic fibrosis in the South African Caucasian population is approximately:

- ☐ 1 in 200
- ☐ 1 in 100
- ☐ 1 in 50
- ☐ 1 in 20
- ☐ Uncertain of the correct answer

20) The frequency of carriers of albinism in the black population in South Africa is approximately:

- ☐ 1 in 200
- ☐ 1 in 100
- ☐ 1 in 60
- ☐ 1 in 30
- ☐ Uncertain of the correct answer

21) Carrier testing for Tay-Sachs disease is recommended in which population group:

- ☐ Afrikaans-speaking individuals
- ☐ Asian individuals
- ☐ Individuals originating from Greece and Cyprus
- ☐ Ashkenazi Jewish individuals
- ☐ Uncertain of the correct answer

Q. No._____

22) A Greek couple is planning to start a family. There is no family history of any genetic disorders but they ask you if there are any conditions which should be screened for. They present a list of disorders they have heard about and you advise them as follows (place a tick after the appropriate answer(s)).

a) Alpha thalassaemia	Yes ____ No ____ Unsure ____
b) Beta thalassaemia	Yes ____ No ____ Unsure ____
c) Porphyria variegata	Yes ____ No ____ Unsure ____
d) Albinism	Yes ____ No ____ Unsure ____
e) Fanconi anaemia	Yes ____ No ____ Unsure ____
e) Myotonic dystrophy	Yes ____ No ____ Unsure ____

23) The percentage of **Major** birth defects in South African live born babies is:

- ☐ Below 1%
- ☐ Between 3% and 5%
- ☐ Between 10% and 15%
- ☐ Between 15% and 20%
- ☐ Uncertain of the correct answer

24) Which of the following disorders are caused by DNA triplet repeat expansions?

a) Fragile X syndrome	Yes ____ No ____ Unsure ____
b) Alzheimer's disease	Yes ____ No ____ Unsure ____
c) Myotonic dystrophy	Yes ____ No ____ Unsure ____
d) Huntington disease	Yes ____ No ____ Unsure ____
e) Spinal muscular atrophy	Yes ____ No ____ Unsure ____

Q. No._____

25) Please answer by **ticking** the appropriate column to indicate the inheritance mode of the following genetic disorders:

GENETIC DISORDER	AUTOSOMAL DOMINANT	AUTOSOMAL RECESSIVE	X-LINKED RECESSIVE	MULTIFAC-TORIAL	UNCERTAIN OF ANSWER
Cystic fibrosis					
Huntington disease					
Familial hypercholesterolaemia					
Albinism					
Myotonic dystrophy					
Haemophilia A					
Neural tube defects					
Cleft lip and/or palate					
Porphyria variegata					
Duchenne muscular dystrophy					
Spinal muscular atrophy					
Tay Sachs disease					

TERATOGENS

26)Which of the following infectious agents may pose significant risks of teratogenesis?

a) Syphilis	Yes ____ No ____ Unsure ____
b) Rubella	Yes ____ No ____ Unsure ____
c) Cytomegalovirus	Yes ____ No ____ Unsure ____
d) Toxoplasmosis	Yes ____ No ____ Unsure ____
e) Influenza	Yes ____ No ____ Unsure ____
e) Adenovirus	Yes ____ No ____ Unsure ____

Q. No._____

27) Which of the following drugs are considered major teratogens and are strongly contraindicated in pregnancy?

a) Warfarin	Yes ____ No ____ Unsure ____
b) Valproic Acid	Yes ____ No ____ Unsure ____
c) Retinoids (for treatment of acne)	Yes ____ No ____ Unsure ____
d) Paracetamol	Yes ____ No ____ Unsure ____
e) Tricyclic antidepressants	Yes ____ No ____ Unsure ____
f) Antimalarials e.g. chloroquine	Yes ____ No ____ Unsure ____
e) Lithium	Yes ____ No ____ Unsure ____

28)Children with Fetal Alcohol Syndrome (FAS) may present with the following features:

a) Short palpebral fissures	Yes ____ No ____ Unsure ____
b) Long smooth philtrum	Yes ____ No ____ Unsure ____
c) Developmental delay	Yes ____ No ____ Unsure ____
d) Normal growth parameters	Yes ____ No ____ Unsure ____
e) Polydactyly	Yes ____ No ____ Unsure ____

Q. No._____

D. GENETIC COUNSELLING INVESTIGATION

The following section aims to gather information regarding your current opinions and practices regarding genetic counselling. Please tick where necessary and comment fully when requested.

1a) Have you heard of genetic counselling before? ☐ Yes ☐ No

1b) If you answered Yes to the previous question, when did you first hear about it?

☐ 0-1 year ago ☐ 1-2 years ago ☐ 2-5 years ago ☐ >5 years ago

1c) How did you hear about it?

☐ Colleagues/other professionals (please specify) _____
☐ Conference/ seminar
☐ Pamphlet
☐ Medical Journal
☐ Medical School
☐ Other (please specify) _____

2) What do you understand by genetic counselling? _____

_____

_____

3a) Have you ever referred a patient for genetic counselling?
☐ Yes ☐ No

3b) If you answered Yes to the previous question please state the approximate number of patients referred and their disorders.

NUMBER OF PATIENTS	GENETIC DISORDER(S)

3c) If Yes was answered for question 3a, describe how the clients were referred:

☐ You made the appointment on their behalf
☐ You supplied the patient with the telephone numbers and left it to them
☐ You referred them to the nearest provincial hospital
☐ You asked your secretary to make the appointment
☐ Other (please specify) _____

4) Do you feel that genetic counselling is an important facet of health care in general practice? Please comment on your choice of answer.

☐ Yes ☐ No
Comment: _____
_____
_____
_____

5) Do you think that patients with hereditary disorders would benefit from genetic counselling? Please comment on your choice of answer.

☐ Yes ☐ No
Comment: _____
_____
_____
_____

6) Should all hereditary disorders be dealt with at a genetic counselling facility? Please comment on the choice of your answer.

☐ Yes ☐ No
Comment: _____
_____
_____
_____

7) Do you know the whereabouts of the nearest genetic counselling facility to your practice?
☐ Yes ☐ No

If Yes, please state where: _____

Q. No _____

8) Do you feel sufficiently prepared to take a full family history from patients and draw pedigrees? ☐ Yes ☐ No

9) Do you feel sufficiently prepared to counsel patients about their genetic risks?
☐ Yes ☐ No

10) Do you feel sufficiently prepared to counsel patients about their genetic test results?
☐ Yes ☐ No

11) How would you deal with the emotional consequences of patients who are either affected or at risk for a genetic disorder?

_____
_____
_____
_____

12a) Would you be interested in attending courses or seminars dealing with current genetic issues? ☐ Yes ☐ No

12b) If answered Yes, which topics in Genetics would interest you most?
Comment: _____
_____
_____
_____

12c) If answered Yes, what type of event do you feel would be most appropriate?

☐ Lecture ☐ Seminar ☐ Individual hands-on instruction
☐ Distance education course ☐ Other (please specify)_____

12d) What day of the week would suit you best?
☐ Monday ☐ Tuesday ☐ Wednesday ☐ Thursday
☐ Friday ☐ Saturday ☐ Sunday

12e) What time of day would suit you best?
☐ Morning ☐ Afternoon ☐ Evening

12f) Individualised genetic teaching is time consuming and may be costly. Would you be prepared to pay for such a course?

☐ Yes ☐ No

APPENDIX C

Interview Assessment Form

GP Interview Sheet

Date: _____ Interview No. _____

Personal details:

First name: _____ Surname: _____

Address: _____

_____

Telephone No.: _____

Relevant personal information:

Specific comments made:

Genetic topics raised:

Any specialized information required?:

APPENDIX D

Genetic Information Sheet

- Fetal Alcohol Syndrome (FAS)
- May be caused by the consumption of more than two units of absolute alcohol (AA) per day (30ml AA) or one or more binges at a crucial embryological time during gestation (>5 drinks of >75ml AA
- Clinical characteristics: growth retardation, short palpebral fissures, short nose, smooth philtrum, thin upper lip, micrognathia, microcephaly, developmental delay, hyperactivity and other behavioral abnormalities
- Four times more prevalent in the Western Cape of SA than reported anywhere else in the world

Genetic Counselling

What is Genetic Counselling?

Genetic Counselling is a comprehensive communication process that deals with the problems associated with the occurrence or the risk of recurrence of a genetic disorder in a family. This process involves a trained person helping an individual or family to: 1) comprehend the medical facts, 2) understand the hereditary implications, 3) understand the options available based on risk of recurrence, 4) choose a course of action and 5) adjust to the disorder in an affected family member and/or to the risk of recurrence.

What does a Genetic Counsellor do?

- Obtains an accurate assessment of the problem and attempts to establish a diagnosis
- Assists the family in the management of the disorder where possible
- Explains the nature and cause of the disorder (genetics and heredity)
- Discusses the psychosocial implications surrounding the disorder
- Estimates and explains the risk of the disorder recurring
- Discusses the concepts of preventing the disorder from recurring i.e. prenatal diagnosis, reproductive alternatives, therapeutic options
- Facilitates decision making regarding future plans and helps the family adjust to these plans
- Assesses the family's needs and refers them to suitable resources (medical, psychiatric, support groups etc.)

When should a patient be referred for Genetic Counselling?

- If there is a family history of some genetic disorder or birth defect e.g. Down syndrome, cystic fibrosis, mental retardation
- If an individual has one or more congenital malformations
- If there have been repeated spontaneous abortions (three or more first trimester) or a previous stillbirth for which no medical reason could be found
- If a pregnant woman is over 35 years of age Advanced maternal age has been implicated in a higher frequency of chromosomal abnormalities such as Down syndrome
- If a pregnant women has been in contact with potentially harmful agents such as infections, drugs, radiation, alcohol, or has diabetes mellitus
- If close relatives of an individual with a genetic disorder wishes to plan a family

Recommended Reading

- Muller, R. F. and Young, I. D. 1998. Emery's Elements of Medical Genetics, 10th Edition Churchill Livingston: London
- Harper, P. S. 1998. Practical Genetic Counselling, 5th Edition. Butterworth Heinemann: Oxford

Genetic Counselling Clinics:

*Tuesday Morning
- SAIMR (clinical cases)
- Johannesburg Hospital, Area 159

*Thursday Afternoons
- C. H. Baragwanath Hospital

*Bookings for Genetic Counselling Clinics: **(011) 489-9223/4**

The South African Institute for Medical Research
University of the Witwatersrand, Johannesburg

SCHOOL OF PATHOLOGY
Department of Human Genetics

Hospital Street, Johannesburg 2001, PO Box 1038 Johannesburg 2000
Telephone: +27-11-489-9000 Telefax: +27-11-489-9226 or +27-11-489-9209

Professor D Viljoen	489-9239	Dr TJL de Ravel	489-9212	Dr H Soodyall	489-9208
Professor M Ramsay	489-9214	Dr A Krause	489-9219	Dr AB Lane	489-9221

Genetics Information Sheet

Mendelian patterns of inheritance

Mendelian inheritance refers to disorders that are caused by single genes. Mendelian inheritance may follow autosomal patterns of inheritance, where the mutant gene(s) is/are on one of the 44 autosomes or it may follow a sex-linked pattern of inheritance where the mutant gene(s) is/are on one of the two sex chromosomes.

Autosomal Dominant (AD) Inheritance

- Usually seen through many generations of a family
- One copy of the mutant gene is required to cause the disorder (heterozygous state)
- There is a 50% risk of an affected parent having an affected child
- Clinical features may show striking variation from person to person
- The *de novo* (new) mutation rate may be high. An individual may present with a unique AD disorder which is not apparent in any other family member
- Both sexes are equally affected
- Examples: Huntington disease, porphyria variegata, familial hypercholesterolaemia, myotonic dystrophy

Autosomal Recessive (AR) Inheritance

- Only manifest when the mutant gene is present in a double dose (homozygous state)
- A family history is rarely found
- Two parents who are both carriers of a mutant gene for an AR disorder have a 25% risk of having an affected child
- Consanguineous (related) parents have a higher risk of having children affected by an AR disorder
- Both sexes equally affected
- Examples: cystic fibrosis, spinal muscular atrophy, albinism and Tay Sachs disease

X-Linked Recessive (XLR) Inheritance

- Mutant gene is found on the X chromosome
- Affects males almost exclusively
- In female carriers, a mutation is present on one of the X chromosomes (heterozygous state) and usually produces no phenotypic effect
- A mutation on a male's only X chromosome (hemizygous state) causes the disorder
- Affected males and their daughters are all obligate carriers (they all receive an X chromosome from their father). Sons of affected males are never affected as they receive the Y (and not the X) chromosome from their father
- In carrier females: 50% of their sons are affected and 50% of their daughters are carriers
- *De novo* mutations may occur. Affected males may occur with no previous family history
- Examples: Haemophilia, Duchenne muscular dystrophy

Non-Mendelian patterns of inheritance

Multifactorial Disorders
- Not caused by a single gene but by both multiple genes and environmental factors
- Examples: cleft lip and/or palate, neural tube defects and *talipes equinovarus* (club foot)

Dynamic Mutations
A new class of mutation identified as causing disease in humans. Triplet repeat sequences occur in increased copy number in affected persons when compared to the general population. These disorders are characterised by:
- Marked variation in clinical symptoms may occur between individuals
- Earlier age of onset may be seen in offspring than was seen in the parents
- Sex of parent influences severity. E.g. Fragile X - more severe when maternally inherited, Huntington disease more severe when paternally inherited
- Examples: Fragile X syndrome, Huntington disease, myotonic dystrophy, Friedreichs ataxia

Aneuploidy
Aneuploidy refers to a numerical chromosomal abnormality involving the loss or gain of one or more chromosomes.

Down Syndrome (DS)
- 47 chromosomes. Commonest karyotypes: 47, XX, +21 (female) and 47, XY, +21 (Male)
- Common clinical features: epicanthic folds, mental retardation, hypotonia and cardiac defects
- Approximately 1 in 700 births (found in all population and ethnic groups) increased risk is seen with advanced maternal age

Turner Syndrome (TS)
- Karyotype is most commonly 45, X. Other variants include: 46 X, r(X) or 46 X, i(Xq)
- Common features: oedema at birth, webbing of the neck, cardiac defects, short stature, infertility, usually mentally normal

Prenatal Diagnosis and Screening
Prenatal diagnosis and screening offers the ability to detect abnormalities in an unborn child. Maternal serum screening, amniocentesis and chorionic villus sampling are a few options that may be offered to expectant parents.

Maternal Serum Triple Screen Test
A blood sample is taken from the pregnant woman at 16-18 weeks gestation. Detects women at increased risk for DS and neural tube defects.
- Measures oestriol, HCG and alpha-fetoprotein (AFP) levels
- The detection rate for DS is ±60% with a false positive rate of ±5%
- It is a screening test, not a diagnostic test
- Other chromosomal abnormalities and up to 85% of open neural tube defects may be detected
- A positive result indicates an increased risk only, and does not represent a confirmed diagnosis

Amniocentesis
- Best performed between 16-18 weeks
- Miscarriage risk: ±0.7%
- Chromosomes and AFP levels are routinely examined
- Chromosome results available after 2-4 weeks, AFP levels after about a week
- Biochemical and DNA analyses may be performed for known genetic disorders
- It is an invasive procedure - Rhesus maternal sensitisation may occur (administer Anti-D to Rh negative women)

Chorionic Villus Sampling
- Carried out between 10-12 weeks
- Miscarriage risk: ±3-5%
- Chromosome, some biochemical and DNA analyses for known disorders may be conducted
- Cannot measure AFP levels
- Confined placental mosaicism may give false results in 1% of cases An abnormal result thus requires confirmation by amniocentesis.

Increased risk for having a child with chromosomal abnormalities
- Previous child with a chromosomal aberration
- Advanced maternal age (over 35 years)
- Advanced paternal age (over 65 years)
- Parents with a balanced translocation

Population specific diseases
Certain populations have higher frequencies of specific genetic disorders than others. Examples:
- Cystic fibrosis - Caucasian populations (Carrier frequency: 1 in 20)
- Albinism - Black populations (Carrier frequency: 1 in 30)
- Tay Sachs disease - Ashkenazi Jewish population (Carrier frequency: 1 in 25)
- Thalassaemia - in individuals originating from the Mediterranean area, the Middle East, the Indian subcontinent and South-East Asia. Between 1 in 7 and 1 in 30 people from these areas may carry the mutations

Birth Defects
- ± 3-5% of all newborns have at least one major structural defect or genetic disorder present at birth, which may lead to premature death or severe handicap.

Teratogens
Drugs - Many drugs are possible teratogens. Examples of proven teratogens:
- Warfarin - nasal dysplasia, chondrodysplasia punctata, microcephaly, deafness
- Valproic acid - neural tube defects, facial and digital abnormalities
- Retinoids - anencephaly, anopthalmia, spina bifida, facial and urogenital anomalies
- Antimalarials e.g. choroquine - chorioretinitis and deafness (rare)
- Lithium - heart and limb defects

Infectious Agents - Examples:
- Syphilis - facial and bony abnormalities, keratitis
- Rubella - mental retardation,cataract, deafness, congenital heart defects
- Cytomegalovirus - microcephaly with mental retardation, chorioretinitis, hepatosplenomegaly
- Toxoplasmosis - chorioretinitis, microcephaly with mental retardation, hepatosplenomegaly

APPENDIX E

GP Thank you letter (Postal replies)

The South African Institute for Medical Research
University of the Witwatersrand, Johannesburg

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Department of Human Genetics

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Telephone: +27-11-489-9000. Telefax: +27-11-489-9226 or +27-11-489-9209

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Professor M Ramsay	489-9214	Dr A Krause	489-9219	Dr AB Lane	489-9221

Dear Doctor

Thank you for participating in the study **"Genetic knowledge, opinions and practices amongst general practitioners".**

Attached to this letter please find a General Information sheet designed to provide fundamental genetic information and assist you with possible referrals. This document will come in handy and we urge you to keep it for future reference. Contained within this sheet you will also find information regarding when and where to book patients for Genetic Counselling.

Your CPD certificate awarding you 1 CPD point in the self-study category for participating is also attached.

Should you have any queries about this study please contact Kelly Trenton, (011) 489-9236.

Thank you once again for your cooperation.

Yours sincerely

K Trenton

Kelly Trenton
MSc (Med) Student

This organisation rejects racism and racial segregation. It is committed to non-discrimination, particularly in the constitution of its student body, in the selection and promotion of its staff, and in its administration.

APPENDIX F

GP Thank you letter (Interview)

The South African Institute for Medical Research
University of the Witwatersrand, Johannesburg

GENETIC COUNSELLING CLINIC
SCHOOL OF PATHOLOGY
Department of Human Genetics

Cnr Hospital and De Korte Streets, Johannesburg 2001 PO Box 1038, Johannesburg 2000
Bookings: Telephone: +27 11 489 9470/1 Telefax: +27 11 489 9226 or +27 11 489 9209

rofessor D Viljoen	489 9239	Dr TJL de Ravel	489 9212	Dr A Krause	489 9219
ls P Craig	489 9243	Sr M Glass	489 9227	Ms C de Vos	489 9236

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Kelly Trenton
MSc (Med) Student

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APPENDIX G

Ethical Clearance Certificate: M991115

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 Trenton

CLEARANCE CERTIFICATE **PROTOCOL NUMBER** M991115

PROJECT Genetic Knowledge, Opinions & Practices Amongst General Practitioners

INVESTIGATORS Miss KM Trenton

DEPARTMENT Dept of Human Genetics, SAIMR

DATE CONSIDERED 991126

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE 991210 **CHAIRMAN** .....(Professor P E Cleaton-Jones)

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

c c Supervisor: Dr A Krause
Dept of Dept of Human Genetics, SAIMR

Works2\lainC015\HumEth97 wdb\M 991115

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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 19/1/2000 SIGNATURE .....

PROTOCOL NO.: M 991115

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX H

Protocol Approval Letter

Faculty of Health Sciences
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

7 York Road PARKTOWN Johannesburg 2193 Telegrams WITSMED Telex 4-24655.SA
FAX 643-4318 TELEPHONE 647-2075
E-MAIL jmainwa@chiron.wits.ac.za

MISS K TRENTON
9 KIEPERSOL ST
FERNDALE EXT 6
RANDBURG
2194

APPLICATION NUMBER 9503300H
STATUS (DEG 65) (MM043) PZZ

2000-03-16

Dear Miss Trenton

Approval of protocol entitled genetic knowledge, opinions and practices amongst general practioners

I should like to advise you that the protocol and title that you have submitted for the degree of Master Of Science In Medicine (Ft).(Coursework) have been approved by the Postgraduate Committee at its recent meeting. Please remember that any amendment to this title has to be endorsed by your Head of Department and formally approved by the Postgraduate Committee.

Dr A Krause, Mrs PA Craig has/have been appointed as your supervisor/s. Please maintain regular contact with your supervisor who must be kept advised of your progress.

Please note that approval by the Postgraduate Committee is always given subject to permission from the relevant Ethics Committee, and a copy of your clearance certificate should be lodged with the Faculty Office as soon as possible, if this has not already been done.

Yours sincerely

JO Mainwaring (Mrs)
Faculty Officer
Faculty of Health Sciences

Telephone 647-2075/2076

Copies - Head of Department____Supervisor/s

The University of the Witwatersrand rejects racism and racial segregation. It is committed to non-discrimination in the constitution of its student body, in the selection and promotion of its staff, and in its administration

Electronic-Database Information

On-line Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/omim/

Census information: http://www.odci.gov/cia/publications/factbook/sf

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