GENETIC COUNSELLING AND ADULT POLYCYSTIC KIDNEY DISEASE: PATIENTS' KNOWLEDGE, PERCEPTIONS AND UNDERSTANDING

VOLUME ONE

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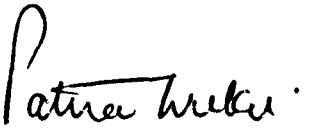
DECLARATION

I declare that this work is my own and has not appeared in any other thesis.



ABSTRACT

Adult Polycystic Kidney Disease (APKD) is a genetic disease transmitted in an autosomal dominant fashion. There is no cure. Treatment is of the symptoms as they appear usually in adulthood. Patients affected by APKD may receive genetic counselling from renal physicians.

The aims of genetic counselling can be described through paradigms which reflect the current understanding of genetics and knowledge of the illnesses. The availability of new diagnostic techniques creates a new paradigm concerned with the ethical issues of genetic testing and counselling.

An investigation into patients' knowledge, perceptions and understanding of genetic counselling was undertaken at the Renal Unit of Glasgow Royal Infirmary, prior to the establishment of a screening and counselling service for those at risk for APKD.

The main findings of the study were: the majority of patients had received some genetic counselling from renal physicians; the majority of patients had relatively good knowledge of the symptoms of and treatments for APKD; nevertheless patients believed that the two most important items to be included in genetic counselling were information about the symptoms and the treatment of APKD; patients did not fully understand the genetic inheritance of APKD; they described the risk of transmission of APKD (50-50) as a medium risk; almost all patients recommended that their at risk relatives and their children be tested for APKD; prior to the availability of prenatal diagnosis, patients thought that their children should be tested between the ages of 16 and 20.

A secondary study, including spouses of those with APKD and also haemophiliacs and their spouses, found that respondents favoured prenatal testing without termination of pregnancy and that both diseases were rated as being of medium severity.

These findings raise ethical issues for those giving genetic counselling, and have implications for the content of genetic counselling.

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CHAPTER 1. INTRODUCTION AND OUTLINE OF THESIS

1.1 INTRODUCTION

Throughout the 1970s there was an increasing interest in genetic diseases and in genetic counselling. According to a WHO Report (1972 p5) this interest in disease of genetic origins stemmed from:

> "the absolute and relative decline in morbidity and mortality attributable to infection, parasitic infection and malnutrition; the relative increase in morbidity and mortality attributable to genetic factors and the development of promising approaches to the diagnosis, treatment and prevention of genetic diseases...".

Genetic diseases were also becoming a subject of discussion in more popular literature with the availability of clearly written books such as Milunsky's *Know your own Genes* (1977), and Etzioni's *Genetic Fix* (1973), which discusses moral and ethical issues raised by the ability to identify genetic diseases. There also appeared books such as Phillips *Living with Huntington's Disease* (1982) which discussed the physical and social problems of Huntington's Disease (or Chorea) as well as problems created by the fact that the disorder is genetic.

By 1982, according to a report of the Clinical Genetics Society, genetic counselling was being offered by clinical geneticists from genetic clinics and was available in most health authority areas in the United Kingdom.

Adult Polycystic Kidney Disease (APKD) is an inherited disease of variable age of onset. There is no cure; the treatment is the treatment of the symptoms as they appear and these symptoms may necessitate renal dialysis and transplantation. It is possible to diagnose the condition in adults by non-invasive ultrasound. Furthermore, the genetic transmission is clearly understood. Once diagnosed, patients with APKD attend a hospital renal clinic on a regular basis.

In 1982, a new service to offer genetic counselling and presymptomatic testing for APKD at the Tenovus Kidney Unit of Glasgow Royal Infirmary was under consideration and the research worker had been employed to ascertain the feasibility of establishing such a service which would be offered by the staff of the renal unit rather than having patients attend a genetic clinic run by geneticists.

At this time, genetic counselling was becoming a subject of interest both to doctors as well as to other non-medical researchers, with interest focused on the definitions of genetic counselling, the aim of genetic counselling and the outcome measures used in the studies (Shaw 1977). The criteria most consistently used by genetic counsellors to evaluate the success of their work were patient knowledge, patient reproductive intentions and/or reproductive behaviour after counselling, with the assessment of patient knowledge mainly focused on the patients' understanding of the risk of recurrence or occurrence of the particular disease.

However some studies into genetic counselling had suggested that the attitudes of many families coming to genetic counselling were determined more by the sense of the burden of the illness (Leonard et al 1972) than by knowledge of the precise genetic risks. Such a finding may reflect the different concepts of illness and health held by the patients on one hand and the doctors on the other hand. It could have implications for the content of genetic counselling in terms of giving information about the problems that may be associated with particular diseases. Therefore, it seemed important from the point of view of the content of genetic counselling to consider how patients perceived the burden of the particular illness. For example a study of haemophilia (Markova and Forbes 1984) highlighted the importance to those with haemophilia of social problems such as employment.

Apart from giving information about the genetic risks, very little was known from the available research about what other information was given to patients in genetic counselling. It was not known whether information about such topics as contraception or about adoption and fostering was routinely given. Moreover it was not known what sort of information patients themselves would consider important to be included in genetic counselling.

At the time of the beginning of this study, it was likely that most genetic counselling was retrospective, ie it was given after the diagnosis of the illness in the individual or after the birth of a child affected by a particular disorder. With regard to APKD, it was assumed that genetic counselling, if given, would have been given after the diagnosis of the illness in the patient.

Prospective genetic counselling involves the identification of the at risk relative who can then be offered counselling and diagnosis. As the success of the identification of the at risk relatives depends on the cooperation of a source patient, it is important to ascertain the views of patients about informing at risk relatives of their risk as well as about the presymptomatic testing of those at risk.

In view of the likely expansion of genetic knowledge and of genetic counselling, the importance of the patients' views of the content of genetic counselling, the perceived burden of the illness and attitudes to presymptomatic testing of a genetic disease seemed serious and worthwhile subjects of an investigation.

The specific focus of this thesis was to assess the knowledge, perceptions and understanding of patients with APKD to their illness as well as to ascertain topics that could be included in a genetic counselling service. A secondary focus of the study was to ascertain the views of patients with APKD and their families to prenatal diagnosis for APKD and termination of pregnancy of an affected fetus. In order to provide a

comparison with a 'control population', the views of male patients with haemophilia, haemophilia carrier women and their families to prenatal diagnosis for haemophilia and termination of pregnancy of an affected fetus was also sought.

The research, therefore, had the following objectives in relation to those with APKD:

1. To ascertain the patients' experience of genetic counselling.
2. To ascertain the patients' knowledge of the symptoms of APKD and the treatments available.
3. To ascertain the patients' knowledge of the genetic inheritance and transmission of APKD.
4. To ascertain the attitude of patients to family limitation.
5. To ascertain the influence of genetic counselling on the patients.
6. To assess the attitudes of patients to testing their at risk children and asymptomatic relatives for APKD.
7. To identify topics that patients perceived to be problems of APKD.
8. To identify topics that patients thought should be included in genetic counselling.
9. To ascertain the views of patients and their families to prenatal diagnosis for APKD and termination of an affected fetus.
10. To offer recommendations on the content of genetic counselling based on the findings of the study.

The research for this thesis took place with the following timetable:

1982: Registered for higher degree with Department of Psychology, University of Stirling.

June 1982: Appointed Research Fellow, Department of Psychology, University of Stirling and Department of Medicine, Glasgow Royal Infirmary, based in the Renal Unit, Glasgow Royal Infirmary.

July 1982 - September 1982: Initial accrual of patients and pilot study.

October 1982 - May 1983: First interviews carried out and accrual of patients completed.

May 1983 - November 1983: Second interviews carried out and completed.

November 1983 - April 1984: Third interviews carried out and completed.

November 1984: Also appointed Research Fellow/HIV counsellor at the Haemophilia Unit, Glasgow Royal Infirmary.

1985: Announcement of discovery of gene marker for APKD on short arm of chromosome 16.

January 1986 - October 1987: Collecting of data for APKD gene marker investigation with Dr Keith Simpson and in conjunction with Department of Medical Genetics, Yorkhill Hospital Glasgow.

January 1986 - March 1987: Secondary study on prenatal diagnosis in APKD and haemophilia carried out and completed.

1986 - 1987: Data from all questionnaires coded and analysed using SPSS at Stirling University.
February 1988: Moved to South East England.
September 1988 - October 1990: Leave of absence from thesis for domestic reasons.
1991: Commenced writing up of thesis.
1991: All data recoded and analysed using SPSS PC.
August 1992: Thesis title lodged with University of Stirling.
September 1992 - November 1992: Data reanalysed using GLIM computer package and analysis using ridits carried out.
December 1992: Thesis submitted to University of Stirling.

1.2 Outline of Thesis

The content of the thesis is outlined below.

In Chapter 2 key themes in the development of genetic counselling from the historical beginnings in the Eugenic movement are described with reference to the literature. The influence of preventive medicine in genetic counselling is discussed as well as the implications of the emphasis on prevention in genetic counselling. The relationship between the availability and type of diagnostic tests and the psychological and ethical implications of these tests for genetic counselling are explored.

In Chapter 3 the development of medical knowledge of APKD from the earliest description to date are examined. The physiology of the illness and the major medical problems are described. A description of the most common treatments available is given.

In Chapter 4 specific issues in genetic counselling in relation to APKD are examined. In particular the availability of accurate diagnosis, presymptomatic diagnosis and gene markers are discussed and the influence that these factors may have on genetic counselling.

Chapter 5 explores lay concepts of health and illness.

In Chapter 6 the methodology of the data collection and the type of interview used are described.

Chapter 7 describes the populations involves in the study. While 83 patients were initially accrued to the investigation, only 71 completed the first interview, and smaller numbers attended subsequent interviews. The reasons for this are given.

Chapter 8 presents an overview of the subsequent analysis.

Chapter 9 examines the demographic and medical explanatory variables. This includes the analysis by age, sex, number of children, education, occupation, housing and religion as well as severity of disease and family history.

In Chapters 10 to 15 the analysis of the main responses is examined. In Chapter 10 the patients' experience of genetic counselling is discussed. Chapters 11 and 12 are concerned with the analysis of the data on the patients' knowledge of the symptoms and treatment of APKD and their knowledge of the inheritance of the illness. In Chapter 13 the respondents' perceptions of the burden of certain problems that could be caused by APKD are examined. In Chapter 14 the results of the analysis of the patients' attitudes to having children, attitudes to screening and testing of at-risk relatives, attitudes to testing of children, the outcomes of genetic counselling, and their views about who should give genetic counselling are discussed. The patients' perceptions of elements that could be included in genetic counselling are analysed in Chapter 15.

In Chapter 16 a secondary study on prenatal diagnosis and termination of pregnancy is described, and in Chapter 17 the results of that study are discussed.

The conclusions of the study are put forward in Chapter 18.

Details and selected tabulations of the basic results and supplementary results appear in the Appendices in Volume 2.

CHAPTER 2: GENETIC COUNSELLING

2.1 INTRODUCTION

The term 'genetic counselling' can be first traced to Sheldon Reed, an American doctor who reputedly coined the phrase in 1947 (Porter 1977). Reed was concerned that the prevailing phrases of 'genetic advice' and 'genetic hygiene' were too eugenic or too socially oriented. In their place he suggested the term 'genetic counselling' to emphasise more the individual one-to-one relationship that he felt should exist between a counsellor and a patient.

The activity that we now call genetic counselling has evolved in the 20th century. The state of knowledge of genetics and genetic diseases has increased during this century due to a greater understanding of the application of the principles of Mendelian inheritance. There has been an increase in the knowledge and availability of diagnostic tests for genetic diseases including both prenatal and presymptomatic diagnosis. There has also been the development of computer technology and the widespread use of computers. In this chapter the association between the state of knowledge of genetics and genetic diseases and the development of four paradigms in genetic counselling is discussed.

2.2 THE USE OF PARADIGMS IN THE ANALYSIS OF GENETIC COUNSELLING

Kessler (1980) first suggested that the history of genetic counselling could be organised around three different paradigms, relating to **eugenics, preventive medicine** and **psychological medicine**, each paradigm being based on a different set of beliefs and assumptions regarding the goals, principles and practices of genetic counselling. The sequence of Kessler's paradigms can be summarised: (1) genetic counselling had its origins in the eugenic movement and in the biological sciences of the early 20th century;

(2) by the 1950s it had become established as a medical activity; (3) during the 1970s a new paradigm emphasising communication and attention to psychosocial issues as an integral part of genetic counselling had emerged.

The adoption of the concept of a paradigm is a useful starting point from which to analyse genetic counselling. These paradigms are based on different sets of ideologies and beliefs reflecting societal attitudes in different historical periods and also reflecting the current knowledge of genetics, the prevailing medical attitudes to genetic disease, the awareness of the psychological needs of patients in genetic counselling, and the awareness of ethical problems created by new technologies.

I suggest that a new fourth paradigm is now emerging in which the emphasis is on the ethics of how genetic information should be used. The widespread use of computers and computer linkage has enabled geneticists to store information easily as well as to transfer information about individuals and families from one genetic centre to another. As evidenced by the Report of the Working Party of the Clinical Genetics Society on Genetic Registers (1978) computerised genetic registers have been developed and used for clinical purposes for some time. These registers are intended to make it easier to recall individual patients for therapeutic purposes or to inform them of advances in treatment or diagnosis. Such registers may also be used to store information about at-risk relatives who may be contacted and offered genetic counselling (Emery and Miller 1976). The use of such registers raises important ethical considerations concerning confidentiality. It is necessary to protect the confidentiality of those about whom information is stored in the register; information about any family member must be confidential to that person alone.

The increase in availability of easy diagnostic tests both for particular genetic diseases and for the identification of carrier status increases the opportunity of conflict for

the genetic counsellor wishing to protect the confidentiality of the patient but at the same time knowing that the information acquired could prevent harm to at-risk relatives.

Presymptomatic screening for genetic disease raises the ethical dilemma of the need to protect the privacy of patients from institutional third parties such as employers and insurance companies. The increasing use of prenatal diagnosis raises the question of the need to respect parental choice which would include the decision either to terminate the fetus or to carry to term a fetus known to have some genetic defect.

The four paradigms, Kessler's three and this fourth paradigm, which I am now proposing, do not form discrete entities. Rather there is an evolutionary development from one to the next, with each paradigm retaining some of the features of its predecessor. For example, a principle of negative eugenics, to prevent or reduce genetic disease, can be found reflected in the writings of many authors and does not belong solely to the first paradigm. In her examination of published studies of genetic counselling Shaw (1977) found that the most frequently stated objective of genetic counselling was to 'prevent' or 'reduce' genetic disease. Rainer (1969) in discussing counselling of single gene disorders says "... weight must also be given not only to the genetic risk but also to the mental health and social responsibility of the prospective parents ... Lowering the incidence or prevention of severe handicap is good for the community ..." (p225). And Lynch (1969) in his suggestion that "genetic counselling is ideally suited to programs of prevention" (p279) is supporting the same philosophy. Similar views are found in the writings of Leonard et al (1972), and the authors of the Report on the Provision of Regional Genetic Services in the United Kingdom (1982 p1) state: "There is increasing evidence that a national network of comprehensive genetic services would provide a real opportunity for disease prevention".

2.3 PARADIGM 1: EUGENICS

The concept and the philosophy of genetic counselling can be traced back to the beginning of the 20th century and the eugenics movement. It is necessary to discuss the historical background first to demonstrate that it is the availability of knowledge of genetics that initially determined the focus of genetic counselling.

2.3.1 Historical background: knowledge of heredity

An understanding of heredity and the practical application of genetics by humans can be traced back to early civilisations. The process of domestication of animals and plants required an understanding of heredity. In early civilisations, individual animals and plants with desirable traits were selected, and by inbreeding them offspring with more of the same trait were produced. The success of domestication indicates that early human cultures understood a simple, but important rule of heredity, that 'like breeds like'.

Early writings provide evidence that early societies had some understanding of heredity. According to Pierce (1990) Hindu sacred books attribute the characteristics of children primarily to the father, but differences between a son and his father were thought to result from the influence of the mother. Early writings also provide rules for choosing a spouse, suggesting that women from families with undesirable traits should be avoided.

The ancient Greeks showed a knowledge of human heredity in their poetry and literature, and also in their medical writings. Euripides in *Electra* (413 BC) drew attention to the physical similarities between relatives, and also to psychological differences. The poet Theognis (6th century BC) described how practical considerations overcame eugenic ideals:

> "we seek well bred rams and sheep and horses and one wishes to breed from those. Yet a good man is willing to marry an evil wife, if she brings him wealth; nor does a woman refuse to marry an evil husband who

> is rich. For men reverence money, and the good marry the evil, and the evil the good. Wealth has confounded the race."

The fact that pattern baldness (alopecia) is sex limited was noted by Hippocrates (ca 400 BC) in his statement that eunuchs neither get gout nor grow bald and by Aristotle (384-322 BC) in his comment that no boy ever gets bald, no woman and no castrated man. One of the followers of Hippocrates, in the 4th century BC, describes conception and the growth of the fetus and observes that "the child must inevitably resemble each parent in some respect", though he attributes the degree of resemblance to the strength and quantity of 'sperm' contributed by each parent (Lloyd 1978).

In early Talmudic writings there is reference to an understanding of the hereditary nature of haemophilia. According to Rabbi Judah, if two children of the same mother died as a result of circumcision or, according to Rabbi Simeon ben Gamliel, if three children died as a result of circumcision, then circumcision of a third or fourth child respectively should not be performed. The same applied to the situation of three sisters. If one son of each sister had died as a result of circumcision then the son of the fourth sister may not be circumcised. This is in accord with Talmudic comment that in regard to circumcision there are families where the blood is loose and others in which the blood is held fast (*Kamit*, easily congealed, Yebamoth 64b, Rosner 1983 p245).

Historically views about inheritance were often confused with popular superstition. In the 19th century, some believed in telegony, the idea that a person's heredity is affected not only by his father but also by other males who had had intercourse with his mother. This belief in telegony was taken to extreme in old British law which held that a man who seduced the wet nurse of the heir to the throne was guilty of polluting the blood of the Royal Family (McKie 1988 p10).

CHAPTER 2: GENETIC COUNSELLING

The problem of heredity in the 19th century was studied by scientists such as Mendel, Galton and Weissmann in different ways. Gregor Mendel (1822-1884) discovered the mathematical law governing dominant and recessive characteristics in hybrids. But the application of this discovery belonged to the 20th century. Mendel fertilised tall plants with pollen from short plants. He noted that a uniformly tall generation of plants was produced. When a second generation was grown from these plants some of the shortness characteristic of the first generation returned in the ratio of three tall plants to one short. Mendel concluded that each of these characteristics must be determined by two distinct factors which acted as physical particles transmitted from one generation to another. One of these factors was inherited from the male, the other from the female. Further, Mendel concluded that one of these factors dominated the other. For the first time an explanation for heredity had been found (Mendel 1959).

However for 35 years Mendel's work remained obscure. In 1900 the botanists Hugo de Vries (1848-1935), Carl Correns (1864-1933) and Erich von Tschermak-Seysenegg (1871-1962) independently rediscovered Mendel's work and recognised its importance. In 1908 Ottenburg and Epstein demonstrated that blood groups were inherited in mendelian fashion and in 1911 Wilson made the first gene assignment in humans by assigning the gene for colour blindness to the X chromosome (Connor and Ferguson-Smith 1988 p4).

Francis Galton (1822-1911) began to investigate heredity experimentally in 1871. His observations on the inheritance of transfused blood in rabbits, of tricoloured spots in the coats of basset hounds, and of stature in humans led him to reject the Lamarckian theory of inheritance. The French biologist Jean-Baptiste Lamarck (1744-1829) had suggested that characteristics acquired by an individual during his lifetime could be passed on to the next generation. Lamarckism was popular in revolutionary France where the

emphasis on an individual's power to impose his or her influence on future generations was popular (Mckie 1988,p10). The theory had flaws which were demonstrated by scientists who amputated the tails of mice who continued to produce offspring with tails.

In *Natural Inheritance* (1889) Galton described the law of filial regression which asserts that the offspring of tall parents regress to the mean. Galton had approached the problems of inheritance through the then infant science of statistics. In the mid 19th century the practice of statistics consisted mainly of the accumulation of socially useful numerical data, with neither theoretical underpinning nor mathematical analysis. By the late 1860s Galton had come upon a quite different approach to statistics, the formulation now called the normal or Gaussian distribution. In 1877 in *Typical Laws of Heredity*, based on sweet pea data, it was clear that Galton realised that the laws governing heredity could be treated mathematically in terms of units of statistical deviation. Galton's work in statistics constituted a sharp and irreversible departure from the mere data gathering that had characterised the science of the mid 19th century (Kevles 1986 p17) and insisted that statistics had to incorporate the theory and methods of mathematical probability. Galton's biographer Karl Pearson wrote in 1930: "Thousands of correlation coefficients are now calculated annually, the memoirs and textbooks on psychology abound in them; they form ... the basis of investigations in medical statistics, in sociology and anthropology ...". The method Galton invented to express the degree of resemblance between parents and children was the 'regression diagram' (Pearson 1914).

Augustus Weissmann (1834-1914) was a biologist who maintained that variation is produced by sexual selection and that acquired characters are not directly transmitted. Garrison (1921) suggested that if Weissmann's theory were true and accepted it would have far reaching social significance as it would seem probable that "moral qualities

cannot be transmitted to children but have to be acquired in each case by intensive early training" (p554).

Weissmann also suggested that the hereditary endowment of the animal, which he called germ plasm, was separate from and protected against influences from the environment. The insulation of the germ plasm from environmental influences called the Weissmann barrier is a fundamental principle of modern evolutionary theory.

Charles Darwin (1809-1882) in *The Origin of Species* (1859) suggested that animals best suited to an environment survive longer and produce more offspring. In his review of the 1867 edition of *The Origin of Species* Fleeming Jenkin, Professor of Engineering at University College London, clarified the problem that Darwin had still to explain. Jenkin pointed out that an individual with a useful trait, which mated with a normal partner, would pass on only 50% of the trait to its offspring, 25% to its grand children 12½% to its great grand children and so on until the trait disappeared. Darwin died in 1882 without realising that a solution to that problem had been found 15 years earlier by Mendel.

2.3.2 The eugenic movement: application of genetic knowledge

The word 'eugenics' was coined by Galton in 1883 and first introduced in his book on Inquiries into *Human Faculty* (1883). He had, however, first published his eugenic ideas in 1865 in a two part article for Macmillans Magazine entitled *Hereditary Talent and Characters*. According to Schuster (1912), Galton was stimulated by the publication of Darwin's *The Origin of Species* in 1859. He was also impressed by the many cases of what he referred to as heredity among the men who were graduates of Cambridge university. In his investigations he drew a sample population of distinguished statesmen, military men, artists, jurists and musicians and found that a disproportionately large

number were related to one another. This observation led Galton to the conclusion that families of reputation were much more likely than ordinary families to produce offspring of ability. Galton believed that superior hereditary lines tended to be diluted by crossing with inferior lines, that human offspring tended to be more like the average between their parental strains than like either parent. He further believed that inferior genetic types, judged mainly by intelligence, tended to reproduce more rapidly than superior ones (Galton *Hereditary Genius* 1869) Galton's ideas indicated that unless strong measures were taken, the human evolutionary course could only be downhill. He argued that the effect of ancestry caused the progeny of one generation to revert towards the centre population and he called that tendency the 'coefficient of reversion'.

The concept of eugenics embodied in *Human Faculty* (1883) was the study of agencies that might improve or impair the racial qualities of future generations either physically or mentally.

The practical measures by which eugenic principles could be applied were often divided into positive and negative eugenics (Haller 1963). The aim of positive eugenics was to secure the multiplication of those individuals above average in physical, mental and moral qualities. Negative eugenics focused on preventing an increase in the stock from which persons inferior in these respects may be expected to be derived (Schuster 1912 p235).

In the preface to the 1892 edition of *Hereditary Genius* Galton acknowledged that "the great problem of the future betterment of the human race is ... at the present time, hardly advanced beyond the state of academic interest ...". He continued: "The processes of evolution are in constant and spontaneous activity, some towards the bad, some towards the good. Our part is to watch for the opportunities to intervene by checking the former and giving free play to the latter" (Kevles 1986 p305).

Galton's eugenic ideas gradually won some degree of commendation from the scientific community in Britain and in the United States as well as among intellectuals such as George Bernard Shaw, Havelock Ellis and Sidney and Beatrice Webb.

In 1904 Galton founded a Research Fellowship at the University of London, the aim of which was research and not for the spread of eugenic ideals. Galton expected the first Eugenics Fellow, Edward Schuster, to establish a register of able families so as to ascertain the hereditary ingredients of ability. Galton, disappointed by the lack of progress made by Schuster, terminated the Fellowship and founded instead the Galton Laboratory for National Eugenics, providing further in his will that the majority of his estate should go to University College London for the support of studies in eugenics.

2.3.3 The Eugenics Society

The Eugenics Society was founded in 1907 as the Eugenics Education Society (the name was changed in 1926) with Galton as Honorary President. The initial aims of the society were:

"1. Persistently to set forth the national importance of Eugenics in order to modify public opinion and create a sense of responsibility, in the respect of bringing all matters pertaining to human parenthood under the domination of eugenic ideals.

2. To spread a knowledge of the laws of heredity so far as they are known, and so far as that knowledge might effect improvement of race.

3. To further eugenic teaching at home, in the schools and elsewhere."

(quoted in Schenk and Parkes 1967 p150).

These aims were modified and expanded over the years so that by 1944 the Aims and Objectives of the Society took up a 12 page leaflet (Hall 1990) and according to Hall, even in its peak years of 1911 and 1932/33, the membership never exceeded 800.

The influence of the Society, however, went further than its small membership, which included members of distinction and influence and also members represented on government committees. The Society held regular meetings, endowed lectures and published *The Eugenics Review*. However, it is difficult to assess the impact of the Eugenics Society in bringing about eugenic awareness. According to Hall (1990 p328), from evidence in letters and documents sent to the Eugenics Society there did appear to be "pervasive but vague notions about good and bad breeding to be found in nearly all levels of British society". From the beginning of the Society there also appears to have been a tension in the aims between positive eugenics, encouraging those perceived as 'suitable' to have more children, and negative eugenics, discouraging or preventing those perceived as 'unfit' from breeding.

2.3.4 Sterilisation

The Society also received requests for information about sterilisation and from evidence held in the Society archives it appears that there was often considerable support for legislative measures such as sterilisation from organisations not necessarily perceived as particularly in sympathy with the Eugenics Society. In 1926 the Society printed 20,000 copies of a leaflet explaining the advantages of sterilisation. Although there was no law against it, British doctors were generally reluctant to perform sterilisation, even on volunteers who wished the operation let alone on those who were unable to decide to have the operation voluntarily (Kevles 1986 p115).

In 1934 the Brock committee reported on sterilisation and stated "that there is no sound scientific basis for sterilisation on account of immorality of character defect. Human conduct and character are matters of too complex a nature, too interwoven with social conditions ... to permit any definite conclusions to be drawn concerning the part that heredity plays in their genesis". The Brock Report declared that there was no case for compulsory sterilisation for eugenic reasons or any other reasons. The Report suggested that sterilisation may be warranted for a few genetic disorders but such sterilisation should be voluntary (Kevles 1986 p167).

2.3.5 Widening horizons

In the years 1910-1914 eugenics took up subjects that had previously been outside the bounds of respectable discussion. For example, many eugenicists considered it important to teach adolescents about the physiology of sex to prevent venereal disease and to give information about sex, heredity and marriage. The scope of genetics adopted by the Society evolved as more knowledge of genetics became available to the scientific community. Until the early 1930s the hereditary nature of many traits now known to be infectious diseases was accepted. In addition good and less desirable moral qualities as well as scientific and artistic ability were treated as if they had simple patterns of inheritance and transmission. In the mid 1930s the Society had begun to appreciate the complexity of inheritance and had adopted the concepts of dominant and recessive transmission. By this time the Society was also distancing itself from the eugenic ideas adopted by Nazi Germany. As Hitler became more anti-semitic, Nazi racial and eugenic policies merged and the extremely barbaric Nazi policies eventually provoked a powerful anti-eugenic feeling.

Organisations to further eugenic ideas were also established at an early date in other countries. In Holland a committee was formed to urge the need for medical research before marriage and to convince mankind that one is morally bound to ask for medical advice before marriage, which ought to be done both in the interests of the enquirers and of the offspring (Schuster 1912 p55).

2.3.6 Genetic advice and genetic hygiene: forerunners of genetic counselling

Until the end of the Second World War, 'genetic hygiene' and 'genetic advice' were the terms used to describe what is now called 'genetic counselling'. The information was given by a variety of professionals, including doctors in public health, sociologists and biologists. Many of these people were zealous social reformers and social philanthropists. Genetic information was aimed at groups in society, e.g. the mentally ill and the feeble minded, through lectures and the dissemination of pamphlets and literature (Huxley 1936, Kevles 1986), rather than directed at individuals.

The principal aims were to prevent the breeding of poor stock and therefore to reduce the social and economic burden to society. There is some evidence in the records of the Eugenics Society (Hall 1990) that information was also given to individuals, but the content of information given to individual people and by doctors to individual patients during this period is not well documented. As the aim was to reduce further harm to society, it is not unreasonable to assume that the personal needs of the individual patient were not necessarily considered (Twiss 1979).

In the period prior to 1945, while individual doctors had an understanding and knowledge of the growing information about the influence of genetics on disease, the main thrust of information, research and interest in genetics came from organisations such as the Eugenics Society and the scientific community. Although members of the Eugenics

Society, the scientific community and social reformers wrote and distributed pamphlets and gave lectures on the implication of heredity and genetic diseases, they did not have the infrastructure to organise genetic counselling service for individual patients. The application of the knowledge of heredity to disease had still to be accepted by the medical profession, who would then provide genetic information and the infrastructure necessary for the further development of genetic counselling.

Thus the period of the first paradigm is characterised by the discovery of Mendelian inheritance and the activities of the Eugenics Society. Their broad aims were to encourage the weaker stock to have fewer children and the more talented to have more, but neither of these groups of people was in the habit of consulting their doctor about how many children they should have. The genetic inheritance of individual diseases was not yet widely understood in the medical profession, and individual patients were hardly affected by the activities of the eugenics movement.

2.4 PARADIGM 2: PREVENTIVE MEDICINE

After the Second World War and with the realisation of the extent of Nazi atrocities, eugenics became a word to be hedged with caveats (Kevles 1986 p251) and many scientists withdrew their support from the eugenic movement (Kessler 1980).

Since 1950 there had also been a decline in infant mortality and childhood morbidity due to the availability of antibiotics and better control of infectious diseases. In addition improved medical and nursing care resulted in the survival of many infants who previously would have died shortly after birth (Connor and Ferguson-Smith 1987).

The reduction in mortality from infectious diseases produced an increase in the proportion of deaths attributed to congenital abnormalities among infants and an increase in the proportion of cases in both childhood and adult morbidity (Emery and Pullen 1984).

Different authors have attempted to estimate the extent of fetal abnormality present at birth and attributable to genetic abnormality. For example, according to Pembrey (1987) at least 1% of all live births have a disorder inherited in a simple Mendelian fashion that is manifest at birth, or will develop later. Pembrey suggests that if the multifactorial conditions where there are substantial genetic influences are included the figure rises to 2-5%.

Furthermore, researchers such as Stickle (1965) have estimated that birth defects, because of their relative early onset, account for a heavier loss or reduction in productive future years than other more widely recognised public health problems such as cardiovascular disease, cancer and stroke. Others such as Wilkie (1980) and Roberts (1991) have pointed to the appreciable contribution made by genetic diseases to the morbidity and mortality load of the community.

After the Second World War the medical profession in Britain was beginning to take an interest in genetic counselling. In 1946 a genetic clinic was established at the Hospital for Sick Children, Great Ormond Street, London (Roberts and Pembrey 1985 p324). It is not surprising that the first genetic counselling centre was in a children's hospital since people tended to seek or were sent for genetic information because they had had a child affected by what either the parents or their doctor suspected was a genetic disorder. This situation is often referred to as 'retrospective counselling'.

Furthermore, by this time the philosophical basis of medicine had broadened to include the concept of prevention (Porter 1977). The application of genetic principles to medical illnesses harmonized well with this extension of the role of medicine. The prevailing ethos in this second paradigm of genetic counselling is one of preventive medicine, but in this period genetic counselling became firmly embodied in the medical

setting in hospitals and carried out within the doctor-patient relationship. In this paradigm the focus is, therefore, on the doctor and the individual patient.

Another feature of this paradigm is that most genetic counselling was still retrospective. Patients were referred for genetic counselling following the birth of a child with a genetic handicap or following the diagnosis of a genetic disease in themselves.

2.4.1 Content of genetic counselling in paradigm 2

The focus in the content of genetic counselling in the second paradigm is on giving information about the diagnosis and the risk of occurrence or recurrence and this reflects the tools and knowledge of the genetic counsellors. Fraser (1968 p928) in his description of what the genetic counsellor does states: "... the genetic counsellor confirms and establishes the diagnosis; takes a family history; performs and arranges for appropriate tests; uses this information to make an estimate of the probability of recurrence; conveys the significance of the probability to the counsellee". However the information that could be offered in genetic counselling at this time was limited to information about the diagnosis and the significance of the risk or probability of occurrence or recurrence of the particular disease. The particular expertise of the medical geneticist was in calculating the risk of transmission. This limitation of knowledge is commented upon by Fraser (1958) "... much new information is needed ... new means of detecting genetic 'carriers' of disease will greatly increase the precision of the counsellor's predictions in many cases. In the meantime the paediatrician consulted about the possibility of family occurrence of a disease must make best use of what information is available ... and exercise proper caution in applying average risk rates to individual situations ..." (p488).

2.4.2 Aim of genetic counselling in paradigm 2

As already noted, by 1940, the philosophical basis of medicine had broadened to include the concepts of prevention (Porter 1977). With their knowledge of heredity doctors were now able to offer genetic counselling to parents affected by a genetic disorder and thereby: "... prevent the unwitting passage of a disease to subsequent generations" (Porter 1977 p23).

While it is unlikely that many doctors offering genetic counselling in this period would have considered themselves eugenicists, the objective of their counselling clearly was to prevent. For example Dice (1952) believed that voluntary abstention from reproduction by those people who carry hereditary defects was consequently the only practical method for eliminating any considerable number of harmful genes from the population of a democracy and he says: "From my experience in giving advice about heredity to families in all walks of life I can affirm that every parent desires his children to be free from serious handicap ... and if there is a known high probability of transmitting a serious defect, it would be an abnormal person indeed who would not refrain from having children." (p2).

The same author considered that there were only two practical ways available for the elimination of harmful genes: "Either those who carry the defective defects may be segregated or sterilised by the state or they may voluntarily refrain from reproduction". The author does not recommend that any pressure be put on prospective parents but that "sterilisation of those persons who carry obvious hereditary defects should continue to be carried out on a voluntary basis" (p2).

In this example there is an assumption that patients would be motivated by societal goals, a feature also of the first paradigm. There is also an underlying expectation that the

patient will be compliant with the authority and recommendations of the doctor within the traditional doctor-patient relationship.

2.4.3 Measurement of effectiveness of genetic counselling

Studies examining the effectiveness of genetic counselling (Shaw 1977, Evers Kiebooms and Van Den Berghe 1979) demonstrate that the criteria most consistently used by genetic counsellors to evaluate the success of their work was patient knowledge and patient reproductive intentions and/or behaviour after counselling.

The assessment of patient knowledge mainly focused on the patient's understanding of the risk of recurrence or occurrence of the particular disease. The results show wide variability in the knowledge of patients about the risk after counselling. Pearn and Wilson (1973} found that only 26% of their sample knew the genetic risks after counselling. Sibinga and Friedman (1971) found that there was no correlation between the education level of parents and their understanding of the genetics of the disorder phenylketonuria with fewer than 20% of parents having an adequate understanding. However, authors such as Emery et al (1972) and Carter et al (1971) reported what they described as effective understanding of risks. According to Leonard et al (1972), 44% of their sample misunderstood, denied, distorted or incorrectly interpreted the genetic information. In spite of the lenient interpretation of their test results, these authors found that only one half of the sample had sufficient information to make informed and rational choices.

It is not surprising that the quantification of the risk was seen as the essential information as this was to a great extent the major expertise that the medical geneticist had to offer patients at this particular point in time. The understanding of the nature of risk is, however, complex. Tversky and Kahneman (1981) suggested that all theories of decision making under risk contain two basic components: (a) the desirability of the

outcomes to the individual or individuals concerned, and (b) the perceived likelihood of the desired result eventuating.

Pearn (1973) in discussing patients' subjective interpretation of risks offered in genetic counselling, suggested that in the genetic context the former of these two factors - the desire for children and in particular healthy children - represents a basic attitude determined before the specific genetic status of the individual is known. Pearn suggested that whether or not at-risk parents following genetic counselling satisfied this universal desire to have children depended very largely on the subjective interpretation of odds given to them.

For example, in a study by Carter et al (1971) two thirds of couples who were at high risk, i.e. greater than 1 in 10, of having a child with a particular genetic disease were deterred from having further children following genetic counselling. Similar results were found by Ives et al (1973). However, in the work of Hsia and Silverberg (1973) as many as 75% of those considered at high risk of having a child with a particular genetic disorder either decided to have more children or remained undecided.

The interpretation by patients of the risk figures given to them may also be influenced by the manner in which risk is explained to them. An explanation that there is a 1 in 4 risk of having a child with an abnormality may be interpreted very differently from the explanation that there is a 3 to 1 chance of having a child without the particular problem. Similarly the explanation that there is a 50-50 chance of developing a disease (in the case of variable age of onset autosomal dominant disorders) may be interpreted very differently from the explanation that there is a 50-50 chance that the patient will not develop the disease. Counsellors may consciously or unconsciously choose to emphasise one fraction or another depending upon how they wish the situation to be interpreted by the patient. Pearn (1973) believed that "... at the core of the subject lies the individuals

ability to appreciate the mathematical symbolism of exact risks, or at least the ability to appreciate relative orders of risk ...". This argument was also supported by Howell and Burnett (1978) who suggested that the formulation of a realistic interpretation of odds is dependent on how well subjects are available to reflect their actual perception of probabilistic events or degrees of certainty.

It is important to appreciate that these studies which have just been discussed fail to point out that while the concepts of risk and probability are useful in aggregate for large numbers of cases, they may cease to be useful in single, individual situations such as in genetic counselling, where other considerations such as the burden of the disorder and other medical, social and economic factors may influence the decision more than the mathematical odds (Wilkie and Sinclair 1977). Rational decision making may be more difficult when only one or a few gambles are to be taken,rather than a large enough number for the 'law of averages' (strictly the law of large numbers) to apply, and decisions then may be quite unrelated to probabilities.

A further problem in the interpretation of these studies is that they do not say precisely what information was given to the patient and how that information was phrased since this may also influence the decision making process.

The measurement of reproductive behaviour after counselling was carried out by several authors (Emery et al 1972, McCrae et al 1973, Carter et al 1971). Carter's study showed that an increased genetic risk tended to deter families from having further children and in this study "no high risk couple in the study had planned a further child with a serious long term handicap". However these couples were not deterred from having further children if the affected child was expected to die young, if treatment was available or if the condition was mild. In a study by McCrae et al (1973) one third of the parents

of cystic fibrotic children reported that they had not received any family planning information.

It is clear from these studies that information about the risk of transmission of a genetic disorder was not the sole factor in influencing subsequent reproductive behaviour. In addition work by Sorenson (1974) suggested that many patients do not remember or understand the genetic information that they have been given. Kessler (1980) argues that those offering genetic counselling were becoming aware of the large discrepancies between their goals as genetic educators and the realities actually achieved.

A direct consequence of the understanding of the limitations of the approach to genetic counselling which emphasised prevention, was a movement away from the medically led genetic counselling based on information and advice, to genetic counselling in which there was a greater awareness of the psychological needs of the patient and which was focused on the needs of the patient. This leads on to the third paradigm.

2.5 PARADIGM 3: PSYCHOLOGICAL MEDICINE

Writing in 1980 Kessler suggested that genetic counsellors were becoming more aware of the dilemmas posed by a model of genetic counselling that emphasised prevention. In particular there was increasing evidence that the goal of prevention of genetic disease was not a realistic one, with authors such as Epstein (1977) suggesting that persons at risk for genetic disorders were sometimes reluctant or resistant to using available prevention technology. There was often a gap between what the counsellors hoped would be the results of genetic counselling and the actual results. For example, in a follow-up of 200 couples seen in a genetic counselling clinic, Emery et al (1979) found that over one third of those couples who had been told that they were at high risk (greater than 1 in 10) of having a child with a serious genetic disorder were *undeterred* and

planned further pregnancies. Writing five years later the same author said: "in the past such behaviour was often regarded as 'irresponsible', a failure on the part of the counsellor and an indictment of counselling in general. But when the couples were carefully questioned their reasons for planning further children were often very understandable." (Emery and Pullen 1984 p4).

It is arguable that in a model of genetic counselling that emphasises prevention, the counsellor is protecting the social good, possibly at the expense of the individual patient. Most counselling is carried out by doctors and in the relationship between a patient and the doctor, it is frequently assumed that the interests of the patient always come first. The British Medical Association in their *Handbook of Medical Ethics* (1984) states that for the individual doctor "the health of my patient will remain my first consideration" (pp70-72), although acknowledgement is given to the principle of service to humanity endorsed in the statement that it is "the mission of the medical doctor to safeguard the health of the people " (pp43-46).

In the period of the third paradigm genetic counsellors were beginning to consider the autonomy of the patient by favouring the rights of individual patients to choose their own reproductive destiny. Counsellors were also appreciating the psychological needs of the individual patient.

The paradigm shift to a more psychologically oriented genetic counselling as suggested by Kessler became evident in the United States some years before such a change was evident in the United Kingdom. This can be explained by the fact that in the United Kingdom, genetic counselling had been given generally by medically qualified staff mainly based in departments of human genetics. By contrast in the United States other professionals, such as psychologists, sociologists and specially trained genetic counsellors or genetic associates in addition to doctors, had already become involved in both the

process and the evaluation of genetic counselling. It is arguable that these professionals brought different skills and different perspectives and raised awareness of the psychological and social components in genetic counselling including the way in which patients acquire information and reach decisions and the coping strategies used by patients in dealing with a difficult medical diagnosis.

The extension of the role of genetic counselling to nurses, health visitors and psychologists in the United Kingdom has been a recent phenomenon. For example the first course in genetic counselling for community nurses started in London in 1991 (Anionwu 1992) although a course for specialist genetic nurses in post had already started in Cardiff.

An acceptance of a wider view of genetic counselling embracing the psychological needs of the patient is reflected in the following widely used definition of genetic counselling written by the Ad Hoc Committee on Human Genetics (1974) and reported in Fraser (1974). Genetic counselling is a "communication process which deals with the human problems associated with the occurrence, or risk of occurrence, of a genetic disorder in the family. This process (Fraser 1974) involves an attempt by one or more appropriately trained persons to help the individual or family to:

(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 risks 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 recurrence of that disorder."

This definition is broad. Counselling is aimed both at those who have already been faced with a genetic disorder as well as those concerned with their risk. Many skills including the ability to communicate genetic knowledge and counselling skills are required. In addition, in order for (3) and (4) to be accomplished counsellors would need to have a detailed knowledge and understanding of the patient including their aspirations and their values. This definition points to the complexity of the process of genetic counselling, and implies what could be the content of genetic counselling as well as what skills are needed by the counsellor.

Furthermore, during the 1970s attention was being paid to the impact that genetic information could have on the lives of patients and their families, and there was an awareness that an understanding of these factors could lead to improved effectiveness in genetic counselling (Reynolds et al 1974).

This impact of genetic counselling on the individual patient began to be discussed in articles in the popular press. For example Tysoe (1983) comments on the difficulties involved in "grappling with the psychological and ethical dilemmas raised in genetic counselling" and goes on to suggest that while theoretically all genetic counselling is non-directive it is "very hard for doctors to do, as their whole training is geared towards giving advice and preventing disease" (p276). Issues such as the cost of treating and not treating genetic disorders and the difficulties in decision making following genetic counselling were debated by the Council of Science and Society in *Life and Death before Birth* (1978).

Authors such as Gaylin (1972 and 1976) and Wilkie (1980) questioned the ethics of genetic screening which gave people information about genetic traits or defects which

cannot be remedied and which may cause anxiety and a feeling of stigmatization, and Shore (1975) emphasised the need for psychological support in genetic counselling by highlighting such adverse reactions of genetic counselling as depression, family disruption and desertion (p170).

By the early 1980s several academic textbooks addressing the psychological dimensions in genetic counselling by American authors, e.g. Kessler (1979), Sorenson et al (1981), Applebaum and Firestein (1983) and also by Emery and Pullen from the United Kingdom (1984) had been published.

This realisation that genetic counselling is not just a matter of giving information including probabilities, to the patient, but that the psychological needs of the patient should also be taken into account leads into the ethical issues that are the heart of the fourth paradigm.

2.6 PARADIGM 4: ETHICS

During the 1980s another conceptual shift took place in which genetic counselling came under greater scrutiny. This forms my fourth paradigm. In this fourth paradigm there is a movement away from what was essentially retrospective genetic counselling (although there will always be a need for retrospective genetic counselling) to a more proactive form of genetic counselling. Proactive or prospective genetic counselling can be defined as an activity in which individual prospective patients are sought out and offered genetic counselling. These may be the relatives of an index patient, i.e. an already identified patient. This is conceptually different from the situation where the patient has sought help and has been referred to a genetic counsellor.

The shift towards proactive genetic counselling has raised a number of ethical issues that were not previously relevant to genetic counselling. Proactive genetic

counselling has been made possible by a number of developments, each of which raises different ethical problems. The availability of computers and the use of record linkage (Benjamin 1977) raises questions about the confidentiality of information and the right of doctors to approach patients who have not consulted them. The availability of prenatal diagnosis for a number of genetic diseases raises questions about the role of termination of pregnancy. The availability of presymptomatic diagnosis raises questions about whether those affected ought to know, and who owns the information. The development of population screening programmes for certain single gene recessive disorders raises similar problems, in respect of those with carrier status. Each of these is discussed in the ensuing sections. Presymptomatic testing raises problems in a specific field, that of life assurance. Finally, the question of the possibility of neutral genetic counselling is discussed.

2.6.1 Genetic registers and record linkage

According to Harper (1983), genetic registers can be established with diverse aims. The main categories of genetic register are: preventive, therapeutic, epidemiological, reference and research. It is preventive registers that are of interest here. The principle aim of preventive registers is to help the avoidance of births of children with a genetic disorder by "recording those families and individuals who are affected or who have a high risk of transmitting the disorder in question" (Harper 1983 p118).

One example of a preventive genetic register was the genetic register system RAPID (Register for the Ascertainment and Prevention of Inherited Disease) (Smith et al 1971). This system involved the ascertainment of individuals in the population who might have been at risk of having a child with a serious genetic disorder, the determination of their risks, the follow-up and provision of genetic counselling and antenatal diagnosis (where applicable) for those found to be at high risk (defined as greater than 1 in 10) of

a serious genetic disorder. It was believed that RAPID was a feasible and relatively inexpensive method of ascertaining and preventing cases of serious genetic disorders (Emery et al 1974).

Another example of a preventive genetic register is the South Wales Huntington's Chorea Register, which as well as providing information on individuals to be seen clinically, has made it easier to monitor the incidence of the illness (Harper 1983).

The use of these registers has enabled doctors to offer proactive genetic counselling systematically, because accurate information is recorded about the index patient as well as about his or her at-risk relatives. In proactive genetic counselling the relatives at risk for a particular disorder are contacted and offered genetic counselling. While such a system could operate without the use of computers, their use has made it very much easier.

The introduction of systematic proactive genetic counselling raises some very serious concerns about the risk of psychological disturbance in those who learn early of their risk of contracting an illness for which there is no effective treatment. Such early knowledge may also affect applications for insurance and even employment opportunities and in this context the question of confidentiality is raised. The power of modern computers means that much information can be easily stored and easily accessed necessitating the need for strict security for genetic registers.

It is also arguable that such genetic counselling should be restricted to those who seek it and who are referred by their doctor and should not include those relatives who have not requested such counselling.

Wilkie and Sinclair (1977) in their study on the acceptability of genetic registers point out that it is not always clear, particularly in prospective or proactive counselling, who is to be the beneficiary of the genetic counselling. Is it the at-risk person or patient

who has been identified, the as-yet-unborn child or the society of the future? Nor is it known whether at-risk individuals wish to know of their own risk or involvement with the particular genetic disorder. It is also not clear whether the advantages to society of telling individuals of their involvement outweigh the possible disadvantages. These authors suggested that the advantages can be seen at both a personal and at a societal level. By telling such individuals of their situation, geneticists hope that individuals will behave 'responsibly', i.e. they will not have children. As a result the burden and the responsibility of having a possibly affected child may be removed, presumably to the advantage of the individual and their partner and to society. The personal disadvantages seem to lie mainly in the anxiety and suffering that may be caused by telling such an individual of their risk and the difficult decision making that is often called for (Wilkie 1980).

2.6.2 Prenatal diagnosis for genetic diseases

There have been very considerable advances in the techniques now available to diagnose genetic diseases prenatally. These techniques and the risks associated with them are discussed in Section 2.7. Prenatal diagnosis for genetic disease followed by termination of an affected fetus, should this be what the parents want, is a choice that is now available to an increasing number of parents.

According to Laurence (1991) terminations for genetic reasons account for approximately 2% of all terminations in the United Kingdom (p79). However, there is already evidence that some women are permitted prenatal diagnosis only if they agree in advance to an abortion should the fetus be abnormal (Farrant 1985 p113). In these circumstances the mother is hardly being offered her own choice. Similarly, according to Rothman (1988), the choice to avoid having a child with a handicap also becomes a forced

choice; she states; "in gaining the choice to control the quality of our children, we may rapidly lose the choice not to control the quality, the choice of simply accepting them as they are " (p191).

It is arguable that prenatal diagnosis both reflects the values of society and also puts pressure on parents to conform to these values. As McIntyre (1987) argues, the language in which prenatal diagnosis is offered to women, "to ensure that the baby is all right", implies that all possible abnormalities will be detected, whereas in reality only certain abnormalities can be identified and not all of these are investigated in any one case. The dilemma for parents is that it is not considered acceptable to allow a newborn handicapped baby to die but it is considered highly desirable to terminate a pregnancy where the baby is known to be affected (Green 1990). A major concern is that parents who decline prenatal diagnosis and parents who reject termination of pregnancy may be seen as having brought the situation on themselves. Such a concern may be more acute in times of economic stringencies and high costs for health services.

Markova (1990) argues that while it is to the advantage of a society that its members be healthy, advances in genetics have put the burden for improving the health status of the country on individuals at risk or affected by genetic disorders and she suggests that these advances raise profound ethical dilemmas.

It is necessary to question what the underlying problem is for which prenatal diagnosis and termination of pregnancy is the solution, and to consider that the views of the parents and the professionals may not be the same.

2.6.3 Presymptomatic diagnosis of genetic diseases

The availability of DNA analysis can now be used to determine the presence or absence of a particular gene in a person postnatally as well as prenatally. These techniques

have, for the first time, allowed a very high degree of accuracy in diagnosis in genetics. It is now possible to use DNA analysis to diagnose such disorders as haemophilia, cystic fibrosis, Huntington's Chorea and adult polycystic kidney disease (APKD).

Both haemophilia and cystic fibrosis affect children and while not all prospective parents may wish prenatal diagnosis followed by termination of pregnancy, prompt and accurate diagnosis postnatally so that treatment can begin is uncontroversial.

The situation with Huntington's Chorea and APKD is very different. They are both diseases of variable age of onset, the symptoms not appearing until middle years. For Huntington's Chorea there is really no effective treatment. The treatment for APKD is of the symptoms as they appear, as described in Section 3.8.

While there are clearly advantages for an at-risk individual to learn that they do not carry the gene for a particular disease, one has to question what the advantages are to the individual of knowing that they are affected before the symptoms begin if it is by a disease for which there is no treatment. The technology is available, but do people wish to use it?

Rosenfield (1984) has argued that the central issue created by these new technologies concerns the question of disclosure of genetic knowledge. Rosenfield was concerned with the amount of pressure that may be put on a person who was, for example, at risk for Huntington's Chorea to be tested. The partner of such a person may want to know what the future holds. Offspring may want to know in order to establish their own genetic status. A decision to disclose genetic knowledge raise a number of further ethical questions including when the information should be disclosed, how it should be disclosed, who should be told and by whom (Harper 1992).

In this respect, and in relation to Huntington's Chorea, it has been suggested that predictive testing for minor children as well as for couples who seek prenatal diagnosis

but hesitate about terminating a high risk pregnancy, should be unavailable (Bloch and Hayden 1990). According to Pelias (1991) parents of minor children would therefore be classified as third parties whose interests in their own minor children would be equated with the interests of "adoption agencies, educational institutions, insurance companies and other third parties" (Pelias 1991 p349). According to Pelias the reason for limiting the interests of parents by classifying them as third parties is to protect the privacy and autonomy of the minor child. As parents are usually considered the sole decision makers for their children's health, this suggestion raises the question of paternalism in genetic counselling as well as challenging the principles of parental autonomy.

The debate about the right to information also applies to the adult. Protocols for molecular genetics predictive tests in Huntington's Chorea have been developed (Went 1990) and they could be used as guidelines in the presymptomatic testing of other late onset genetic diseases for which there is no effective treatment. Such protocols point to the need for pre-test counselling, a period of consideration before taking the test and the availability also of post-test counselling.

2.6.4 Population screening for genetic disease

Prospective counselling of large groups in society involves identifying people with incipient disease so that prompt treatment may avert harm (Beck et al 1974). Population screening can also be used to identify otherwise healthy persons who may be heterozygous carriers of certain genetic diseases and to explain to them their risk of having affected children if they mate with another heterozygous carrier of the same gene (WHO 1972). This approach has become used widely in populations where the frequency and severity of a particular disease is high. For example there are programmes directed against sickle cell disease in populations of Afro-Caribbean descent (Massarik and Kaback 1981), against

Tay-Sachs disease amongst Jews of Ashkenazi descent (Kaback 1977), and against G6PD deficiency and thalassaemia in populations of Mediterranean descent (Bundey 1991). Individuals identified as carriers of recessive genes are told that they may have a child with a particular disease if they mate with another carrier.

What are the implications for the individual of being confirmed as a (heterozygous) carrier of a genetic disorder? To be a carrier of a genetic disorder does not mean illness or disability. With very few exceptions carrier status does not carry with it any observable indices of being different, unlike having the disease itself. But it is possible that to be identified as a carrier may cause the development of psychological disabilities. These disabilities would result not from being a carrier but from the personal and social meanings which may become attached to carrier status. It is, therefore, the carrier's perception of the carrier status that is important.

The time in a person's life when they are identified as a carrier may significantly affect the psychological and social meaning of carrier status. For example, if screening is carried out before marriage the knowledge that the person is a carrier may affect whom that person marries and whether he or she has children. Further, the scientific label of carrier status could acquire a psychological interpretation for the person, threatening their sense of personal worth and integrity (Sorenson 1974). For some, carrier status may be perceived as stigmatising, as described by Goffman (1968). This perception of stigma is similar to the stigma perceived by the asymptomatic HIV carrier (Anderson 1992) or by the person with epilepsy (Edwards et al 1986). Furthermore, once a person knows of their carrier status they are no longer able to deny this information. Prior to learning of their carrier status the person was able to say that there was a possibility that they were a carrier and there was equally a possibility that they were not a carrier.

In establishing population screening programmes consideration has to be given to the factors that would motivate an asymptomatic individual to comply with a screening test. There is increasing awareness that such factors as the person's perception of the susceptibility to and their perception of the seriousness of the inherited condition could influence their decision to agree to a screening test (Ivker et al 1974).

2.6.5 Genetic testing and life assurance

The increased understanding of genetic inheritance and the availability of presymptomatic testing has a significant effect on life assurance. Before there was any understanding of genetic inheritance a presymptomatic individual who had no other impairment could obtain life assurance at the ordinary premium rates. The same still applied after genetic inheritance became understood, if the applicant had no knowledge of the family history that might cause him or her to be at risk, if the life assurance proposal form did not elicit this information in its questions, or if the life underwriter was insufficiently knowledgable or alert to the significance of the information that had been elicited.

However, once life assurance underwriters came to understand the principles of genetic inheritance, if applicants gave sufficient information for them to be identified as being at risk of developing a particular disease, for example by stating that one parent had died of APKD or Huntington's Chorea, they became uninsurable. They had a one half chance of developing the disease, but even though they also had a one half chance of not developing the disease neither the applicant nor the underwriter knew which chance would fall out.

Now that presymptomatic testing is available for certain diseases further considerations arise. If the applicant is tested, he (or she) may discover that he is not

affected with the relevant gene, and he becomes insurable at ordinary premium rates, provided he has no other impairment. But if it is discovered that he is affected, then he becomes certainly uninsurable, quite apart from any other problems that may ensue from this knowledge.

There are similarities with HIV testing, though there are also differences. Inability to get life assurance and hence (in many cases) a loan for house purchase is frequently stated to be a serious disadvantage for an individual who is found to be HIV antibody positive and it is particularly problematic for the asymptomatic HIV positive patient (Wilkie 1987). It has become widely believed that an insurance company is likely to decline to insure anyone who has had an HIV test, whatever the result, even though the insurance companies themselves deny that a negative test by itself would prove adverse. What they really mean is that a negative test for an applicant who is gay and who was tested because he was worried would be treated adversely, whereas a negative test for an applicant who required one for travel to some particular country would not be; but it would be insensitive of the insurance companies to say this explicitly.

The situation for those who have had a genetic test for a disease of later age of onset may appear to be not dissimilar. Just as there was evidence that people were deterred from being tested for HIV because of their fear that they would subsequently be unable to get life assurance regardless of the results of the test, there is now some evidence of the same concern, however illogical, regarding genetic testing. For example the Health Council of the Netherlands (1989), quoted in Harper (1991), stated: "If it is felt that the suspicion that fear of insurance problems may deter some individuals from genetic testing is well founded in an atmosphere of growing uncertainty, genetic testing could be perceived as threatening" (p7).

2.6.6 Neutrality of counselling

Emery and Pullen (1984) refer to the neutrality of genetic counselling when they say: "we are moving away from entirely factually oriented counselling to person oriented counselling. ... It is only in this way that counselling is likely to be really meaningful and couples helped to make decisions which are the right ones for themselves. There is no place for directive counselling" (p vii).

There is an assumption here that it is possible to have non-directive, neutral, genetic counselling. Counselling is seldom neutral. The counsellor comes with genetic knowledge. That knowledge is not necessarily neutral. For example, Anderson (1992) has pointed out in relation to AIDS that the "facts about HIV and AIDS do not represent some unquestionable reality, but are the products of complex processes of social construction". Similarly, in genetic counselling it is extremely difficult for counsellors to avoid communicating their own values and beliefs, if not by what they say, then by their body language, tone of voice or choice of words.

For example the patient may be told that prenatal diagnosis and termination of an affected fetus is available. The counsellor may think that the information was delivered in a neutral fashion for the patient to reach their own decision. But unless the patient was also given sufficient information about the treatment and facilities for a child who may be affected by the particular disease should she (or he) decide not to have prenatal diagnosis followed by termination of an affected fetus, the patient is unable to make an informed choice. Furthermore she may perceive that she is expected to have prenatal diagnosis because she was not given any other information.

Giving the patient information in a way that respects the patient's own ability to reach a decision empowers the patient. The concept of patient empowerment has been highlighted particularly by those involved in HIV counselling (Anderson 1992).

The process and content of genetic counselling is now under wider scrutiny. For example, in 1987 the King's Fund ran a forum on screening for fetal and genetic abnormality and published a consensus document (King's Fund 1987). Consumer organisations such as GIG (Genetic Interest Group) have recently been invited to discuss the organisation of genetic counselling services with the Royal College of Physicians, London (Hunt 1992).

2.6.7 Characteristics of paradigm 4

The new knowledge (of testing) and the new equipment (computers) have caused genetic counselling to move into another phase, in which it can be seriously questioned whether the application of the new technology is in fact beneficial to those affected with, or who are at risk of being affected with, a particular disease.

Counselling patients who come for advice is one thing; seeking out patients to counsel is another. Obtaining information from a patient about those who are not yet patients is questionable. Offering prenatal testing with the threat of termination of an affected fetus may not be the way to give choice to parents. Those who are presymptomatic but affected and for whom no treatment is available may prefer to remain in ignorance until treatment becomes necessary. Those who are carriers of a recessive disorder might pass their whole lives without ever discovering this fact; do they need to be told? And is it possible to provide wholly neutral, non-directive counselling of any kind, genetic or other? All these issues are now under discussion and the answers are not yet resolved.

2.7 TECHNIQUES USED IN PRENATAL DIAGNOSIS

In the final section of this chapter the procedures now available for the detection of prenatal abnormality are described. There are four of them: amniocentesis, ultrasound, fetoscopy and fetal blood sampling, and chorion villus sampling. Two of these procedures, amniocentesis and ultrasound, have been available for some time. Ultrasound is the only procedure that is non-invasive and as far as is known carries negligible risk to the fetus.

2.7.1 Amniocentesis

Amniocentesis was first introduced some 20 years ago and is the most widely used invasive prenatal diagnostic technique (Rodeck 1987). The procedure is usually carried out at 16 weeks gestation. Under ultrasound guidance, a needle is passed through the abdominal wall to draw off amniotic fluid from the amniotic sac that surrounds the fetus in the uterus. Amniotic fluid contains fetal cells which can then be sent for examination. The investigations that can be performed include chromosome analysis, biochemical and DNA studies and alphafetoprotein and acetylcholinsterase estimation. Cytogenetic reports are available in approximately three weeks. The most common reason for amniocentesis is fetal chromosomal analysis in mothers at increased risk of having a child with Down's syndrome. All the numerical and many of the structural chromosomal abnormalities such as Down's syndrome (Trisomy 21) can be detected by culture of cells obtained by amniocentesis.

The main complication of amniocentesis is miscarriage. However amniocentesis at 16-17 weeks gestation is considered quite a safe procedure with the risk of causing a miscarriage that would not have otherwise occurred being of the order of 1 in 150, with the risk increasing if repeat amniocenteses are required (Roberts and Pembrey 8th edition 1985). According to these authors, studies have failed to demonstrate any risk to the

mother's health, or any evidence of a significant risk of damaging the fetus with the needle, provided that amniocentesis is carried out under proper conditions and under ultrasound control.

Prenatal diagnosis of the major neural tube defects, anencephaly and open spina bifida can be diagnosed by a raised level of alphafetoprotein in amniotic fluid at 17 weeks gestation.

2.7.2 Ultrasound

Ultrasound examination plays a critical role in prenatal diagnosis allowing the detection of structural abnormalities and the detection of abnormal growth by regular ultrasound examinations. Ultrasound can reveal the internal anatomy of the fetus, whether the fetus is alive, and how many fetuses there are and it can confirm gestational age. Ultrasonography is used for the guidance of all invasive investigative procedures. There is no evidence that diagnostic ultrasound is harmful.

2.7.3 Fetoscopy and fetal blood sampling

Fetoscopy is used for direct observation of the fetus. The procedure involves the insertion of a fetoscope through the abdominal wall into the amniotic sac. The fetoscope has a channel for withdrawing fluid or blood in addition to the fibreoptic and lighting system. Fetoscopic examination can be used to confirm a diagnosis by ultrasound as well as being the primary means of prenatal diagnosis for example to diagnosis such abnormalities as small or absent ears.

Fetal blood obtained by fetoscopy is used in the prenatal diagnosis of beta-thalassaemia and it has also been successfully used in the prenatal diagnosis of Von Willebrand's disease and various red cell enzyme defects.

Fetal blood sampling cannot be carried out until 18 weeks gestation and analysis takes about one week. Fetal blood sampling is associated with a fetal mortality of between 2 and 5 per cent and an increased maternal morbidity due to infection and haemorrhage (Weatherall 1991 p257).

2.7.4 Chorionic villus sampling

Chorionic villus sampling (CVS) is a method of obtaining a small sample of tissue from the region of the chorion frondosum where the villi persist and eventually form the placenta. The procedure was introduced in 1982 and is carried out in the first trimester of pregnancy, usually at about 10 weeks gestation, by a suction tube inserted transcervically or transabdominally. The range of possible investigations is similar to amniocentesis and includes chromosomal, biochemical and DNA analysis. Alphafetoprotein for neural tube defects cannot be measured from chorion villus. The precise risks of chorion villus sampling are not known but fetal loss is probably increased by 2% (Rodeck 1987).

Chorion villus sampling has greatly advanced the ability to diagnose certain genetic disorders prenatally by DNA analysis. DNA samples can be obtained from chorion villus and results can be available in 48 hours.

There are several ways to analyse fetal DNA for single gene disorders like APKD. Currently prenatal diagnosis using restriction fragment length polymorphisms (RFLPs) is being used successfully in the diagnosis of diseases such as APKD, Huntington's chorea and neurofibromatosis (Weatherall 1991). The limitations of this approach are the complexity of the investigation and hence the expense. Furthermore this technique can only be offered to women where linkage has previously been established in appropriate family members (Gabow et al 1992).

A major problem associated with amniocentesis, fetoscopy and fetal blood sampling is that these procedures cannot be carried out until the second trimester of pregnancy as many of the conditions for which prenatal diagnosis is required necessitate the growth of amniotic cells in culture for several weeks. Parents, therefore, not only have to consider the risks of the individual procedures but also the implications for termination when the diagnosis is made late in the second trimester. By the end of the second trimester the mother will have experienced fetal movement and may have already bonded with this baby. In addition her pregnancy will have become obvious, which may exacerbate her difficulties should she decide to terminate. Psychological trauma following a late second term termination may not be inconsiderable (Green 1990).

CHAPTER 3: ADULT POLYCYSTIC KIDNEY DISEASE

3.1 Introduction

This chapter is divided into three main parts. After a short section (Section 3.2) in which Adult Polycystic Kidney Disease (APKD) is described, the first main part (Section 3.3) describes the development of the knowledge and understanding of APKD from the 19th Century to date in terms of symptoms, diagnosis, clinical history and understanding of genetics as applied to APKD. The second part (Sections 3.4 and 3.5) describes the functions of the normal kidney as well as some common renal function tests. The third part (sections 3.6 to 3.9) describes the diagnosis and symptoms of APKD, the treatment for end stage renal failure (ESRF) and the prognosis for APKD.

3.2 Description of APKD

3.2.1 APKD: the illness

Adult Polycystic Kidney Disease (APKD) is the most common inherited renal disease leading to end stage renal failure (ESRF) and the need for renal replacement therapy. It is estimated that APKD is responsible for 6-9% of cases of ESRF in Europe (Robinson and Hawkins 1981). Prior to the need for dialysis there is likely to be a period of some years of declining health which can present major problems for the affected persons and their families in terms of reduced quality of life, reduced working life, reduction in earnings, and chronic ill health in middle age (Wilkie et al 1985). The age of onset of symptoms of APKD including hypertension, urinary tract infection (UTI), loin pain and chronic renal failure is variable with most authors agreeing that there is a long asymptomatic period. It is estimated that approximately 14% of deaths amongst patients with APKD are attributed to subarachnoid or intracerebral haemorrhage (Zeier 1988).

3.2.2 APKD: genetics

APKD is transmitted in an autosomal dominant fashion, which means that each child of an affected parent has a 50-50 chance (one half chance) that he or she has inherited the defective gene. Diagnosis of APKD is the confirmation by ultrasound of the presence of bilateral renal cysts in individuals in families with a positive family history. In 1985 a gene marker for APKD was localized to the short arm of chromosome 16 assisting in the presymptomatic diagnosis in families where there is sufficient family linkage information.

3.2.3 APKD: terminology

Historically many terms have been used to describe polycystic kidney disease including: congeneries of renal cysts, cystic degeneration of the kidneys, conglomerate cysts of the kidney, cystic metamorphism of the kidney, polycystic disease of the kidney, bilateral polycystic kidney. According to Davis (1925) all the above terms have been used to describe congenital, bilateral cystic degeneration of the kidneys. The most common terminology now used is adult polycystic kidney disease, usually abbreviated to APKD, although some authors (Torres et al 1988, Parfrey et al 1990) refer to APKD as autosomal dominant polycystic kidney disease (ADPKD). APKD is not to be confused with infantile polycystic kidney disease (IPCD) which is transmitted in an autosomal recessive fashion (Mandell et al 1983).

3.3 Historical Background

3.3.1 Development of knowledge of APKD in 19th and 20th centuries

According to Lejars (1888 p7) a polycystic kidney was first described by Hufeland and then by Rollet after an autopsy had been carried out on a woman, not known to suffer

from other illnesses, who had been found dead in the street. Bilateral polycystic kidneys, however, were first described by Rayer. In the middle of the 19th century with the expansion of scientific pathology, investigators such as Virchow (1856) were beginning to describe polycystic kidneys as a specific condition. In the second half of the 19th Century, authors focused on a description of the kidneys as they appeared in autopsy. In the advanced stage of the condition, the kidneys take on a very characteristic appearance (see Figure 3.1), which seldom failed to arouse great interest when discovered and frequently a very graphic description. For example, Dickinson (1885) described the appearance of polycystic kidneys in the following way: "The kidneys are transformed into collections of cysts so completely that it is difficult to discern with the naked eye any remnants of the proper tissue which may be destroyed by extension and distortion. The increase in bulk is usually great and renal shape is more or less preserved as if the addition of substance were distributed with some uniformity. The cysts protrude from the surface as circular bosses raising the capsule, which, together with the cyst wall is so transparent that the variously coloured contents can be seen from without. The external appearance roughly resembles that of a water worn mass of conglomerate or pudding stone, the prominent pebbles resembling the cysts, which appear to be lined with a smooth, translucent membrane. The contents of the cysts are various in colour and kind: they are generally pale or deep yellow and highly albuminous often viscoid, treacly or even colloid; they are sometimes purplish, variously blood tinged, purulent or caseous." (p844).

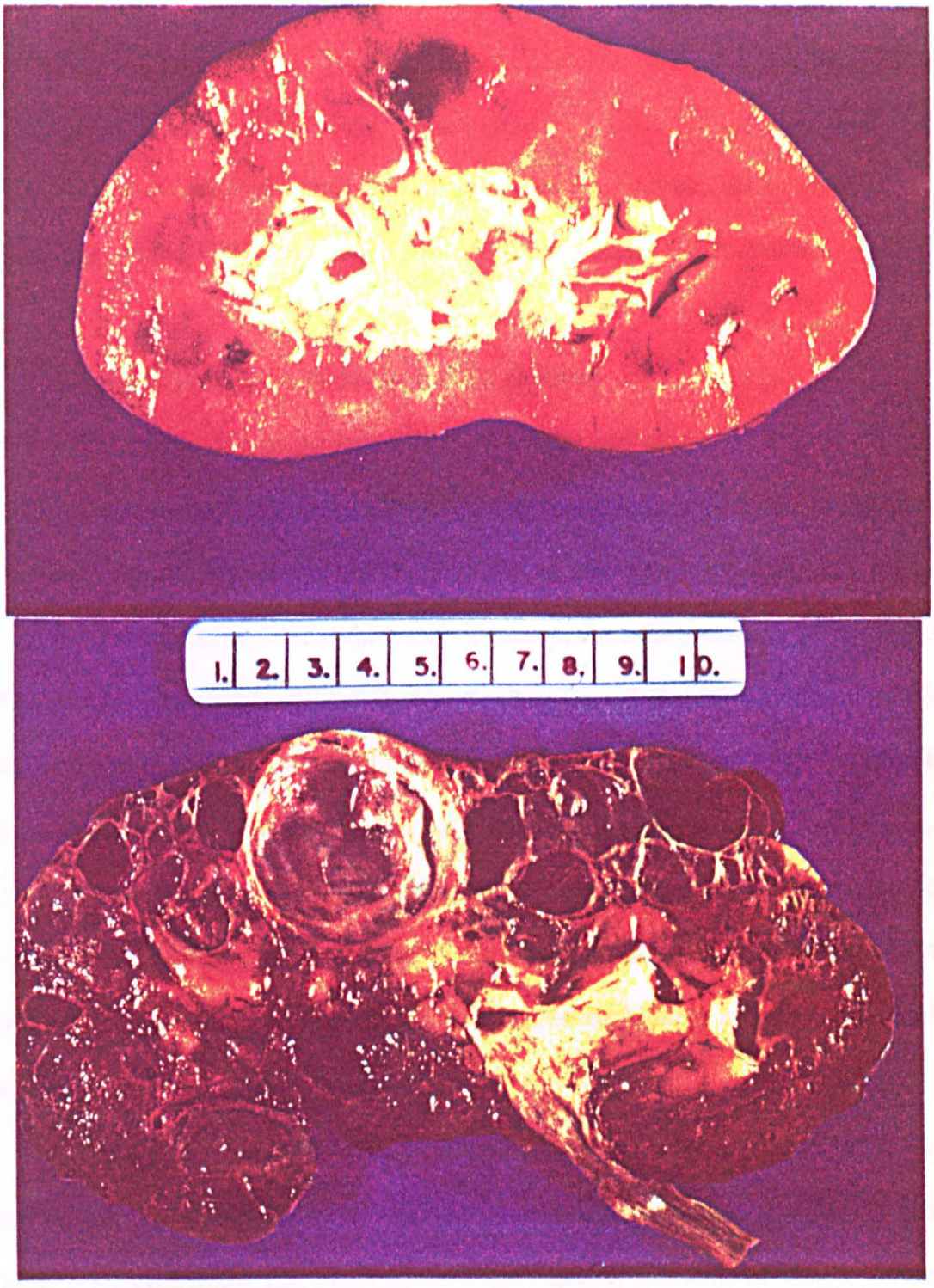

Figure 3.1. A normal kidney (above) and an APKD kidney (below).

3.3.2 Causes of APKD

By the mid 19th century explanations were also being offered as to the cause of the cysts. Virchow (1856) first suggested that tubular casts or insoluble calcium salts might be sufficient to obstruct the urinary flow and so lead to cystic dilation. Later, in 1892, Virchow attributed the formation of cysts to fibrous tissue occlusion of the excretory tubules which he thought resulted from prenatal inflammation.

3.3.3 Polycystic kidneys in adults and in children

Polycystic kidneys appeared in both infants and adults. In infants the condition usually leads to death at birth or shortly afterwards (Kaplan et al 1989). In the case of the newborn, it was easy to see that the majority of the cysts were distended nephrons or enlarged portions of nephrons which were separated from the excretory tubules (Beckmann 1856). Lambert (1947) suggested that in the case of the adult technical difficulties encountered in the reconstruction of the nephrons in the past had made it difficult for a thorough investigation of the topography of the distorted structure to be carried out. In the infant with polycystic kidneys other forms of known congenital abnormality such as polydactyl, anencephaly, meningocele and congenital defects of the urinary tract were often observed (Wigand 1899). Cystic condition of the kidneys in infants was the first to be described as congenital.

Throughout the second half of the 19th century, there were references to cystic kidneys in infants having been observed in several members of one family (Virchow 1856). Attempts were also made in the second half of the 19th century to differentiate between the adult cystic kidney and that found in the infant. Dickinson (1885) described adult cystic kidney as an acquired chronic disease somewhat resembling in its incidence the granular kidney and congenital kidney fatal about or before birth. A few years earlier

Virchow (1869) had traced the history of the congenital cystic kidney of the infant and attributed the degenerative cystic kidney of the adult to a persistence of the infant disorder at least in a number of cases. In 1876, Laveran stated that the degenerative cystic kidney of the adult must be treated as a "maladie speciale qui doit être distinguée de la dégénéresce kystique des nouveau-nés." (quoted by Lejars 1888 p8).

3.3.4 Clinical history of APKD in 19th century

Towards the end of the 19th Century several scholarly articles detailing the clinical history of adult polycystic kidneys appeared.

Dickinson (1885) reviewed 33 cases and described the condition as frequently latent until an advanced age is reached and often not revealed until post mortem. This author suggested that the symptoms included marked loin pain, haematuria, palpable kidneys and in the advanced stage all the symptoms of uraemia. Dickinson found it difficult to estimate the duration of the disorder because of the "indefinite beginning". He assumed that it must be considerable. Treatment was the treatment suitable for uraemia. Lejars (1888) stated that for a definitive diagnosis of APKD both kidneys must be affected, ie the condition was always bilateral, and the condition was compatible with a long period of general good health. During this period, the cystic kidney was seen as an isolated occurrence.

In the latter part of the 19th century the association between polycystic kidneys and cerebral haemorrhage was highlighted (Lejars 1888). The association was described as sudden death of a young patient with no previous history of illness.

3.3.5 Clinical history of APKD in 20th century

In 1933 Braasch and Schacht described data from 193 patients attending the Mayo Clinic. They observed that symptoms did not usually appear until the third decade of life, and that the clinical picture varied considerably depending upon the stage which the disease had reached. Their description of the symptoms was very clear: "As the cystic disease progresses, symptoms caused by renal insufficiency will appear, such as weakness, periods of malaise, headache and gastric distress. Occasionally, cerebral haemorrhage occurs in cases where there was hypertension which had previously caused no distressing symptoms. Complications from intercurrent disease may appear as a result of decreased vitality and lowered values for haemoglobin, and may add rapidly to the patient's decline. With increased vascular disturbance there may be symptoms caused by hypertension with cardiac failure, which usually appears late, there may be oedema and dyspnoea. Patients may be unaware of the gradual progressive enlargement of the kidneys. After a varying period the kidneys become insufficient, the cardiovascular system is impaired and death will follow as a result of uraemia or vascular accident." (p469). These authors concluded that "the hereditary nature of the disease should discourage the having of progeny and sterilization should be considered" (p474).

3.3.6 Development of knowledge of genetics of APKD

It has already been stated that Virchow as early as 1856 had pointed to the familial nature of polycystic kidney disease in infants. Lejars (1888 p55) referred to both 'acquired' and 'congenital' polycystic kidneys. Mohne (1896, quoted in Bunting 1906 p273) reported on the removal at operation of a cystic kidney from a 20 year old girl whose mother had had bilateral cystic kidneys and cysts in liver and ovaries. However,

according to Dalgaard (1957), Steiner (1899) was the first to conclude that an outstandingly hereditary character was the cause of polycystic kidney disease.

David and Jacobsohn (1900) and Beck (1901) both reported that heredity was the cause of polycystic kidney disease. Bunting (1906) reviewed the state of knowledge about congenital cystic kidney and liver and in a much quoted sentence stated that "the attempts to explain the pathogenesis of the congenital cystic kidney have been so numerous and so varied that one is inclined to question whether pathologists have been dealing throughout with a single pathological process" (p276). He concluded that "from the marked hereditary and family tendency shown in the disease, one is led to search for the etiological factor in the parents and that where the condition has appeared in two generations it has generally been transmitted from father to son and mother to daughter." (p287).

In 1925 Cairns concluded that APKD was a hereditary disease. In 1925 Davis, supported by Fuller (1929), suggested from the evidence from his study that polycystic kidney disease was caused by defective protoplasm which may be inherited or congenital in obedience with the same biological laws governing the recessive characteristics illustrated in phylo-genetic changes and in other congenital deformities. In 1933 Braasch and Schacht pointed to the hereditary nature of polycystic kidney disease. However, it was Bell (1935) who expressed the opinion that polycystic kidneys were inherited in Mendelian dominant fashion. Oppenheimer (1934) suggested that the hereditary predisposition of APKD appears to be equally transmitted by either sex and this suggestion was supported by Ferguson (1949) who investigated the incidence of polycystic kidneys in hospital practice and demonstrated an equal distribution of the disease between the sexes. Ferguson also attempted to isolate some distinguishing factors e.g blood group, saliva, hair and eye colour. Fifty relatives of affected persons were investigated but no other genetic factor

was isolated. Ferguson concluded his investigations with the hope that a genetic linkage would ultimately be found.

Dalgaard (1957) in his study of polycystic kidney disease in Denmark demonstrated that polycystic kidney disease in adults was transmitted in an autosomal dominant fashion and that penetrance could reach 100% should the individual reach 80 years.

In Dalgaard's study only 60% of patients with APKD had a positive family history of the illness. As a result, Dalgaard assumed that spontaneous mutations occurred frequently. According to Gabow (1990) a negative family history more commonly reflects failure to diagnose APKD in the parent rather than absence of the disease and this was substantiated by the work of Iglesias et al (1983) who found that half the cases of APKD in their study population had been diagnosed on autopsy.

3.3.7 Discovery of a gene marker for APKD

A major breakthrough in the genetics of APKD came with the work of Reeders et al (1985) who used gene linkage techniques and localized a gene for APKD on the short arm of chromosome 16. In gene linkage the gene itself is not discovered but DNA markers near the gene are identified. For each family, it is necessary to identify the form of the marker linked with the gene. In order to identify which form of the marker is linked with the APKD gene in the particular family, the affected and unaffected parents must have different markers. Furthermore, in the particular family there must also be at least two affected people whose gene status has still to be established. When these criterion can be met, the gene marker can be applied and can demonstrate the status of gene carrier to a 99 to 1 chance. Without gene marker technology the risk status for offspring of an affected parent is 50-50 (Gabow 1990).

In 1988 Kimberling et al were the first to identify a family whose gene for APKD was not found on chromosome 16 and since then other families have been identified (Romeo et al 1988). The gene located on chromosome 16 has now been called APKD1 and the other gene on the as yet unidentified chromosome has been called APKD2 or non-APKD1.

3.4 THE NORMAL KIDNEY

The kidney is one of a pair of organs which lie towards the back of the body. The upper part of the kidney lies under the ribs which offer some protection for them. The kidneys are bean shaped organs measuring approximately 12cm by 7cm by 3cm with some variation from individual to individual and weigh 150-170g (6ozs) each in the average male and a little less in the female. The length of the kidney is equivalent to 3½ vertebrae and on respiration the kidney moves up and down the length of one vertebrae. The kidneys receives their blood supply from a branch of the aorta, the renal artery from which blood is passed to the outer parts of the kidney in blood vessels which form a fan shape (Fig 3.2). The blood is passed back into the main vein, vena cava, by the renal vein. The whole kidney is covered by a thin fibrous capsule which is joined to the renal vein, renal artery and pelvis at the hilum. Urine is passed from the kidneys through the ureter into the bladder.

A kidney is made up of approximately 1 million nephrons. A nephron consists of two parts: the glomerulus which is the filter of the kidney and the tubule. The glomeruli lie in the cortex or outer part of the kidney and are composed of tufts of capillaries with very thin walls which allow the glomerulus to function as a filter. The tubules drain the glomerulus into the calyces which join to form the pelvis. The inner part of the kidney, the medulla, contains only tubules and no glomeruli.

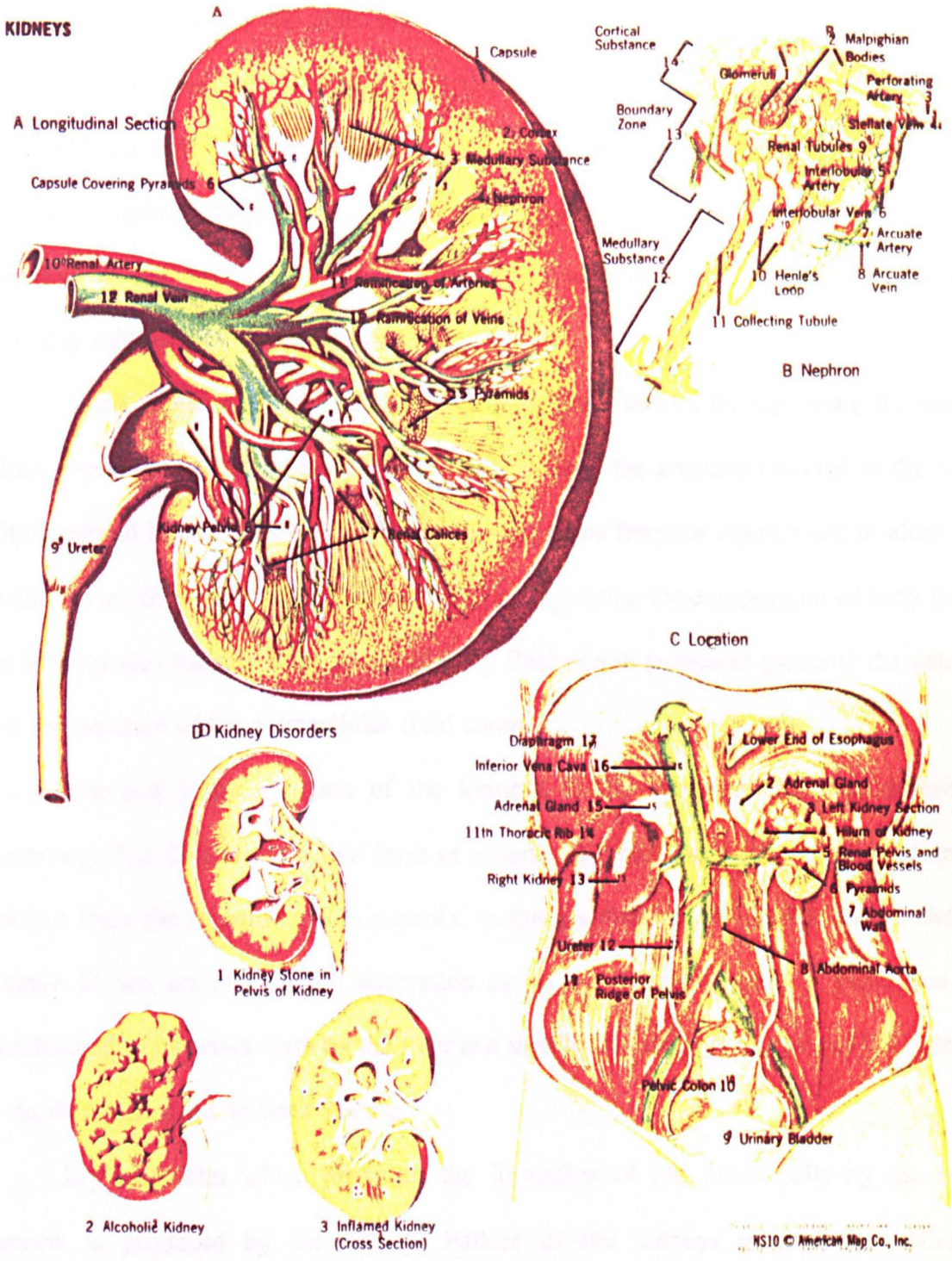

Figure 3.2. Details of a normal kidney.

The nephrons function in the following way. The glomerulus takes in blood and filters off about one fifth of the water and its dissolved substances. The volume of this filtrate is approximately 200 litres every 24 hours. Most of this filtrate is then reabsorbed by the tubules, reduced in volume and the waste transformed into urine. In normal circumstances, 1½ to 2½ litres, or 3 to 5 pints of urine is passed daily. Through this process the kidneys carry out the function of disposing in the urine the waste products of metabolism, the chemicals urea, uric acid and creatinine, as well as regulating and retaining substances vital to the body water content.

Urine contains several water soluble body constituents. By regulating the rate at which these substances are excreted, the kidneys keep the amounts retained in the body within normal limits. Clearly the kidneys have to make frequent adjustments to allow for variations in dietary and fluid intake. As well as regulating the composition of body fluid, the kidneys also maintain the volume of body fluid and in particular preserve the volume and composition of the extracellular fluid content.

The last major function of the kidneys is the secretion of some important hormones. The first is the active form of vitamin D which promotes the absorbtion of calcium from the intestine and is essential in the maintenance of healthy bones. Before vitamin D can act on calcium absorbtion or on bone development, it must first be transformed to its active form by the liver and then by the kidneys. Failure of the kidneys to do this may result in bone disease.

Erythropoietin which promotes the formation of red blood cells by the bone marrow is produced by the kidney. Failure of the kidneys to produce sufficient erythropoietin may result in anaemia.

The kidneys also produce renin which stimulates the production of angiotensin and aldosterone which are important in the regulation of blood volume and blood pressure.

Finally the kidneys are responsible for the production of several prostaglandins some of which also regulate blood flow and blood pressure.

3.5 RENAL FAILURE

Renal failure describes the situation when the kidneys are no longer able to carry out their function. Renal failure can be acute or chronic. Chronic renal failure is almost always caused by an irreversible impairment of renal function, such as APKD. For patients with progressive chronic renal failure the outcome is death unless treatment such as dialysis or transplant is given.

As the function of the kidneys fail, high levels of waste products accumulate in the blood causing uraemia.

Various tests are used to investigate kidney disease and to assess the degree of renal impairment; these are described below.

3.5.1 Glomerular filtration rate

The glomerular filtration rate (GFR) is a measurement of the amount of water being filtered at the glomeruli and is the single most important functional test in renal medicine. GFR is measured by a clearance study. The renal clearance of any substance represents the theoretical volume of plasma which is completely cleared of that substance in a given period of time. A clearance is usually expressed in ml/min and is calculated from the formula UV where U=urine concentration, V=volume of urine and P=plasma concentrate. The most frequently used clearance substance is creatine an end product of muscle metabolism, which accumulates in kidney failure and is filtered at the glomerulus. A 24 hour urine collection ie all urine passed over a specific 24 hour period and a blood

sample are needed for this test. The degree of renal failure according to creatinine clearance can be described as;

mild	100-60
moderate	60-40
severe	40-20
ESRF	20 and less

3.5.2 Serum creatine

Another method of measuring renal function is to calculate the amount of serum creatine in the urine. This is a simpler test than creatine clearance and a less accurate assessment of renal function. The degree of renal failure according to serum creatine can be described as;

mild	0-200
moderate	200-400
severe	400 and over
ESRF	

3.5.3 Volume of urine

Urine: the volume of urine passed by an adult with healthy kidneys is approximately 2.25 litres per day (4-5 pints). Passing urine at night (nocturia) may be an indication that the usual fall in volume during the night is not taking place. This is a symptom of renal failure when the volume of urine to be passed has increased and the concentrating power of the kidney is impaired. Passing urine frequently particularly if accompanied by pain burning or smarting is frequently due to a urinary tract infection (UTI). In APKD this may be caused by rupture of the cysts.

Frequent blood tests are carried out on renal patients to assess the degree of urea, creatine, uric acid and phosphates in the blood as well as the level of blood electrolytes such as sodium, bicarbonate and potassium.

3.6 DIAGNOSIS OF APKD

3.6.1 Autopsy

In 1888 Lejars wrote that the signs of a certain diagnosis of polycystic kidneys were loin pain, haematuria, palpable kidneys combined with a detailed analysis of antecedents but that certainty of diagnosis remained on autopsy.

3.6.2 Intravenous pyelogram

By 1927 Braasch and Hager were using urogram as a method of confirming a diagnosis and by 1933 Braasch and Schacht were recommending intravenous urography as the "ideal means of diagnosis in many cases" (p473). De Bono and Evans (1977) suggested that the most common diagnostic technique for APKD was excretion urography. However, there was evidence that this technique gave equivocal or misleading results and Fischer and Doust (1972) showed that there was a small but realistic risk of a major reaction to the contrast material used in excretory urography.

3.6.3 Ultrasound

It was not until 1983 that ultrasound was recommended by Sahney et al as the optimum diagnostic method for presymptomatic polycystic kidney disease. These authors suggested that if ultrasonography showed multiple cysts bilaterally in a person with a family history of APKD no further investigations were necessary. There is a problem of ascertaining the diagnosis in a patient in whom ultrasonography has raised the possibility

of some abnormality but no definitive evidence of cysts were seen. In these circumstances, Sahney et al (1983) suggest that intravenous pyelogram with nephrotomography could be considered while Watson et al (1990) recommend that such patients return for ultrasonography on a yearly basis.

Ultrasound has several advantages over other invasive investigative procedures. It is easily and quickly performed without the use of needles and the patient is caused little or no discomfort. There is no radiation as there is with excretory urography. It is safe and cheap and the results of ultrasound examinations can very quickly be given to the patient.

As it has become possible to diagnose APKD more accurately by ultrasound so it has become easier to offer early diagnosis to the asymptomatic members of families who are at risk of inherited polycystic kidney disease.

3.6.4 Computed axial tomography

Computed axial tomography (CT scan) can also be used to diagnose APKD. CT scan may be more sensitive than ultrasound in the detection of small renal cysts. (Levine and Grantham 1981) but it is more expensive than ultrasound and exposes the patient to radiation.

3.6.5 Gene marker

The discovery of a gene marker by Reeders et al (1985) on the short arm of chromosome 16 enables, if sufficient family data can be obtained (Bear et al 1992), a more accurate diagnosis to be given to asymptomatic patients prior to the identification of cysts by ultrasonography. The gene marker can also be used for prenatal diagnosis. However the use of gene marker technology is still expensive and moreover requires the involvement of other family members in order to establish the diagnosis.

3.6.6 Family history/family pedigree

The taking and development of a detailed family history is important in the diagnosis of APKD. A positive family history by itself cannot diagnose APKD in the asymptomatic. But when a patient is suffering from some of the symptoms often associated with APKD, the presence of a positive family history can facilitate an accurate an early diagnosis.

3.7 SYMPTOMS OF APKD

3.7.1 Symptoms of APKD

The most recent clinical studies of polycystic kidney disease have not added substantially to knowledge of the symptoms of the disease as documented by 19th century authors Lejars (1888) and Dickinson (1885). The major symptoms, when they appear, are urinary tract infection, haematuria, hypertension, loin pain, gastrointestinal complications and eventually end-stage renal failure (Wilkie 1992). It is now generally agreed that in patients with a positive diagnosis of bilateral polycystic kidneys there is a symptom free period with the studies of Higgins (1952), Simon and Thompson (1955), Dalgaard (1957), and Mitcheson et al (1977) all suggesting that for the majority of people with APKD, symptoms develop in their 30s and 40s with authors agreeing that there is likely to be a long asymptomatic period prior to the onset of symptoms.

3.7.2 Urinary tract infection

Urinary tract infection (UTI) is a common symptom and recurrent urinary infection (more than three infections in one year) were found to be more common in female patients (De Bono and Evans 1977).

Most workers suggest that as many as 75% of patients develop urinary tract infection during the course of their illness (Dalgaard 1957, Simon and Thompson 1955). De Bono and Evans (1977) and Milutinovic et al (1984) found the frequency of UTI significantly higher in females than in males. Urinary tract infections does not appear to be related to kidney size.

3.7.3 Haematuria

Frank, painless haematuria is a presenting symptom in as many as one third to one quarter of patients studied (De Bono and Evans 1977 and Funck-Brentano et al 1964). Haematuria may be microscopic, macroscopic, intermittent or virtually continuous. Danovitch (1976) suggested that haematuria was frequently precipitated by trauma and physical exertion.

There does not seem to be consensus amongst authors whether haematuria affects the sexes equally.

Milutinovic at al (1984) showed that haematuria was related to kidney size in patients of either sex. In this study one or more episode of haematuria occurred in 14% of the 22 patients with radiographically measured longitudinal kidney sizes of 15cm or less in contrast to 43% of the 100 patients with kidney sizes larger than 15cm ($p=0.001$).

Most workers suggest macroscopic haematuria seldom lasts more than 2 days. The average duration is 2 days and haematuria is seldom sufficiently severe to require blood transfusion.

3.7.4 Hypertension

Hypertension occurs in approximately 60% of patients with APKD prior to the development of renal impairment (Milutinovic et al 1984, Valvo et al 1985). Gabow

(1990) suggests that since APKD is a systemic disease, the pathogenesis of early hypertension could be attributed to renal factors, extrarenal factors or both.

Hypertension is very frequently associated with renal disease as is left ventricular failure (LVH) and pericarditis.

Blood pressure depends upon the relationship between the level of output of blood from the left ventricle of the heart and the resistance in the peripheral blood vessels. Two blood pressures are measured. The systolic pressure which corresponds to the peak pressure as blood is pumped from the heart and the diastolic pressure which is the low point between contractions of the heart. The convention is to record systolic over diastolic in mmHg. The units are millimetres of mercury from the height of the column of the sphygmomanometer. At birth blood pressure is about 80/40 and rises with age to reach 120/70 at age 20 approximately 140/80 at age 40 and continues to rise with increasing age. A persistent rise in blood pressure, hypertension, if left untreated, is known to be a cause of increased mortality and morbidity.

In his study of impaired lives Leighton (1987) demonstrated that there is extra mortality for moderate hypertension but a marked increase in risk for high blood pressure readings whether systolic or diastolic or both and in particular as soon as the systolic pressure exceeds 170 or the diastolic pressure exceeds 95 (Table 3.1). Persons with untreated hypertension are at high risk of dying of myocardial infarction, cerebral haemorrhage, heart failure or renal failure.

Almost all patients with APKD will develop hypertension (De Bono and Evans 1977) if the disease runs its course (Dalgaard 1957, Danovitch 1976, Rall and Odel 1949, Hatfield and Pfister 1972) with blood pressure higher than 140/90 in 70%-75% of all cases. Some authors suggest that hypertension in polycystic kidney disease is relatively mild and in most patients susceptible to treatment (Hamburger et al 1968).

Table 3.1

Excess mortality from hypertension

		% excess mortality	
S.A.P.	D.A.P.	1974-83	1964-73
155-170	under 95	+38%	+26%
155-170	95-105	+53%	+60%
155-170	over 105	+53%	+103%
over 170	under 95	+89%	+106%
over 170	95-105	+91%	+136%
over 170	over 105	+161%	+193%

Excess mortality among lives insured by Prudential Assurance Company, entering at ages 40-59, not overweight, policies in force for more than two years, as compared with policyholders accepted at normal premium rates.
Source: Leighton (1987)

The cause of hypertension in APKD is unclear. It cannot be explained merely on the basis of chronic renal disease since it occurs much more commonly in the presence of polycystic kidneys than in chronic pyelonephritis with equivalent functional impairment (Schacht 1931, Calabrese et al 1982).

The relationship between hypertension and renal disease is twofold. Untreated hypertension causes renal impairment and renal disease such as APKD causes hypertension. The result of hypertension if left untreated is steadily rising hypertension and progressive renal damage.

Hypertension is frequently the symptom which brings patients to the attention of the renal physician (Dalgaard 1957 and De Bono and Evans 1977) and as a presenting symptom is frequently related to age. In women, it may first be recorded in pregnancy (De Bono and Evans 1977).

Hypertension is known as an early symptom in three quarters of patients with polycystic kidney disease when kidney function measured by serum creatinine is still normal (Hansson et al 1974).

The relationship between serum creatine and hypertension in patients with APKD was studied by Hansson et al (1974). In patients with normal serum creatine the incidence of hypertension which was defined as a resting recumbent blood pressure of 160/100 mmHg was 75% indicating that an increased blood pressure normally precedes impairment of renal function. A lower incidence of hypertension had previously been found by Dalgaard (1957) who regarded hypertension as a late phenomenon in the progression of polycystic kidney disease occurring concomitantly with an advancing impairment in renal function.

It is also known that hypertension, untreated, causes renal damage. To date there has been no comprehensive screening and treatment of early hypertension in patients with APKD. Therefore, the effect of early treatment of hypertension on otherwise asymptomatic patients with APKD and on morbidity and mortality is unknown. However, the effect of early treatment of hypertension in other fields is well documented.

3.7.5 Pain

In many studies pain represents the most frequent complaint of patients with APKD (Dalgaard 1957, Danovitch 1976, De Bono and Evans 1977). The pain is frequently described as a nagging, dull, aching pain in the lumbar or lateral abdominal area. The pain is frequently unilateral and may radiate to the back. It is frequently very acute. Danovitch (1976) suggests that the relationship to exertion and other variables is inconsistent as is the success of the measures of pain. Pain may or may not be accompanied by haematuria or urinary tract infection. A variety of theories for the

aetiology of pain in the presence of polycystic kidneys has been suggested. For example the cysts have swollen producing pressure or stretch of the renal parenchyma or capsule. Braasch and Schacht (1933) suggest that pain is caused by the excessive weight of the enlarged kidney while Dalgaard (1957) and Simon and Thomson (1955) suggest that the enlarged kidney puts pressure on adjacent organs and traction on the renal pedicle and that it is this that causes pain.

3.7.6 Gastro-intestinal system

Common symptoms are nausea, loss of appetite, weight loss, sickness and peptic ulceration. Many patients complain of an unpleasant taste in the mouth which may be due to urea in the saliva and gastric juices.

3.7.7 Bone disease

In addition to the above symptoms, bone disease may appear due to the disturbance in the production of vitamin D and parathyroid hormone. This can be particularly problematic in younger patients. Joints may become inflamed and painful due to deposits of calcium and phosphate.

3.7.8 Anaemia

Anaemia is one of the early symptoms of renal failure due to failure of the kidneys to produce erythropoietin which stimulates the bone marrow to manufacture red blood cells.

3.7.9 Skin

In renal failure the skin becomes dry and flaky as a result of the failure of the skin to form normal secretions. Frequently the skin becomes very itchy. The cause of the itchiness is still unknown. People with chronic renal failure often appear pale due to anaemia. In end stage renal failure the skin often takes on a muddy brown colour due to the presence of pigments which normally colour urine being present in the blood.

3.7.10 Other lesions or symptoms associated with APKD

The finding of cysts in other organs of the body in patients with APKD is not uncommon. Hatfield and Pfister (1972) question the diagnosis of APKD in the absence of cysts in other organs. Cysts in patients with APKD have been found in the liver, pancreas, lungs, spleen, ovaries, testes, epididymis, thyroid, uterus, broad ligament, and bladder (Danovitch 1976). Of these hepatic cysts appear to be the most common (Milutinovic et al 1980). Gardner (1976) suggest that polycystic disease of the liver is present in 33% of patients with APKD. These figures vary according to the different series of autopsies carried out (Melnick 1955) and to the range of investigations at diagnosis. Hepatic cysts are seldom symptomatic although nausea, vomiting and discomfort in a sitting position may develop after some years (Rettiri 1969). Cysts in organs other than the liver occur in approximately 2% of patients (Danovitch 1976). It has not yet been shown conclusively whether the occurrence of cysts in organs other than the liver in patients with APKD is a chance finding or not.

Patients with APKD have an increased risk of intracranial aneurysm or subarachnoid haemorrhage (O'Crowley and Martland 1939).

The discovery of the existence of intracranial aneurysm in the region of the circle of Willis was reported by Lejars (1888) and Borelius (1901) and has since been described

in studies by Dalgaard (1957), Brown (1951), Bigelow (1953), Ditlefsen and Tonjum (1960). Bigelow and Dalgaard also reported an increased incidence of subarachnoid haemorrhage without aneurysm. However the relationship between subarachnoid haemorrhage, Berry aneurysm and APKD has not been clearly defined.

3.8 END STAGE RENAL FAILURE AND ITS TREATMENT

A major symptom of APKD is end stage renal failure (ESRF). In the study by Dalgaard (1957) 50% of patients developed ESRF by age 50 while Churchill et al (1984) found that 70% of patients in their study had not developed ESRF by age 50 and 50% had not developed ESRF by age 73.

When the kidneys are damaged to a degree that renal function is described as ESRF, the patient will die unless some form of renal replacement therapy (RRT) is introduced to carry out the function of the kidneys. Haemodialysis, Continuous Ambulatory Peritoneal Dialysis (CAPD), Intermittent Peritoneal Dialysis (IPD) and successful renal transplantation all perform this task. In many hospitals IPD is used mainly as a holding measure until a more permanent form of RRT is found and is therefore not discussed any further.

In haemodialysis, the dialyser is the mechanism by which waste products are removed from the patients blood. The dialyser consists of two separate compartments separated by a semi-permeable membrane. Blood from the patient goes into one compartment and the waste products from the blood pass through the membrane into the fluid of the dialysis machine and are pumped out of the body. Blood cells are too large to pass across the membrane. The purified blood is then pumped back into the body. This system requires a mechanism by which blood from the patients body is passed to the dialysis machine and back again into the body. The usual method of vascular access is the

fistula which is a direct connection between an artery and a vein. This connection is made under the skin by attaching a vein in the forearm to the digital artery which runs down towards the base of the thumb. The vein eventually grows large as some of the blood that previously went to the hand passes through it. To dialyse, blood is taken from the patient by passing one needle, the arterial, into the fistula. This blood goes to the dialysis machine and is passed back into the body through a second needle, the venous needle in a different part of the fistula. The process of inserting the needles, often referred to as needling, is carried out every time the patient dialyses.

The principle of haemodialysis is that waste and water products that the kidney is no longer able to dispose of cross a synthetic semipermeable membrane and are pumped out of the body. In peritoneal dialysis water and waste products cross from the blood stream through the peritoneum which is a natural semipermeable membrane and into the dialysate which has been inserted into the abdominal cavity. Access for peritoneal dialysis is by a Tenckhoff catheter, often made of silicone rubber, which is inserted into the abdominal cavity with about two inches of catheter left outside the body. To dialyse a sterile tube is attached to the Tenckhoff catheter and warmed dialysate is passed into the abdominal cavity where it is left for a short period to allow the transfer of waste products. The fluid is then allowed to drain out by gravity and the catheter capped off until the next time.

Each form of dialysis has its adherents within the medical profession and there may be medical reasons why one form of dialysis is preferred for an individual patient. Haemodialysis has been tried for longer. The longest surviving time for a patient to be on haemodialysis in Scotland is 25 years (Henderson 1988). Haemodialysis can be done at home where it is cheaper or in hospital. Approximately 12-15 hours of dialysis per week are needed and this will vary from patient to patient.

Some of the psychological disadvantages of haemodialysis include the loss of independence during dialysis, concern about the cosmetic effects of the shunt and problems relating to the restrictions on the amount of fluid that the patient can take.

Peritoneal dialysis has been developed during the last 20 years. CAPD is normally carried out 4 times per day every day and takes about three quarters of an hour to do. From the patients points of view the amount of time spent on either system per week is approximately the same. A major difference is that in peritoneal dialysis the patients are entirely responsible for their own care ie they could live alone and dialyse themselves. This is in contrast to haemodialysis where the patient requires the assistance of another. Patients on CAPD are prone to peritonitis and some patients put on weight. Some patients would argue that the need to dialyse daily in CAPD is more intrusive on their time than the 3 times per week sessions required for haemodialysis. However patients on CAPD can have a relatively 'normal' dietary and fluid intake and dialysing on CAPD can be more flexible than haemodialysis for the patient.

Dialysis treatment is a way of life for the patient and his family in that the patient has to fit their life around the regular need to dialyse and the time that it takes. For some patients the psychological problems of adjusting to the restrictions that dialysis imposes may be considerable (Hardiker et al 1986).

3.9 Prognosis of APKD

In the studies of Dalgaard (1957), Rall and Odel (1949) and Braasch and Schacht (1933) the mean life expectancy following clinical presentation ranged from 4 to 13 years with the time being considerably shorter for patients older than 50 years at the time of presentation to medical attention. Mitcheson et al (1977) estimated that 70% of patients with APKD would develop end stage renal failure (ESRF) if they survived to age 65. On

the other hand Hatfield and Pfister (1972) suggested that many persons with APKD remain asymptomatic and have a normal life span. Churchill et al (1984) studied 17 APKD kindreds to calculate the prognosis for affected members. Their results indicated that the person with ultrasonographically detectable APKD may be told that their chances of developing ESRF before the age of 40 years are about 2% rising to 23% by the age of 50 years and to 48% by the age of 73 years. These authors conclude that the prognosis for patients with APKD is therefore much better than previous reports have suggested. In their study of the epidemiology of APKD in Olmsted County, Minnesota, Iglesias et al (1983) found that approximately only half of patients with APKD were diagnosed during their lifetime. They attributed this finding to the completeness of the authors case ascertainment, to the use of advanced diagnostic techniques and to the high proportion of deaths that came to autopsy in the population of Olmsted County (p638). These authors also discovered that there was a significant improvement in kidney survival in patients diagnosed after 1956 compared with those whose disease was diagnosed between 1935-1955. These authors conclude that these improvements may be attributed to the more effective antihypertensive therapy and that early diagnosis of APKD combined with good medical attention may "improve patient survival" (p638).

It has already been stated that patients with APKD have also an increased risk of intracranial aneurysm. Levey at al (1983) estimated the risk in APKD of rupture of intracranial aneurysm at 2% a year. Once rupture of intracranial aneurysm has occurred both the short and long term prognosis is poor (Nishioka et al 1984). It has also been suggested that patients with APKD and a family history of intracranial aneurysm or subarachnoid haemorrhage have a greater risk of having an aneurysm themselves than those without such a family history (Saifuddin and Dathan 1987).

CHAPTER 4: GENETIC COUNSELLING AND ADULT POLYCYSTIC KIDNEY DISEASE

4.1 Introduction

There are rather few studies concerned with genetic counselling and adult polycystic kidney disease (APKD). This may be because patients with APKD in the United Kingdom are cared for by renal physicians and may not be referred to genetic departments from where most research about genetic counselling in the United Kingdom comes. Furthermore renal physicians may not be familiar with some of the problems inherent in genetic counselling nor with the literature referred to in Chapter 2.

4.2 Background

From studies of APKD such as Danovitch (1976) and Chester and Argy (1979) it is evident that the management of APKD has four facets: management of complications between diagnosis and the onset of end stage renal failure; dealing with end stage renal failure; selection and preparation of patients for kidney transplantation; and the screening and counselling of relatives. De Bono and Evans writing in 1977 point out that APKD "has persisted because its effects are often not manifested until after the peak reproductive period in life" (p363). These authors usually told patients that they had a hereditary disease which "may on average affect one in two of their sibs or children" (p363). Normally relatives were not screened unless there were clinical grounds for suspecting a diagnosis when treatment could begin or if the relative requested screening. These authors were not offering proactive counselling as described in Chapter 2, but reacting to requests from at-risk relatives.

4.3 STUDIES OF GENETIC COUNSELLING IN APKD

By the early 1980s the majority of studies of APKD were particularly concerned with the reliability of non-invasive ultrasound in the diagnosis of APKD in both the symptomatic and presymptomatic patient as compared with the longer established but invasive method of diagnosis, intravenous pyelogram (IVP) (Milutinovic et al 1980, Hogewind et al 1980, Sahney et al 1983, Rosenfield et al 1980).

One of the early problems in genetic counselling in APKD and described by workers such as Hogewind et al (1980) was the lack of availability of age specific detection curves for APKD for any of the four possible diagnostic procedures, IVP, nephrotomography, sonography, arteriography.

Hogewind et al (1980) set out to assess the reliability and sensitivity of ultrasound for the detection of APKD in the asymptomatic offspring of patients with known APKD. They suggested that ultrasound appeared to be at least as sensitive as IVP for identifying carriers of the APKD gene and recommended that this be the diagnostic procedure for asymptomatic carriers of APKD. These findings were supported by Sahney et al (1983) who recommended that ultrasound of the kidney and the liver be the initial screening procedure for APKD. They further recommended that if there was evidence on ultrasound of multiple bilateral cysts and there was also a family history of APKD no further investigations were required. They also suggested that if the patient was under 20 and the ultrasound was normal a further ultrasound could be carried out in a few years time. The authors thought that this approach would reduce the need for unnecessary IVP in many at-risk individuals but would still identify the asymptomatic individuals with APKD so that they could receive genetic counselling sufficiently early to be of value in planning their family. These authors did not discuss what should be included in genetic counselling. Nor

did they comment on any psychological problems that could occur by informing the asymptomatic at-risk individual of their risk status.

As it became evident from these studies that ultrasound appeared to be just as reliable in diagnosing APKD, particularly in the presymptomatic patient, some authors began to consider the implications of early diagnosis of an illness in which the symptoms may not appear for some years. For example Milutinovic et al (1980) suggested that early testing of relatives at risk for APKD has the following potential benefits:

1. early detection of gene carriers should theoretically lead to better therapeutic management of complications;
2. subjects over the age of 20 who know that they are at risk for APKD and who are found to be unaffected can be reassured that they will not develop the condition and that they cannot transmit APKD to their offspring.

However, these authors did point to the possibility of problems as a result of establishing a diagnosis in some asymptomatic people many years before they would otherwise have known. They suggested that physicians and genetic counsellors would need to balance these factors when deciding whether to recommend unsolicited early testing of persons at risk for APKD.

In 1982 Sahney et al published a study which had set out to

a) assess knowledge of the hereditary nature of APKD in 22 patients with end stage renal failure due to APKD and
b) to determine whether these patients had received adequate genetic counselling.

Their findings showed that patients were neither sufficiently informed of the familial nature of the disease nor had they received adequate genetic counselling. This

study, like many of the studies described in Chapter 2, assessed knowledge of the disease by measuring both the patients' knowledge of the genetics of APKD and the symptoms of the illness. The emphasis was on whether the patient was aware of the presence of kidney disease in the family and whether the illness was passed from generation to generation. The investigation did not focus on the understanding of risk and probability as frequently happened in studies described in Chapter 2 and falling into paradigms 2 and 3. Indeed the authors stated that " ... effective counselling should not only emphasise the risk of recurrence of a genetic disease but should help the family cope with the genetic burden" (Sahney et al 1982 p466). Although the authors did not describe what they thought should constitute genetic counselling they made several references to the psychological component in genetic counselling. The authors referred specifically to the possible psychological impact of learning of the genetic nature of APKD and in this respect this study fits into the third paradigm described in Chapter 2.

4.4 Issues in presymptomatic and prenatal diagnosis

By the mid 1980s ultrasonography had become the recommended method of diagnosing APKD presymptomatically.

The announcement in 1985 of the discovery of two genetic markers closely linked to APKD on chromosome 16 (Reeders et al 1985) greatly increased the potential for early presymptomatic diagnosis of APKD. Later in 1986 Reeders et al carried out prenatal diagnosis of APKD in a fetus by chorion villus sampling.

These authors point out that the inclusion of presymptomatic diagnosis of APKD has not yet been established in the management of patients with APKD. This is not surprising when one considers the short time scale between the establishment of non-invasive ultrasonography as an accurate method of presymptomatic diagnosis of APKD

and the discovery of gene markers that can also be used prenatally. Reeders et al pointed to the need to define the place of both prenatal and presymptomatic detection of APKD in genetic counselling.

In 1990 Hodgkinson et al described a study into knowledge, experience and attitudes to prenatal diagnosis amongst patients with APKD. The work was carried out in Manchester between 1987 and 1988. The authors contacted 352 subjects aged between 18 and 45 who were on a confidential genetic register held by the North Western Regional Genetic Centre. Their subjects included patients affected by APKD, those at high risk, ie 50%, of developing APKD, those classified at low risk, which was defined as one or more negative presymptomatic tests by a consultant radiologist, and spouses of any of the above. The take-up rate for the whole population was 54% but only 19% for those at high risk.

Respondents were asked whether they themselves would be interested in a prenatal test for APKD. 29% of the whole population said that they would, compared with 25% of those affected, 13% of those at high risk and 47% of those at low risk, for whom the question was more hypothetical. The high non-response rate for those at high risk should be noted as it is this group whose perceptions of the implications of presymptomatic and prenatal diagnosis are particularly important.

The relationship between the respondents perception of the severity of APKD and interest in a prenatal test was examined. 65% of those who said that they were interested in a prenatal test and who were also at high risk of inheriting APKD considered that APKD was "extremely serious" compared with 34% of those respondents who were affected by APKD but who were not interested in a prenatal test. However the authors do not discuss how the perception of seriousness was ascertained. While a majority of the respondents in this study felt that the development of a prenatal test was acceptable, only

a minority of the sample would personally be interested in using it. The authors also found that a higher proportion of those at low genetic risk for APKD said that they would have had a prenatal test for APKD if they had been at high risk which led the authors to suggest that prenatal diagnosis for APKD may be more appealing in the abstract.

The authors concluded that " ... even for persons with a realistic perception of the disease and a good recall of the recurrence risk, the demand for prenatal diagnosis will be low" (p557).

Another study into attitudes of at-risk and affected individuals regarding presymptomatic testing for APKD using gene linkage analysis was carried out in the USA and also reported in 1990 (Sujansky et al 1990). This study involved 141 affected respondents and 137 at-risk respondents. Ninety seven per cent of the at-risk group stated that they would want to know their own gene status if gene linkage were available, and the majority of respondents said that they would like to confirm the genetic status of a child postnatally with regard to APKD. While 65% of the affected and 50% of those at risk would consider using prenatal diagnosis, only 4% of affected respondents and 8% of those at risk would terminate a fetus with APKD. The authors explored respondents' attitudes to termination and found that the participants' attitudes to termination of pregnancy for APKD was different from their view of termination of pregnancy for "a very serious medical problem" in the fetus. They found that significantly more respondents, including both those at risk and those affected, would be definitely willing or would consider termination of a pregnancy for "a very serious medical problem" than would consider termination of pregnancy for APKD. The authors concluded that many of their respondents did not perceive APKD as a serious medical problem. The authors were also surprised that the severity of the disorder in the family did not appear to influence the desire of the respondent for prenatal diagnosis and termination of pregnancy.

These authors do point to the apparent inconsistencies in their results in the desire for fetal genetic knowledge on the one hand but the reported lack of take-up of termination of an affected fetus on the other hand. They state that their data did not indicate that this was caused by lack of medical or genetic understanding of APKD and assume that the late onset of APKD influenced judgements of respondents about prenatal diagnosis. The authors conclude that from their data earlier presymptomatic diagnosis will have little effect on the frequency of the disorder as it will only occasionally alter reproductive plans. This study highlights the great complexity of attitudes that should be considered by clinicians before offering presymptomatic diagnosis or prenatal diagnosis for those at risk for APKD.

4.5 AWARENESS OF ETHICAL AND PSYCHOLOGICAL PROBLEMS CREATED BY PRESYMPTOMATIC DIAGNOSIS

The three studies discussed above all point to possible difficulties that may be caused by presymptomatic diagnosis of APKD. Sahney et al (1982) clarify some of the problems when they state: "If young people who are at risk of developing end stage renal disease are identified early, the psychological problems created in them and their parents during the long asymptomatic period will have to be carefully weighed against the benefits of early diagnosis." (p467). These authors see the potential benefits of presymptomatic diagnosis as rational reproductive decision making and the remote possibility of delaying renal failure by monitoring and controlling urinary tract infections and hypertension.

However, in their study of the attitudes of those affected by or at risk for APKD to presymptomatic testing for APKD, Sujansky et al (1990) found that only 40% of those affected and 30% of those at risk would consider altering their plans to have children because of APKD. The authors assumed that these respondents did not consider APKD

to be a serious condition and they concluded that presymptomatic testing for APKD would not substantially modify the incidence of APKD since it "may only occasionally alter reproductive plans" (p510).

Hodgkinson et al (1990) suggest that the diagnosis of an adult onset condition many years before the onset of symptoms could have adverse consequences, including the possibility of discrimination in employment and difficulties in acquiring life assurance, as well as psychological problems.

4.6 Third parties, ethical implications and informed consent

There is an ethical issue raised by the practice of acquiring information about other family members from the index ie the affected patient. In order to develop a family tree or pedigree it is customary to start with the patient and to ask them whether their parents are alive and if not what was the cause of their death. The same questions are then applied to siblings, having first established how many there are and their sex, as well as to uncles, aunts and cousins. What is the obligation on the patient to give information about other family members when that information is not necessary for the diagnosis of the illness in the patient? The cooperation of the patient in the task of developing a family tree may depend on a variety of factors including their comprehension of the problem, their actual knowledge of other family members, their relationship with these other family members, the presumed benefit of the investigation and their desire to protect these family members from investigation. In turn their willingness to give information could depend upon the point in time that the patient was given the diagnosis.

In APKD the diagnosis has frequently been given to the patient when symptoms first appear or when the patient is unwell. In these circumstances the patient has firstly to absorb information about what is to happen to himself or herself and, as Sahney et al

(1982) point out, the patient may then be unable to assimilate all the information that is given. These authors raise the ethical question of collecting information about the extended family when they state: " ... because the patient may deny the reality of the disease, the counsellor must persist in order to identify and trace family members at risk and have them evaluated." (p467).

There are two important ethical issues raised implicitly in the study by Sahney et al. The first is embodied in the statement quoted above " ... the counsellor must persist in order to identify and trace family members at risk ... ". In these circumstances is the patient giving information voluntarily and has informed consent been sought? It is appreciated that some patients may find it very difficult to remember biographical details of their family.

The second problem concerns what is done with the information about other family members and whether the doctor should divulge information to a third party, the relative. This situation also raises the question of medical confidentiality. The norms of medical confidentiality require that doctors do not divulge information given to them by their patients and which these patients wish to keep secret (Gillon 1988). Both the GMC (1987) and the BMA (1984) describe the few exceptions to the situations where a doctor may divulge information given to them by a patient. These include situations such as when it is medically undesirable to seek the patient's consent, when disclosure to a third person not a relative is in the best interests of the patient, certain court requirements to disclose and when it is in the interest of the public to disclose. Gillon (1988) argues that at present it seems likely that definitions of medical confidentiality as described by the BMA and the GMC do not permit the giving of medical confidences to third parties unless there is what is described as "harm equivalent to a grave or very serious crime" (p172). Neither the

BMA nor the GMC recommendations specifically mention whether genetic disorders would fall into this category but it is unlikely that they would.

It becomes important, therefore, that information given to doctors by patients about their relatives and partners so that appropriate relatives can be informed of their genetic risk must be based upon informed consent. And this importance of informed consent is emphasised by Pelias (1991) when she states: "The geneticist should have the consent of both his client and the participating collateral relative before revealing any information to the relative. Any fortuitous information about non-participating relatives should *ideally be kept in confidence until an inquiry is initiated by that relative himself*" (my italics). Pelias suggests that the geneticist is in a position to encourage communication among family members, but the geneticist is obliged to respect the privacy, autonomy and confidentiality of those with whom he has direct contact (p350).

The importance of informed consent in screening for fetal and genetic abnormality was also emphasised by the King's Fund Forum Consensus Statement (1987).

The use of DNA markers in the testing of genetic diseases such as APKD requires blood samples not only from the patients but also from several relatives. Relatives who do not wish to "be involved" or to receive any genetic information about themselves, can, at least theoretically, not participate by not giving a sample of blood. However it is not known to what extent pressures may be put on these relatives to participate. Nolan and Swenson (1988) suggest that family pressures on even distant relatives to participate in genetic diagnosis can result in harm to individuals and to family relationships.

The problems of genetic counselling for APKD fall fully into those described in Chapter 2 as part of the fourth paradigm.

CHAPTER 5: LAY PERCEPTIONS OF HEALTH AND ILLNESS

5.1 Introduction

In the studies into genetic counselling and APKD discussed in Chapter 4, there is reference to the 'genetic burden' of APKD (Sahney et al 1982), and also to patients who have 'realistic perceptions' of APKD and to patients who did not 'perceive APKD as a serious medical problem' (Hodgkinson et al 1990). APKD is a chronic illness for which there is no cure. The development of symptoms is normally gradual but the symptoms of chronic renal failure can be distressing and the treatment of end stage renal failure is complicated and creates restrictions for the patient.

In the these studies there is the assumption that those at risk for APKD would wish to take advantage of presymptomatic diagnosis 'so that appropriate reproductive decisions can be made' and that pregnant women with APKD would take advantage of prenatal diagnosis followed by termination of an affected fetus. The assumption here is that patients with APKD and those at risk of APKD perceive APKD as a sufficiently serious illness that they would wish to prevent. And yet the conclusion of Hodgkinson et al (1990) is that earlier presymptomatic diagnosis will be unlikely to have an effect on reproductive decisions.

There are two problems inherent in this assumption. The first concerns the interpretation that patients perceive APKD in the same way as the doctors looking after them. Doctors and many others undoubtedly perceive APKD as a serious illness that people would wish to prevent. In the present climate of increasing health costs, doctors also may be concerned about the cost of treating the illness and this may influence their perception of the illness. The second problem is that patients with APKD cover a broad spectrum of symptoms from the asymptomatic person to patients in end stage renal failure

and that the symptoms and the available treatment for these symptoms may influence patients' perception of the illness. Furthermore, although APKD is a genetic or family condition, some patients may not have been in contact with a relative with more advanced symptoms of the illness. In this chapter specific aspects of lay perceptions that may be relevant to APKD are explored.

5.2 LAY AND BIOMEDICAL CONCEPTS OF ILLNESS

In western society, the medical definition of ill health is largely based on objectively demonstrated physical changes in the structure or function of the body and these changes can be quantified by reference to some standard of physiological measurement. This medical perspective assumes that diseases are universal and will be the same in whichever country or society they appear. However, as Helman (1986) points out, this perspective does not include the social and psychological dimensions of health and illness which determine the meaning of the disease for the patient and his family.

Authors such as Engel (1980) have suggested that the dominant model of disease is biomedical, with molecular biology its basic scientific discipline. This model assumes disease to be fully accounted for by deviations from the norm of measurable (somatic) variables. It leaves no room within its framework for the social, psychological and behaviourial dimensions of illness (p196).

Helman (1986) reminds his readers that not only do medical models change over time as new discoveries are made and new technology becomes available but also that medical models are neither homogeneous nor consistent. Any one doctor may use a number of different perspectives when making a diagnosis, including lay health beliefs. For example, according to Stacey (1988), GPs may collude with the lay model when they

negotiate with their patients on the basis of a lay model and for example agree that 'there is a bug going around'. As Stacey (1988) comments, this is not a scientific explanation.

However, this is not to say that patients and professionals will hold quite different beliefs about illness. For example, there is evidence that lay ideas about the causation of illness, if not paralleling scientific theories (Calnan 1987), are influenced by them (Helman 1986). According to Helman an increasing number of people use the germ theory, where the cause of illness is external to the body, as an explanation for their illness. Helman has observed that such explanations are particularly common amongst his younger patients and he links the spread of the germ theory in lay models of illness causation with the introduction of antibiotics and the establishment of the National Health Service.

There is also evidence that to some extent biomedical concepts are used by patients. For example Blaxter (1983) demonstrated that the respondents in her study adopted biomedical concepts and ideas although their logical framework followed a different model. Similar findings were also described by Cornwell (1984)

5.3 LAY CONCEPTS OF HEALTH AND ILLNESS

For some time, social psychologists and sociologists have examined the ways in which patients explain, perceive or try to make sense of, their illness.

In an analysis of why people with APKD do or do not take certain actions and take particular views about the illness, it may be helpful to examine studies of lay concepts of both health and illness. The diagnosis of APKD in a presymptomatic person does not necessarily make that person ill. The pathology has been identified but the person may not have experienced any symptoms or changes in him or her body nor defined him- or herself as ill. For example Cassell (1978) describes illness as the problem the patient has

when he goes to the doctor: disease is what the patient has when he leaves the doctor. Disease is something attributed to an organ or part of the body, while illness is the subjective response of the patient to being unwell.

Blaxter (1990) examined perceived links between health and lifestyle. The majority of her respondents expressed multiple concepts of health. The types of definitions offered varied mainly by stage in the life cycle and also by sex. For example younger people spoke in terms of physical fitness or vitality while in middle age ideas became more complex with a greater emphasis on total mental and physical wellbeing. In old age there was a greater emphasis on function, on being able to manage for oneself. There were also social class differences in the self- assessments of health, with the most disadvantaged and the poorest respondents most likely to say that their health was poor.

Locker (1983) examined how people construct definitions of illness. He suggested that illness is one explanation of patterns of action described as 'illness relevant behaviours', which were used in the construction of the definitions of illness and in prescriptions for action, such as going to bed, calling the doctor, not going to work. These actions characterise people who are ill; those who follow these actions will be described as being ill, and those who say that they are ill can be expected to behave in this way. Locker also suggested that illness has a moral component in that those who are labelled as ill are usually absolved of responsibility for their actions because the major cause of illness is believed to be outside the control of the individual. Illness, therefore, involves judgements about the extent to which a person has control over his actions.

Blaxter (1983) in her study of attitudes of Scottish women to health and disease, found that the most commonly cited cause of illness was family susceptibility and heredity including ideas about family similarity and inherited weaknesses. Blaxter argued that this focus enabled the women to deny that could in any way be responsible for their own

illness and this is similar to Locker's explanation that the cause of illness was outside the control of the individual. Blaxter found that the women distinguished between illness and disease. Illness for these women was weakness, 'lying down to it', being functionally unfit and giving in to disease. The women also offered explanations from the environment such as bad working conditions, poor housing and poor climate. Blaxter suggested that it was more acceptable for her respondents to find a cause or explanation for their illness in the environment rather than to locate the responsibility in their own body.

Blaxter also widened the scope of investigations into chronic illness by examining both the way in which the individual perceives his or her place in society and the relationship between this self-perception and the structures that surround and constrain the individual. For example, Blaxter (1983) described the administrative structure, which, she suggested, forces doctors " ... to choose between 'sick' or 'well' for a certificate, to adjudicate whether a man is 'fit' to work and not whether he wants to work or whether it would be best for him to work" (p240). "By convention, the actions of doctors are given arbitrary meanings: a patient has to wait for the final review of his condition before he has recovered." (p239). This administrative structure also imposes a timetable on the patient. For example an individual can be 'off sick' from work for up to 5 days before having to supply a medical certificate and be recognised as officially sick, while short term sickness lasts for three months.

Pill and Stott in a series of studies between 1981 and 1987 examined beliefs about health and illness amongst Welsh working class mothers with specific focus on the distinctions construed between inferences of internal causality (ie individual responsibility) and of external attributions (fate and the influence of powerful others). They developed a salience of lifestyle index which they used to distinguish between people whom they described as 'lifestylists', those who saw health as under their own control, and others

whom they called 'fatalists' who felt that they had little control over their health, seldom reported trying to improve it and were likely to rely on the expertise of the doctor. Lifestylists reported taking regular exercise and seeking to reduce stress. They were knowledgeable about the causes of such illnesses as heart disease and cancer but they commented on the need to evaluate medical advice. These authors were careful to point out that their respondents were neither totally fatalists nor did they believe that leading a healthy lifestyle would grant them immunity from illness. While the respondents in these studies had no doubt that there is a link between behaviour and lifestyle and health and illness, health was not seen as a matter of personal responsibility. These respondents argued that if people lived in circumstances which reduced choices of courses of action, individuals could not accept blame for their illness. Pill and Stott have suggested that while this interpretation may be seen as 'fatalism' from one perspective, from another it may be seen as a realistic appraisal of the complex variables involved in the aetiology of illness.

A question raised by the work of Pill and Stott concerns the extent to which those respondents described as lifestylists acquire the more positive self-perceptions as a consequence of overcoming adversity or whether they overcome difficulties because of the attitudes to life that they adopt. Similarly do those who were described as fatalists believe that life has been hard, or is life hard for them because their attitude does not encourage them to help themselves? An alternative approach is to accept that these two different explanations are themselves explanations of health and illness.

Amongst the respondents in the Pill and Stott study the notion of heredity was stated as an explanation of the cause of illness. Blaxter (1983), who had similar findings, commented that there appears to be a greater readiness to involve genetic causation in lay culture than in medical science. She suggests that patterns of shared illness in families can

offer a powerful source of ideas of inheritance. However, it is not known how widespread this interpretation is, nor whether it is an interpretation that would be accepted by individuals from families where there is a known inherited illness.

Dingwall (1976) accepted that illness was a socially determined state and that people from all social groups engage in the active construction and interpretation of reality for themselves. He suggested that people try to make sense of health and illness through what he calls the concept of 'ordinariness'. To be ordinary is to do usual, expected, normal things at usual times in usual places and this requires familiarity with commonsense knowledge. Therefore, according to Dingwall, our understanding of illness is dependent upon our conception of ordinariness.

5.4 CONCEPTS OF ILLNESS AS SOCIAL REPRESENTATIONS

When we label people as 'ill' what is happening is a process of social definition in human terms. Illness is only meaningful as an illness when it has particular implications for the person. Illness is, therefore, a product of a particular social reality. Berger and Luckmann (1967) suggest that knowledge in any culture is distributed within socially segregated sub-universes of meaning (p103) which are developed within specialized groups. According to Berger and Luckmann such sub-universes of meaning compete within society for dominance and that in advanced industrial societies "pluralistic competition between sub-universes of meaning becomes the normal state of affairs". The authors argue that as these sub-universes become more complex they become sealed off from one another. They illustrate this with the following example (p105):

> "It is not enough to set up an esoteric sub-universe of medicine. The lay public must be convinced that this is right and beneficial and that the medical fraternity must be held to the standards of the sub-fraternity. Thus the general population is intimidated by images of the physical doom that follows 'going against the doctor's advice'; it is persuaded not to do so by

> the pragmatic benefits of compliance, and by its own horror of illness and death. To underline its authority the medical profession shrouds itself in the age-old symbols of power and mystery, from outlandish costume to incomprehensible language, all of which, of course, are legitimated to the public and to itself in pragmatic terms. Meanwhile the fully accredited inhabitants of the medical world are kept from 'quackery' (that is, from stepping outside the medical sub-universe in thought or action) not only by the powerful external controls available to the profession, but by a whole body of professional knowledge that offers 'scientific proof' of the folly and even wickedness of such deviance. In other words, an entire legitimating machinery is at work so that laymen will *remain* laymen, and doctors doctors, and (if at all possible) that both will do so happily."

Berger and Luckmann argue that it is possible to distinguish between four different levels of legitimation. The first is built into the language, the second is the impact of everyday explanations, the third are explicit theories of a particular collection of knowledge, and fourthly there are symbolic sub-universes themselves. These are whole bodies of knowledge which integrate different provinces of meaning into coherent wholes. By legitimation, the sub-universe of biomedical knowledge becomes the property of individuals.

Herzlich (1973), in her study mainly of Parisians with some country people from Normandy, set out to examine the way in which people made sense of the concepts of health and illness. Herzlich, who was influenced by the work of Moscovici (1961) on social representations, analyzed the content of respondents' accounts of health and illness. Herzlich argued that health and illness are experienced and thought of by the individual in reference to society. She found that illness was conceived of as being produced by a mainly urban way of life, whereas health came from within the individual. Illness was conceived of as something external to the individual and in terms of pathological agents such as germs, which were perceived as products of modern life. Certain illnesses such as cancer and mental disorders were also conceived as products of the way of life.

Herzlich identified three kinds of perception of illness:

1. illness as destructive;
2. illness as a liberator and
3. illness as an 'occupation',

and suggested that "in terms of these the individual expressed his relation to illness or to health as this relation is established in society, and his relation to society as this relation is established through health or illness" (p105).

The concept of illness as destructive, according to Herzlich, appeared characteristic of active people for whom the essential part of illness was perceived as inactivity, as exclusion from their social group, changed professional and family and financial problems. Herzlich identified two possible responses to destructive illness, denial and passivity. Denial can be seen as representing victory over the illness. To reject illness behaviour is to get better and to maintain one's life through social integration. The maintenance of activity as long as possible is important. The refusal to take special care or to go to the doctor was seen as a desire to deny illness as was the refusal to 'know' or find out about one's condition. As one of the respondents in Herzlich's study said " ... there's nothing like telling people that they are ill to make them feel even iller ... When you know, that's it, you have got your illness and I think that makes it worse ... ". Denial does not need to be complete but any adoption of illness behaviour has to remain hidden or discreet. If the illness becomes established the patient may become powerless to deny and this, according to Herzlich, is when passivity often takes precedence over denial.

For some people illness appeared as a kind of liberation where it was possible to relinquish certain social constraints and responsibilities thus 'freeing' oneself to think and to be alone.

Illness was also seen as an occupation where the patient is occupied in fighting the illness with the aim of getting better.

Cure is the normal outcome of illness. In contrast health was conceived as something internal to the individual and the major factors determining health were temperament and heredity. Herzlich identified three categories of health which she called: health in a vacuum, reserve of health and equilibrium.

Health in a vacuum simply means the absence of illness. Reserve of health was seen as something the individual had and childhood was seen as a good opportunity to develop a reserve of health. Equilibrium was sometimes referred to as real health when 'the body functions like a well oiled machine'. Equilibrium means physical and psychological well being and absence of fatigue.

Herzlich's respondents also referred to heredity. Some referred to the inheritance of weak or strong points, of fragility or robustness requiring certain precautions. Other respondents tended to restrict the role of heredity "... we don't really know why some people have abnormal children ... there is heredity ... but there are parents who are drunkards and others whose parents aren't drunkards, who are still abnormal." (p25). There were also respondents for whom hereditary diseases were much rarer than those diseases due to the way of life: "There's heredity if you like, but it doesn't count for all that much ... in the cities you come across so many queer folk in the street you don't really notice them." (p25). Herzlich suggests that while this respondent did consider heredity as an explanation for some illness he abandoned it for the view shared by many other respondents that the way of life was the cause of much illness.

5.5 CONCEPTS OF CHRONIC ILLNESS

APKD is a chronic illness. Authors such as Charmaz (1983) have suggested that the onset of chronic illness represents an assault on both the person's physical self as well as on the sense of identity held by the person and calls into doubt the person's self-worth.

Chronic illness by definition is a long-term and possibly permanent event in a person's life. Bury (1991) suggests that the 'meaning' of chronic illness is to be found both in the consequences for the individual in, for example, the effects of the onset of symptoms on everyday life at home and at work as well as in the significance of the chronic illness. Significance of a chronic illness according to Bury means that different illnesses carry with them different connotations and different imagery, and that these differences may have a profound effect on how individuals regard themselves and on how they think that others perceive them. This is evocatively described by the author, Susan Sontag, in her work on the metaphors used to describe tuberculosis and cancer (1983) and more recently AIDS (1989)

The meanings surrounding illness often change as they interact with different stages of life. Changes in symptoms over time may affect social responses, and these in turn will influence experience. Bury (1991) suggests that chronic illness creates what he describes as 'meanings at risk' by which he means that in responding to chronic illness, individuals "test the meanings attached to their altered situation against the reality of everyday experience" (p454). This is a situation of risk, as individuals cannot be certain that their own developing perception and definition of the situation will be shared by others. For example, Shelley (1985) in his description of his life with haemophilia learned that "as long as people were ignorant of my condition I was welcomed anywhere, but as soon as they became aware of the truth I was an alien who made them feel uncomfortable ... I must invent plausible excuses that the normal person could relate to, such as having a

bleed. I had to remember never to tell them that I had had a bleed" (p115). A similar situation is described by Iphofen (1990 p462) in his study of *petit mal* where some patients alternate between concealing their situation and revealing it, depending upon their situation.

Uncertainty is another feature of chronic illness and this may be particularly disruptive at the time of diagnosis. This is particularly true in conditions like Huntington's Chorea where at the beginning of the illness symptoms of the illness overlap with a range of what could be considered normal symptoms and behaviour (Phillips 1982). A raised sense of uncertainty also features in chronic illness when people consider employment (Markova et al 1980). In patients with renal failure this raised sense of uncertainty was evident when considering social and holiday arrangements and kidney transplantation (Morgan 1988).

The term 'legitimation' is described by Bury (1991) as the process whereby the individual attempts to establish an acceptable place for the chronic illness in their life. The diagnosis of Huntington's Chorea can be seen to represent official validation of a series of problems that have faced the patient. Similarly Robinson (1988), in his study of multiple sclerosis, suggested that people might use the diagnosis of multiple sclerosis to overcome the feelings of being regarded as mentally ill.

In APKD there are now not only better forms of diagnosis but also more treatment. Gerhardt (1990) suggests that the new and more effective forms of treatment that are now available for many chronic conditions have extended the role of medicine to affect the quality of life as well as the clinical outcomes. She suggests that expectations of medicine have been raised in an area where previously the use of medicine had been limited. This raised expectation of what medicine may have to offer can lead patients into searching for

more and more information that makes sense to them. This situation is described very clearly by Jobling (1977), who has psoriasis himself, in his study of that disease.

5.6 CONCEPTS OF SERIOUSNESS OF ILLNESS

What does 'serious' mean? Herzlich (1973) found amongst her sample that seriousness of illness was most frequently associated with the danger of dying. But seriousness was also associated with the duration of the illness and with its irreversibility. Herzlich suggests that the seriousness of the illness is not something specific but "indicates an accentuation of one of the features of a disorder" and that this will vary from disease to disease, for example incurability in the case of cancer but duration in the case of tuberculosis, frequently considered as curable by respondents in Herzlich's study. Herzlich argues that the attributes used by her respondents to define the seriousness of the illness differed from medical classifications of seriousness. They are not related to the aetiology of the illness nor for example, is there a distinction made between diseases of the digestive system and diseases of the circulatory system. Herzlich suggested that the attributes have all the function of indicating the implications of the illness for the present or future life of the individual and rendering them meaningful by defining their relationship to the individual.

In their study of HIV and AIDS in people with haemophilia, Markova et al (1990) showed that people with haemophilia who were HIV antibody positive did not consider HIV such a serious condition as did people with haemophilia who were HIV antibody negative. The authors offer different explanations for this finding. Denial of the seriousness of HIV could be a coping strategy on the part of those affected which would also give them some feeling of control over their illness. Alternatively those who were HIV antibody positive were also those more severely affected by haemophilia and because

of the severity of their illness were likely to have overcome life-threatening episodes of illness. For these patients, therefore, HIV infection could be perceived as of relatively smaller importance when compared with other patients with haemophilia less severely affected.

This is similar to Stainton Rogers' (1991) idea of 'the body as a machine'. She suggests that within this system illness is regarded as naturally occurring and modern biomedicine is seen as the only valid source of effective treatment for any kind of serious illness. In this model the medical profession are seen to have the expertise to cure all problems. This image is also reflected by the media both in newspapers and in television in programmes like *Tomorrow's World* (Murrell 1987). Furthermore it is an image adopted by such disease-related voluntary organisations as the Haemophilia Society (Madhok et al 1991) and the Kidney Patients Association (see *Outlook* 1984) in their bulletins to members as well as for use in fund raising.

Murrell (1987) argued that programmes such as *Tomorrow's World* are not neutral windows through which science can be viewed but that they impose approving glosses on explanations which constructs an image of "an autonomous science which naturalises the 'impartiality' and, in a material sense, the inevitability of the consequences of 'scientific progress'" (p100).

Moscovici and Hewstone (1983) suggested that this message that proclaims how wonderful science is gives people second hand knowledge which fulfils a psychological need. These authors suggest that biomedical theorization which promises effective cure and turns illness into disease gives a sense of safety as well a fulfilling the desire to know of the cause and the suitable treatment advised for a particular illness.

Stainton Rogers (1991) suggests that an implication of this interpretation is that it can increase dependency and an unwillingness to assume responsibility, since from this

perspective "medicine is seen as able to patch people back together after they become ill, making preventive actions unnecessary" (p 210).

Another consequence of this view of modern medicine is that the expectations of the public are likely to be raised, with the resulting increase in demand for more expensive treatments. This in turn puts very considerable financial pressure on health services. Currently policy makers in the United Kingdom and in other western countries have been forced to develop principles for prudent health care allocation. For example the Oregon Experiment (Lansdown 1992) has attempted to develop a system, based on the views of the public of which health services should be available, and, therefore, to prioritise resources for medical care by rational rationing. This idea has created very great interest and controversy. In the United Kingdom there have been recent changes in the organisation of health services with the introduction of general practitioner (GP) Fund Holding Budgets and the adoption of trust status by certain hospitals. There has been considerable focus on the cost of the service. A result is that some patients are seen as being expensive and because of this may not be accepted as patients by GP practices (Patients Association 1992).

It is not known whether such financial restraints will alter the common expectation of patients that something can be done for them and that they can be cured, thus negating the need for the patient to take responsibility for his health and to take appropriate preventive action. This point was emphasised by Ehrenreich and Ehrenreich (1978) in their comment that these unrealistic expectations of what the medical profession can do has led to the inability of (North) American medicine to deal adequately with problems that require the patient's willed participation in the cure.

5.7 CONCEPTS OF ILLNESS AS STIGMATISING

Chronic illness can also be stigmatising. Goffman (1968) describes some of the consequences of the stigma (pp5-6):

> "The individual who might have been received easily into ordinary social intercourse possesses a trait that can obtrude itself upon attention and turn those of us whom he meets away from him, breaking the claim that his other attributes have on us. He possesses a stigma, an undesired differentness from what we anticipated — we believe the person with a stigma is not quite human. On this assumption we exercise varieties of discrimination, through which we effectively, if often unthinkingly, reduce his life chances. We construct a stigma theory, an ideology to explain his inferiority ... We tend to impute a wide range of imperfections on the basis of the original one ... Further, we may perceive his defensive response to his situation as a direct expression of his defect."

The visibility of symptoms has long been noted as important in this context. For example MacGregor (1951) describes the problem in the following way (pp629-630):

> "Except when the disfigurement is accompanied by a functional impairment such as harelip with cleft palate, these facially deformed individuals do not necessarily suffer from organic or functional inability to perform the normal activities of daily living. Nevertheless they are handicapped because of the way they look. The twisted mouth, the conspicuous port wine stain or the peculiarly shaped nose may well be a barrier to the privileges and opportunities available to the non handicapped. Such an affliction, therefore, is more of a social handicap than a physical one for the suffering of the individual results from the visibility of the defect and what it means to others as well as to himself."

In her study of rectal cancer, MacDonald (1988) found that there was a high degree of perceived stigma in patients who had been treated for rectal cancer by colostomy. However patients with rectal cancer who did not have a colostomy also felt stigmatized and this Macdonald attributed to the stigma of cancer.

The stigmatising effect of illness has implications not only for the affected person but also for others close to them. Burton (1975) describes the implications for parents and non-affected siblings of having a child in the family with cystic fibrosis. And Voysey (1975), in a perceptive analysis of parents' responses to having a disabled child, showed

how parents attempt to make normal, and in doing so to compensate for, the stigma associated with disability.

5.8 GENETIC IDENTITY AND DISEASE

A strongly held belief in modern medicine is that the earliest diagnosis of a condition is the most desirable so that appropriate treatment can begin. Early diagnosis of a disease such as APKD, where symptoms develop later, raises questions about how this asymptomatic person is perceived. Will this asymptomatic person be 'classified' as having a disease even though they have no symptoms and will they have to face early medicalisation of daily life.

Nelkin and Tancredi (1989) describe early diagnosis of a presymptomatic illness as 'diagnostic labelling' (p169), and suggest that once a person is labelled as having a specific condition, even though they show no symptoms, the way is open to discrimination, stigmatisation and vulnerability. This suggests that the situation for the asymptomatic carrier would be similar to the situation where someone is already showing symptoms of the illness. The problem for asymptomatic persons is that it may be several years before they develop symptoms of the particular illness and, according to Natowicz et al (1992), such patients are prone to what they call 'genetic discrimination', in particular by insurance companies and by employers (p465).

Authors such as Mennie et al (1990) and Wexler et al (1985), writing about the predictive test for Huntington's Disease (Chorea) prior to the use of the test, commented on the benefits for those who would receive results which reduced their risk of Huntington's Disease. Huggins et al (1992) describing the Canadian experience in the use of the predictive test in Huntington's Disease found that 10% of the patients who learned that they had a decreased risk experienced great difficulties in coping with this altered risk

status. Genetic counsellors had assumed that patients would be relieved to receive a risk reduced, in this study, from 50% to 11%. The perception of the patients was different. An explanation offered by Chapman (1992) was that the patients described by Huggins used their risk status as a 'crutch' on which to place or blame some problems they were facing.

In this chapter different lay perceptions of health and illness have been explored, including perceptions of chronic illness, seriousness of illness and of genetic identity. Not all of the studies referred to may appear relevant to the study of genetic counselling in APKD. But together they form an appropriate framework which may help to explain patients' attitudes to APKD. Specific studies are referred to throughout the thesis.

CHAPTER 6: METHOD OF DATA COLLECTION

6.1 Background to the study

In June 1982 a study of patients with APKD began in the Renal Unit of Glasgow Royal Infirmary (GRI). Professor Arthur Kennedy head of the Renal Unit and Muirhead Professor of Medicine, University of Glasgow, had had a long-standing interest in APKD and supported the establishment of the study which was initially funded by a grant from the National Kidney Research Foundation.

The objectives of this study were to assess the medical and psychological problems of the population, to determine the total number of patients with APKD attending GRI, and to determine the extent of the at risk population with a view to planning a genetic counselling service for patients with APKD and a screening and counselling service for those at risk of developing APKD.

Approval for this study was given by the Ethical Committee of GRI.

A secondary purpose of the study was to collect data for this doctoral thesis which would investigate the patient's knowledge, perceptions and understanding of genetic counselling in APKD.

6.2 Where the study was carried out

6.2.1 The Renal Unit

The study was carried out at the Tenovus Kidney Unit, also referred to as the Renal Unit, GRI. The Renal Unit was spread over three sites and consisted of an eight bedded 'admission' and diagnostic ward which was closed at the weekends, laboratory, secretarial facilities, consulting rooms and seminar room on one site. The haemodialysis

ward with ten dialysis units and the CAPD unit were on another site. And there was an acute six bedded renal ward in another part of the hospital.

The Renal Unit at GRI is a major renal referral centre and patients came to the hospital from all areas of the city of Glasgow as well as from other parts of the West, South West and Central Scotland. The Renal Unit at GRI offered diagnosis and treatment for patients with APKD including hospital haemodialysis and Continuous Ambulatory Peritoneal Dialysis (CAPD). Patients were transferred to the Western Infirmary for a kidney transplant and to Stobhill Hospital for home haemodialysis.

6.2.2 Staff

At the beginning of the study, there were three full time consultants, Dr Marjorie Allison, Dr Michael Boulton-Jones and Dr Jim Dobie (who left during the study), one senior registrar, Dr Iain Henderson, and two registrars who also changed during the study. In addition Professor Arthur Kennedy took a ward round once a week and retained a special interest in certain patients. There were two junior doctors attached to the Renal Unit and these changed every six months.

There were five nursing sisters who rotated round the different sections of the Renal Unit. These senior nursing staff were assisted by staff nurses, state-enrolled nurses and some student nurses.

Other relevant staff included a senior research scientist, Mrs Mary Smith, and a technician in the laboratory, a senior renal dietician, Miss Patricia Campbell, and two secretaries. A senior social worker in the hospital, Mr Bob Paisley, spent a part of his time servicing the Renal Unit.

At the commencement of the study a senior house officer, Dr John Gribbon, was asked by Professor Kennedy to assist with the study. Dr Gribbon left during the first year

of the study and his place was taken by a registrar, Dr Keith Simpson, who remained with the study until the end.

6.2.3 Location

Glasgow Royal Infirmary is situated at the east end of the centre of Glasgow in an area in which there has been considerable demolition of inner city housing and rehousing of the population in peripheral housing estates. It is still considered a 'local' hospital by those who live nearby and it evokes considerable loyalty and affection. It has 976 beds and it is one of the two major teaching hospitals in Glasgow, the other being the Western Infirmary. Although some early parts of the hospital were built in the 18th century, the major part of it was built around 1900. A new section containing all the out-patient departments and some wards was opened in 1986.

6.3 WHO WAS INCLUDED IN THE STUDY

6.3.1 APKD patients at GRI

At the beginning of this study there was no systematic system in GRI by which patients with Adult Polycystic Kidney Disease could be identified. There was neither a system where manual records of patients with a diagnosis of APKD could be easily identified nor was there yet in existence a hospital computerised system which could identify patients with APKD. Before the commencement of the study different members of the medical staff of the Renal Unit could identify at least 40 patients with a diagnosis of APKD; it was expected that more could be found.

Professor Kennedy had, over the years, encouraged junior medical colleagues to collect data about APKD. However, there had been no consistent attempt to ascertain the numbers of patients with this illness.

6.3.2 Identification of the study population

The first task was to identify patients with APKD. The three consultants in the Renal Unit were approached and their cooperation gained to carry out a study of patients with APKD. Permission was sought from the renal unit at the Western Infirmary and the home dialysis unit at Stobhill Hospital to contact former patients of GRI.

Two methods of identifying patients for the study were used. The first method identified patients retrospectively from the medical notes. A systematic search of medical notes of all patients attending renal clinics at GRI was made to identify those patients with a diagnosis of APKD. Case notes were examined both by the researcher and by the physician attached to the project.

The criterion used to identify patients was a stated diagnosis of adult polycystic kidney disease confirmed by either intravenous pyelogram or ultrasonography. The criteria recommended for the confirmation of the diagnosis of APKD is the establishment of bilateral renal cysts either by IVP or by ultrasound and the presence of a positive family history. As on only a very few occasions was there evidence in the notes of attempts having been made to take a family history, it was necessary to rely on diagnostic evidence.

The second method used to identify patients involved the cooperation of doctors to inform APKD patients of the study and to pass on the names of these patients when such patients with APKD came to the attention of doctors at an out-patient clinic or when they were admitted to hospital as in-patients. Junior doctors were also informed of the study and their cooperation sought.

6.3.3 Location of patients' notes

Prior to the beginning of this study patients' medical notes had been kept in the Renal Unit. At the beginning of the study a system to centralise patients' medical notes in the Medical Records Department began, making it difficult to identify renal patients, since medical records were classified by patient number and not by clinic or department attended or by disease. The process of keeping track of notes was extremely time-consuming as notes moved between the Renal Unit, clinics and wards, medical records, central typing pool, Renal Unit secretaries and individual doctors. Furthermore, where renal patient notes were kept depended upon which clinic the patient had attended. It was therefore decided that the notes of patients with APKD should continue to be retained in the Renal Unit regardless of which clinic they had attended. The cooperation of Renal Unit secretarial staff, medical records clerical staff and doctors was sought.

6.3.4 Professional collaboration

Informal talks were given at departmental staff meetings in the Renal Unit which were attended by many Renal Unit staff including doctors, nurses, dietician, laboratory and social work staff. An objective of these talks was to inform Renal Unit staff of the aims of the study and to gain their interest and support. All the consultants gave the names of patients with APKD as did both the senior laboratory scientist and the renal dietician. As the study developed, the opportunity was taken to inform Renal Unit staff of the progress of the study as well as to tell new staff about the study and its aims. Draft questionnaires were shown to staff for comment. In addition as the study developed invitations to talk to staff of other departments including radiography and urology were accepted, with the intention of increasing knowledge of the study and possible future referral to the Renal Unit of patients with APKD.

The researcher attended the major renal out-patient clinic every week and spent time explaining the study to out-patient nursing staff. Lectures were given to nursing staff in the School of Nursing, on issues surrounding the early detection of genetic disease and the social and psychological problems associated with chronic illness.

In addition the opportunity was taken to talk to members of the local Kidney Patients' Association about the study and its progress.

6.3.5 Study population

As it was not known how many patients with APKD there were, it was decided to invite all patients with a diagnosis of APKD who were attending the Tenovus Kidney Unit GRI to assist with a project to determine the total number of affected patients and the extent of the at risk population, with a view to developing a genetic counselling service and a screening programme for at risk relatives. Patients were approached by letter and offered an appointment to attend a special clinic established at the Tenovus Kidney Unit. For the duration of the study patients would attend this special clinic and those current patients of GRI would cease to attend the renal out-patient clinics for the duration of the study. In order to reduce travelling time and expense for the patient, appointments were offered when the patient would be due to attend an out-patient clinic.

It had been intended at the outset of the investigation that a specific time would be set aside when the designated physician would be seeing patients. This proved to be impractical. Both the doctors allocated to assist with the study were junior and were not allocated nor able to negotiate specific time to service this clinic. Furthermore the time for the medical consultation was relatively short in comparison with the time required to conduct the study interviews for which one to one and a half hours was required.

Following discussions with Professor Kennedy and all consultants in the Renal Unit, it was decided that it was desirable that study patients should attend a special clinic at the Renal Unit and that patients would be seen by the doctor allocated to the study or by another renal physician. It was the responsibility of the researcher to make arrangements for the medical consultation.

Patients with the following criteria were included in the study:

(1) patients with a stated diagnosis of APKD in their notes who were currently attending the Renal Unit at GRI;

(2) patients with a stated diagnosis of APKD who had formerly attended the Renal Unit at GRI and who had been transferred to the Western Infirmary for kidney transplant;

(3) patients with a stated diagnosis of APKD who had formerly attended the Renal Unit at GRI and who had been transferred to Stobhill Hospital for home haemodialysis treatment.

The reasons for including patients in this way were to have patients at each stage of APKD including asymptomatic patients, those with mild symptoms, those in end stage renal failure, those being treated with hospital haemodialysis, home haemodialysis, CAPD and those who had had a transplant, as well as to determine the extent of the at risk population.

Patients were excluded from the study if they were in the terminal stages of illness or if it was known that there was some major problem which made attending the hospital difficult. These proved also to be reasons why patients dropped out during the course of the study.

Each patient was assigned a study number and added to a master list in alphabetical order. Records were kept in a locked filing cabinet in a consulting room, which was primarily used for the study, in the Renal Unit.

As it was not known how many patients with APKD there were and as it was anticipated that numbers might drop through illness or death, the initial target was to accrue all patients until 100 people with APKD had been included. In the event fewer than this were identified in the time allocated to the study.

6.4 METHODS OF DATA COLLECTION

6.4.1 Interviews and questionnaires

The nature of the subject under investigation, a genetic disease, genetic counselling and the patient's understanding and perception of these topics, required an extremely sensitive approach to data collecting. There is some evidence that respondents may answer questions of a personal or potentially embarrassing nature more willingly and accurately when not face to face with an interviewer whom they do not know well (Cannell and Fowler 1963). This would indicate the use in certain circumstances of self-administered questionnaires rather than interviews. This did not seem appropriate for the major data collection of this study.

There were several reasons why the use of interviews rather than of self-administered questionnaires was preferred. It was important to ensure confidentiality and to establish that the patient's name and address were accurate. Patients move house and one cannot rely on the accuracy of hospital records. In any family the same forename may be used by more than one family member. Furthermore in a study about a genetic disease it is likely that there will be patients with the same surname (and even the same forename), thus necessitating the need for great accuracy in diagnosis and record keeping.

6.4.2 Family history or pedigree

Patients in whose notes the diagnosis of APKD was recorded and where this diagnosis had been confirmed by intravenous pyelogram (IVP) or ultrasonography were approached. According to Sahney et al (1983), an accurate diagnosis of APKD is confirmation by IVP or ultrasound of bilateral renal cysts and a positive family history. An examination of a few sets of notes showed that a family history was seldom taken or at least that there was no record of this having happened and this observation was confirmed by medical staff. Doctors who had worked in the Renal Unit for some time may have known several affected patients from one family. Comments such as 'Mrs Brown's sister' might appear in the notes, but a detailed pedigree was seldom included.

It was essential, therefore, to interview patients to develop a pedigree both to confirm the accuracy of the diagnosis and to assess the numbers of relatives at risk of developing APKD. In addition, the accuracy of the diagnosis had to be determined before asking detailed questions about the patient's understanding of the genetic implications of APKD and questions about genetic counselling.

Furthermore, it was felt that the process of developing a family pedigree could be distressing for some patients as they realised the number of people in their family who had APKD or who had possibly died as a result of APKD. It seemed therefore, important that this information was collected in the presence of the patient.

The development of a pedigree was started in the first interview. All patients were willing to cooperate. As some patients knew very little about their ancestors and their cause of death, the family pedigree could take some time to complete. Many patients became extremely interested in tracing their family history and presented large family

trees in some cases going back as far as the 17th century. In these cases, however, the cause of death was usually not known.

A strong family history where there are sibs, cousins and offspring affected by APKD could have an effect on the way in which patients answered certain questions and on the way they perceived APKD. A grading was given to the pedigrees so that the family history could be used as a variable in the analysis of the data. How this grading was constructed is described in Section 9.12.

6.4.3 Type of interview

A major advantage of interviews is their flexibility. It is possible to probe for more specific answers and questions can be repeated when the response indicates that the respondent has not understood the question. In the interview it is possible to control the order in which questions are answered and to ensure that all questions are answered, or, if appropriate, omitted. The interviewer can observe body language and respond appropriately (Bailey 1987). In the interview it is possible to use language that is understandable to and part of the frame of reference of the person being interviewed (Patton 1980).

It was probable that some patients would find talking about APKD and about relatives who had already died from APKD distressing. A formal or structured interview with the need to ask each question as it is worded (Judd, Smith and Kidder 1991) was therefore considered inappropriate.

A less structured interview, similar to the personal history interview described by Selltiz (1976) was chosen. Each interview would have a theme and a questionnaire would be designed to reflect that subject. The importance of this type of interview is that the questions do not need to be asked in the order that they appear in the questionnaire. There

is flexibility in that the interviewer can probe. The chief function of a probe is to lead the respondent to answer more fully or more accurately. Another function of a probe is to enable the interviewer to ensure that all relevant topics have been covered, or not, as appropriate, as well as to structure the answers. There are a variety of ways of probing including repeating the question, repeating the answer, indicating interest and understanding and pausing (University of Michigan 1969).

This type of interview provides a framework within which respondents can express their own understandings in their own terms (Patton 1980 p205). Genetics is a complex subject which some patients may have difficulty in comprehending. Questions which use the respondent's own language are the questions which are most likely to be clear to the respondent. The type of interview model adopted needed to allow a degree of flexibility for the investigator in order to maximise comprehension by the respondent. The flexibility of these semi-structured interviews allows for a full exploration of unanticipated factors. This may mean that different questions are asked of different patients and may cause problems when comparing data. It is arguable that this type of interviewing may introduce more bias than for example a highly structured interview. Gorden (1969) suggested that it may be necessary to return to a topic on several occasions within one interview to enable respondents to remember. Gorden is referring to respondents who may have memory failure. Memory failure may also be a problem for some people with uraemia. However it is possible that the subject matter of this study may be distressing. In these circumstances respondents who felt hurried by a highly structured interview may be unable to remember accurately. It is arguable that the unstructured interview is less stressful for respondents than the highly structured interview where respondents may feel the urgency to move on to the next question.

6.4.4 Procedure for interviewing

All interviews were to be carried out by the one researcher, myself. From previous experience of interviewing patients with serious genetic diseases in the Genetic Register System Acceptability Study (subsequently referred to as the Acceptability Study, Wilkie and Sinclair 1977), I appreciated the sensitivity of the subject matter for the patient. I also anticipated that the study interview might be the first occasion or the first formal occasion when the patient had an opportunity to talk about APKD in detail as well as its genetic transmission. I believed that having sufficient time and a quiet place to carry out the interview were important considerations for the success of the study. One and a half hours was allocated for each interview although it was calculated that the actual interview would take less than that time. A quiet consulting room through a double door off the main corridor of the Renal Unit was acquired for interviewing. The room was warm (some patients attended for interview when they were in-patients) and easy chairs were arranged in a comfortable manner. Occasionally the interview was interrupted when medical staff felt that the room was needed by them to see a patient.

I had learned from the Acceptability Study that patients may disclose information that they did not wish discussed with anyone else. Patients were therefore reassured at the beginning of the study that any information that they gave was confidential to the study and that any publication that resulted from the study would not be able to identify individual patients. Patients were also reassured that any information gained during an interview would not be discussed with Renal Unit staff unless with the express permission of the patient. I realised that difficulties could arise with staff, in particular medical staff, who might wish information about particular patients and who believed that either the researcher had information or that the researcher could get particular information.

Nevertheless, I believed that it was crucial to maintain the confidentiality of patients and their trust.

I was aware of the importance of developing a rapport with the patient of the manner in which the study was introduced to the patients and of creating a non-judgmental atmosphere in which the patient felt secure.

As a trained counsellor, I was familiar with the need to promote a good relationship and to show empathy, openness and acceptance. Within the interview, the skills of probing, reflection, clarification and summarising (Nelson-Jones 1982) were used.

6.4.5 Tape recording of interview

The form of interviewing adopted for this study requires very considerable concentration on the part of the interviewer. The social process of the interview is important, particularly the way in which the interviewer interacts with the patient. It was also felt that to give full attention to the person being interviewed was important and this militates against constant note taking. It seemed appropriate to consider tape recording all interviews so that recording and transcription of data could be done at a later date. It was explained to the patient prior to the beginning of the interview that tape recording enabled the interviewer to concentrate on what was being said and to fill in the questionnaire accurately. The permission of the patients to record the interview was sought. In addition patients were reassured that the tape would only be used for this purpose and would be erased when data had been transcribed.

6.5 DATA VERIFICATION AND PROCESSING

6.5.1 Reliability and validity

Reliability is defined as the ability of the data gathering instrument to obtain consistent results (Oppenheimer 1972). One measure of reliability used was to compare information collected from different sources, for example the demographic information collected in the first interview and the information in the medical notes. It is recognised that hospital records are not always accurate. When there were inconsistencies between the study interview and the patient's medical records, the patient was asked again at the next interview.

Within each questionnaire there was an internal check on consistency by repeating certain questions in a slightly different form. For example in Questionnaire 1, Section 5, questions 4 and 8 asked for the same information in a different way.

Questions were also repeated over time. For example section 8 in questionnaire 1 on problems associated with APKD was repeated in questionnaire 3. Similarly the section on factors considered important in genetic counselling, section 3, questionnaire 2, was repeated in questionnaire 3.

Validity is concerned with the extent to which the instrument actually measures what it sets out to measure. Content validity was assessed in a number of ways. Previous experience on the Acceptability Study, knowledge of work in genetic counselling in Haemophilia, knowledge gained from a literature review and my experience of working in a voluntary capacity with families with Huntington's Chorea identified the major areas of investigation. Prior to the beginning of the study, a small pilot study was carried out to ascertain the validity for renal patients of the social and medical questions. Content validity was exposed to peer and interdisciplinary review. Draft and final questionnaires were circulated to Renal Unit colleagues for comment.

6.5.2 Interviewer bias

All the interviews were carried out by the one researcher. Skill was used in asking questions and listening objectively. Listening included observing and sensing generally and was not limited to the aural modality. Care was taken to hear the exact words used by the patient as it was appreciated that terminology could reflect an important orientation (Yin 1984). The researcher was assisted by being able to listen again to the interview on tape. It is understood that, however skilful the interviewer is, there will always be the possibility of some interview bias.

6.5.3 Data processing

All the interview schedules were coded. Some of the coding was done by two research assistants from Stirling University. All coding was then checked by the researcher. Analysis of the data was initially carried out using SPSS, and later by using *ad hoc* programmes specially written for this analysis; some of the statistical calculations were carried out using GLIM.

6.6 THE INTERVIEWS: CONTENT AND QUESTIONNAIRES

The study involved three separate interviews with each patient. Each interview lasted approximately 1-1½ hours and was for the majority of the study carried out in a quiet consulting room dedicated to the study. At the beginning of the study no room had been allocated for this work and some early interviews were conducted wherever a quiet corner could be found. This was very unsatisfactory for both the patient and the interviewer.

On a very few occasions when the patient was an in-patient and immobile, the interview was carried out behind screens at the bedside.

The data used for this thesis is taken from each of these questionnaires. Not all the questions asked were central to the subject of the thesis and were therefore not used in the analysis.

Each of the three interviews was structured around a written questionnaire which was later filled in by the researcher with the aid of the tape recordings. The content of the three questionnaires is now described. Copies of the forms appear in Appendix A.

6.6.1 Interview 1 and questionnaire 1

During the first interview, the first task was to establish accurate demographic information to identify the patient. This included current and previous surnames and in the case of married women their maiden name.

The patients age, sex and marital status were recorded and also the number of both live and deceased children and adopted children. This information was necessary to develop a family pedigree. An accurate family pedigree is essential to confirm the diagnosis in genetic disorders.

In **Section 2** questions were asked about age on leaving school, qualifications obtained at school and since leaving school and the educational qualifications of father and spouse. This information along with some information from section 3 would be used to identify the educational level of the patient and their parent. Educational level might be an important independent variable in the analysis of the data. Furthermore there is some evidence (Paterson and Inglis 1975) that the presence of chronic illness in the family may result in downward social mobility. The employment of father was asked as a guide for comparison.

In **Section 3** the focus was on occupation and employment. There is evidence (Townsend 1979) of higher unemployment amongst those with chronic illness. A person's

employment history, their difficulties in getting work and the degree of unemployment may influence that person's attitude to the particular illness. Respondents were asked the name of their current employment and to describe what they did. Details of previous employment history, length of time in the post and reason for leaving were asked. Those unemployed were asked the length of time since last employment and the reason for unemployment; those in employment were asked whether their employer knew about their condition.

Section 4 was concerned with housing. Questions were asked about the type of accommodation, whether it was privately owned or rented and whether the accommodation was a house or a flat. These questions were asked as it is known that housing is a good indicator of income and it was felt that the type of housing occupied by the patient added to the qualitative description of the population.

In **Section 5** questions about the patient's knowledge of the inheritance and transmission of APKD were asked. Respondents were asked to describe how they got the condition and whether it ran in the family. They were asked whether the condition was inherited and whether it could be passed on to children.

This was the first set of questions to ascertain the respondent's knowledge of the genetic nature of APKD.

Section 6 focused on knowledge of the disorder and treatment available. Respondents were asked when they were first diagnosed as having APKD, and what treatment, if any, they were currently having. Respondents were also asked if they knew what forms of treatment were available.

There were ten questions in Sections 5 and 6 relating to the patients's knowledge of APKD. The answers to these knowledge questions have been grouped together and the results scored in terms of accuracy of knowledge.

Respondents were asked when they first learned about APKD and what they were told about the condition. Patient case notes were examined for reference to the information given to the patient.

Section 7 was concerned with social and statutory support. Patients were asked about the main source of their income, whether they got help with rent and rates and whether they received any form of disability allowance. Respondents were asked what sort of transport they normally used, whether they received a mobility allowance and how they got to hospital. In this section there were also questions about contact with general practitioners and other members of the community health team and questions about life insurance.

The questions in this section were asked in order to be able to describe the effect of APKD on the study population.

Although section 7 may appear to be logically out of sequence it was desirable to move back to factual questions to take the patient's mind away from the genetic questions in section 6.

Section 8 was concerned with problems that could be associated with kidney disease. It was designed to be self-administered, i.e. completed by the patient, but often the researcher assisted the patient in completing it. Respondents were asked to identify on a six-point scale how problematic certain issues were for the person affected by APKD. The questions covered areas such as physical problems often associated with severe kidney disease, the genetic nature of the disease, financial issues associated with chronic illness, any restrictions on physical and social activity that may be attributed to chronic illness and whether APKD has an effect on family life and sexual relationships. It was hoped that answers to these questions would give some indication as to the focus or content of future genetic counselling.

6.6.2 Interview 2 and questionnaire 2

Section 1 of the second interview and questionnaire was concerned with the respondent's experience of genetic counselling. Genetic counselling was defined as a discussion about the inheritance of APKD, the effect on the patient and their children and about what they can do about it.

Questions were asked about whether the patient had received counselling and if so how had this been arranged. As a test of consistency the patients' experience of counselling was compared with what they reported they had been told in questionnaire 1. Patients were asked to identify which topics from a list of topics that could be included in genetic counselling had been discussed with them. The topics chosen were those seen as important in other studies of genetic counselling. Respondents were also asked how often they had discussions about the inheritance of APKD and its effect on them and their family, whether other members of the family were involved and whether they had taken any decisions as a result of genetic counselling.

Section 2 was concerned with attitudes to genetic counselling. Questions were asked about whether knowledge of APKD had affected the number of children they had or wanted to have. Respondents were asked whether at risk relatives should be told of their risk and whether they thought that at risk relatives should be tested for APKD. They were asked whether their children should be screened and at what age people should be screened for APKD. Respondents were asked how helpful genetic counselling was in relieving stress and anxiety, in giving information about the risk of inheritance, in helping to decide whether to have a family, in giving information about the symptoms of APKD and in giving information about the available treatment. Patients were also asked what sort of person, GP, social worker, nurse, doctor in renal unit or specialist genetic counsellor should give genetic counselling.

In Section 3 respondents were asked to rank on a six-point scale how important were topics that could be included in a genetic counselling consultation about APKD, its inheritance and its effect on the patient and their family. These topics included the risk of transmission of APKD, the advantages and the disadvantages of testing for APKD, how to tell those at risk, possibility of adoption, fostering, voluntary childlessness, deciding to have no more children, available family planning methods, sterilisation, vasectomy, Artificial Insemination by Donor (A.I.D.), the prevention of APKD and telling partners and in-laws that there was an inherited disorder in the family, and information about the symptoms and the treatment available.

6.6.3 Interview 3 and questionnaire 3

The third questionnaire began in Section 1 with further rather general questions about the patients' knowledge of APKD, including the problems of it, how it is acquired and discovered and how it can be prevented.

In Section 2 respondents were asked questions about how many children they had and how many they would like, about whether they would like grandchildren, and about whether APKD had affected their ideas about children.

Section 3 contained questions to elicit the patients' opinions of presymptomatic screening and testing at risk relatives and the children of those affected, the advantages and disadvantages of testing, and their views on the ownership of genetic. Section 4 went on to the consequences of APKD on the patients, and the effect it had had on their lives.

Section 5 contained detailed questions about the inheritance and transmission of APKD and the risks involved, in a precise 'multiple choice' form. Section 6 covered detailed knowledge of the symptoms and treatment of APKD.

In Section 7 respondents were asked to complete again a section on problems associated with kidney disease previously asked during the first interview. This was done because the condition of many of the patients had deteriorated quite considerably over the course of the study as well as to test for consistency.

In Section 8 respondents were asked to complete again the section previously completed in the second interview on topics that could be included in any genetic counselling consultation.

6.7 DATA FROM MEDICAL RECORDS

6.7.1 Medical data

There was no systematic collection of medical data about patients with APKD in GRI. There had been two major studies of APKD, Dalgaard in 1957 and De Bono and Evans in 1977. There was no reason to believe that there would be any significant differences in this population. It is possible that the degree of severity of a genetic illness could influence patients' attitudes to screening and prevention of that illness (Ekwo et al 1987). It was decided to collect medical information in order also to assess the severity of illness in the patient. Medical information was collected about the date of first diagnosis, family history, stage of illness and treatment. This information was taken from medical notes in order to establish a detailed profile of the patient and to confirm consistency of data.

Medical information about each respondent was collected from the medical notes. Information was collected about symptoms, treatment including drugs, the method and date of diagnosis of diagnosis and genetic information.

6.7.2 Symptoms

Information was collected about loin pain, haematuria, urinary tract infection, hiatus hernia, duodenal ulcer, subarachnoid haemorrhage. Blood pressure and creatinine clearance levels were recorded from the time of diagnosis to date.

6.7.3 Treatment

The information recorded about treatment included diet, whether the patient was on diet and or fluid restriction, whether they were receiving dialysis and what type of dialysis, and whether they had had a transplant. The type of drug treatment was recorded under the headings of antihypertensive therapy and pain killers. The date when diagnosis was first confirmed and the diagnostic method for confirmation of diagnosis were recorded.

6.7.4 Genetic information

Genetic information is part of the medical information about APKD and evidence of a positive family history was sought from the records including the sex of the affected parent, age of parent when parent started dialysis and age of parent's death. The number of affected and at risk children was recorded. When available, information about affected sibs was recorded as well as deaths in the family attributed to APKD. Early in the study it became clear that the availability in the medical notes of this genetic information was very erratic. Frequently there was no genetic information recorded for individual patients. Furthermore when information was recorded, it appeared to be inconsistent with information given by the patients in the research interview. It was therefore decided to use the information from the family trees made during the research interviews, to develop a family history grade, as described in Sections 6.7.4 and 9.12.

CHAPTER 7: THE STUDY POPULATIONS

7.1 INTRODUCTION

In this short chapter, the numbers of patients who were interviewed at each stage of the study are identified, so that the 'populations' considered in the later analyses are made clear.

7.2 PATIENTS CONSIDERED FOR THE STUDY

During the period from July 1982 to May 1983 all patients with a diagnosis of APKD who were registered or came to be registered at the renal clinic of Glasgow Royal Infirmary were initially included in the study. Although the original intention had been to accrue 100 patients to the study, only 83 patients (50 female and 33 male) with a diagnosis of APKD could be identified from the medical notes or came fresh to the clinic. Of these 83:

7 (2 females, 5 males) were found to have died before being interviewed,

1 (female) had emigrated before the beginning of the study, and

4 (3 females, 1 male) declined to cooperate in the study,

leaving 71 patients. Of the 4 patients who declined to cooperate the male replied that he had multiple social problems and did not wish to cooperate in the immediate future, two females replied that they were infirm and housebound, and the third female gave no explanation.

7.3 THE FIRST POPULATION

A total of 71 patients (44 females and 27 males) were interviewed at the first stage of the inquiry and these are described as 'the first population', included in the analysis of Questionnaire 1. These interviews were carried out at a special clinic established at the Tenovus Kidney Unit, Glasgow Royal Infirmary between the summer of 1982 and the spring of 1983.

7.4 THE SECOND POPULATION

A second interview for each of these 71 patients was arranged at the end of the first interview and was made around a time when the medical profession would wish to see the patient again, approximately 3 months after the first interview. Only 65 (40 females and 25 males) of the original 71 were included in this interview, at which Questionnaire 2 was completed. The six who dropped out included:

3 (2 females, 1 male) who had died,

1 (female) who was now too ill to be interviewed,

1 (female) who was found not to be affected with APKD, and

1 (male) who had moved to another district.

Those included in the second interview are described as 'the second population', and are included in the analysis of Questionnaire 2. These interviews were carried out between March 1983 and November 1983.

7.5 THE THIRD POPULATION

A third interview for each of these 65 patients was arranged approximately six months after the second interview. As with the second interview, patients were asked to return for the third interview around the time when the medical profession would wish

to see them again. Only 47 (32 females and 15 males) of the 65 in the second population were included in this 'third population'. The 18 who dropped out included:

5 (3 females, 2 males) who had died,

2 (1 female, 1 male) who were now too ill to be interviewed,

2 (males) for whom the journey to the interview was now too far,

1 (female) who was pregnant and lived some distance away,

5 (2 females, 3 males) who were found not to be affected with APKD, and

3 (1 female, 2 males) who had moved to another district.

These interviews were carried out between October 1983 and April 1984.

7.6 HOSPITAL RECORDS

The hospital medical records for each of the patients in the study were inspected, and details were extracted relating to their medical history and to their family history in relation to APKD. These hospital records were not always available or complete (see Section 6.7) and in respect of family history they did not always agree with the information obtained from the patients during the interviews. In particular the hospital records were not available for:

12 who were not included in the first population,

6 (3 females, 3 males) who were found to be not affected by APKD,

1 (female) who died before the second interview.

Reasonably complete hospital records were therefore available for:

64 (40 females, 24 males) out of 71 in the first population,

61 (38 females, 23 males) out of 65 in the second population,

all 47 (32 females, 15 males) in the third population.

From these records a grade of severity of illness for each patient was defined, as described in Section 9.11.

7.7 FAMILY TREES OR PEDIGREES

During the series of interviews described above a family tree or pedigree for each patient was drawn up by the researcher. In some cases these interlocked with the family trees for other patients in the study. Partly as a result of this work certain patients were found to be not affected with APKD, there being no family history and no conclusive symptoms of the disease. From these family trees additional information about the extent of family history of the disease was derived, as described in Section 9.12.

CHAPTER 8: OVERVIEW OF THE ANALYSIS: RESPONSE AND EXPLANATORY VARIABLES

8.1 Introduction

In attempting to understand what are the perceptions of patients with APKD to genetic counselling it is necessary to differentiate between two sets of variables which have been investigated and used in the analysis of the data, which is discussed in subsequent chapters. In accordance with statistical terminology, these can be described as 'response variables' and 'explanatory variables'. Response variables contain the material which is of inherent interest for the study; explanatory variables consist of those which, not being of relevance in themselves, may help to explain variations in the response variables.

The response variables in this study concern the following main areas of interest:

experience of genetic counselling;

knowledge of symptoms and treatment of APKD;

knowledge of the inheritance of APKD;

perceptions of problems that may be associated with APKD;

screening and testing of at risk relatives;

testing of at risk children;

attitudes to having children;

decisions taken as a result of genetic counselling;

patients' perceptions of the importance of elements that could be included in genetic counselling.

These response variables are discussed in more detail below, followed by discussion of the second set of variables, the explanatory variables, which are mainly medical and demographic.

8.2 EXPERIENCE OF GENETIC COUNSELLING

One objective of this study was to ascertain the patients' **experience of genetic counselling.** The experience of genetic counselling covered questions not only about the content of the counselling that the patient had received but also questions concerned with the 'environment' of the genetic counselling. These questions focused on such areas as whether a special time had been set aside for the genetic counselling or whether genetic counselling had been given during a routine clinic visit, the number of occasions that the patient had received genetic counselling and whether the patient was alone or was accompanied by his or her partner, other relative or friend.

The respondents in this study were very likely to have received their genetic counselling in the renal unit from renal physicians. It takes time to cover the important factual elements of genetic counselling as well as to have a discussion of any psychological issues that may be relevant. A national study of genetic counselling services by Sorenson et al (1981) in the United States found that the average length of time of a counselling session to be 45-60 minutes which, according to Griffin et al (1977), may not be sufficient. The timing of genetic counselling is also important. Evidence from studies such as Leonard et al (1972) suggested that if counselling was given too soon after the emotional shock of receiving a diagnosis, then respondents tended not to recall the information that had been given to them.

8.3 KNOWLEDGE OF SYMPTOMS AND TREATMENT OF APKD AND KNOWLEDGE OF THE GENETIC INHERITANCE OF APKD

Many studies into genetic counselling have assessed the patient's knowledge of the symptoms and the treatment for the disease being studied as well as the patient's knowledge and understanding of the genetics of the disease (Chapter 2). The success of genetic counselling was often measured by the amount of information about the disease and its transmission that the patient had retained post counselling (Chapter 2). However an understanding of the knowledge of the disorder that the patient suffers from could be an important factor in how the patient perceives problems that may be caused by the illness and hence the patient's attitude to genetic counselling. In this study questions about the knowledge of inheritance and transmission were asked in questionnaire 1, section 5, and in questionnaire 3, section 5. In the analysis of the data, these questions were grouped together and subsequently referred to as knowledge of genetic inheritance.

There are difficulties in assessing the knowledge of the symptoms of the disease. APKD is a disease of variable age of onset and has several symptoms. Not all patients experience all the symptoms. Questions about the knowledge of symptoms of APKD and the treatment available were asked in questionnaires 1 and 3. A knowledge score was developed and the degree of consistency of knowledge was assessed by comparing the results of the knowledge questions in questionnaires 1 and 3.

8.4 PERCEPTION OF PROBLEMS ASSOCIATED WITH APKD

The perceived burden of the disease is often used to explain attitudes of patients to genetic counselling and to the decisions that they may take as a result of genetic counselling. However it is not clear what the factors are that influence patients in coming to a decision about whether or not the disease is a burden. It is not known how important

the genetic nature of the disease is in the patient's perception of the burden of the disease nor what is the importance of the physical symptoms or social implications of the illness. It is also possible that the patient's perceptions of the burden of APKD may not be the same as the perception of the burden as defined by medical or health care professionals.

In order to assess the respondents' perceptions of the burden attributed to APKD, patients were asked to rank on a six point scale how problematic they perceived particular items to be. These items included certain medical problems associated with APKD, items concerned with income maintenance, items about the genetic implications of APKD and items about the effect that APKD may have on both social and sexual life. This section on the problems of APKD, which were asked twice in the study, gives some indication as to what patients perceive as problematic about APKD.

8.5 Screening and testing of at risk relatives

Genetic diseases run in families but not all family members know of their risk. Contacting the at risk relatives through the source patient or consultand to offer them screening and genetic counselling is carried out by many departments of human genetics. It seems, therefore, relevant and important to assess the views of existing patients as to whether they think that their relatives should be tested for APKD. It is likely that when an illness can be effectively treated, patients would be happy to give the names of their relatives so that they could be offered the relevant screening test. However, in the case of APKD the treatment is only of the symptoms as they appear and it has not yet been conclusively demonstrated even that early treatment of hypertension in the otherwise asymptomatic patient with APKD will improve the overall morbidity of patients with APKD (Bear et al 1992).

There are many factors which could influence patients' views on testing those at risk. The severity of disorder as perceived by the individual, the stigma associated with the illness and the degree of knowledge of the illness in the extended family (the degree of family history) may all be relevant factors. On one hand the more severely affected the patient, the more important the patient may think it is for their relatives to know. On the other hand the patient may wish to protect the relative and may not wish to be the source of potentially unpleasant information. Knowledge and educational levels could also influence patients' views, since more knowledge and possibly higher educational levels could make people more aware of the disadvantages as well as the advantages of testing and hence make their decision more difficult.

8.6 TESTING OF AT RISK CHILDREN

It may be acceptable for patients to suggest that their at risk relatives, which would include sibs and cousins, should be tested for APKD. However it may be less acceptable for patients to recommend that their own children be tested as this could remind the patients that they may have transmitted APKD to their child and kindle or rekindle feelings of guilt. Since there is as yet no effective treatment for APKD it seemed important to ascertain at what age parents thought it appropriate for their offspring to be tested.

8.7 ATTITUDES TO HAVING CHILDREN

It was important to assess whether knowledge of APKD would influence respondents' attitudes to having children. For example, in a study by Sahney et al (1982) 56% of those asked said that they would not have had children had they known that they had APKD. This is similar to the findings of Zerres and Stephan (1986), who found that

46% of a group of at risk and affected individuals would not have had children had they been aware of their status. The Sahney study was published before the commencement of the work for this thesis and the Zerres and Stephan study was published towards the end of the data collection for this investigation. In contrast to these two studies the more recent study of Sujansky et al (1990) found that only 18% of their sample would not have had children had they been aware of their status, although 57% of these patients considered the 50% risk of passing on the gene to be a high risk. Respondents in the present study were asked whether they had planned their children and whether APKD had affected their plans, and also how many children they would like to have and whether their knowledge of APKD had affected their view.

8.8 DECISIONS TAKEN AS A RESULT OF GENETIC COUNSELLING

Studies of genetic counselling often examine the decisions taken as a result of genetic counselling. It was known at the outset of this study that, while there had been no comprehensive genetic counselling system for patients with APKD, some patients had received some genetic counselling. Questions were asked about the reproductive decisions that patients had made as a result of genetic counselling.

8.9 DEMOGRAPHIC AND MEDICAL EXPLANATORY VARIABLES

Studies by social scientists and geneticists into the knowledge, perceptions and understanding of genetic diseases in general and APKD in particular have sought factors that may help explain how patients perceive the illness (Zerres and Stephan 1986, Harris 1987) (See Chapter 5). Factors that may affect patients' perceptions of APKD may include the demographic and medical variables collected in this study: sex, age, marital status,

number of children, education, occupation, housing, religion, severity of disease and family history.

8.9.1 Sex

Sex could be an important explanatory variable, particularly when examining patients' views of genetic counselling. It is not known whether the same information in genetic counselling is given to males and females. It is possible that counsellors may give more information about the prevention of an illness to female patients than to male patients because it is the female who has the children. On the other hand males and females may take different messages from the same information. It is also not known whether there is any difference in the information that males and females want from genetic counselling.

8.9.2 Age

The age of the patient may have an influence on their perceptions both of the disease and of genetic counselling. Younger patients are more likely to be asymptomatic themselves and because of their age may be less aware or less concerned about APKD related illness in older members of the family. Younger patients may show more knowledge of medical problems generally in keeping with their generation. In APKD older patients are more likely to be symptomatic as well as being more aware of any APKD related illness in the family. Older patients may also have a child who has already been diagnosed as having APKD or whom the parent fears may be affected or who has still to be tested.

8.9.3 Marital status and number of children

It is possible that **marital status** combined with whether the patient has had children and the **number of children** they have had may have an influence on attitudes to having children. The views of older single patients who have never had children may be different from those who have a family and do not intend to have more children and from younger patients who have not yet had children or completed their family. In addition the number of children that the patient has may be an important influence.

8.9.4 Education

The **education** of the patient could be an important influence on the amount of information and the knowledge of APKD that the patient has. Studies in other chronic illnesses such as haemophilia have pointed to the importance of good education which may lead to enhanced occupational opportunities and jobs that are more flexible and less physically demanding (Markova et al 1980). Questions were asked about the age at leaving school, qualifications gained at school, and qualifications gained since leaving school. For the purpose of analysis each patient was classified into a particular 'educational level'.

8.9.5 Occupation

It is likely that the education of the patient would be related to their **occupation.** Each patient was asked questions about their current occupation, and also about their former occupations. Occupations were classified using an adaptation of the extended classification of occupations of the Registrar General for Scotland since this system gives a wide range of occupations as well as including the categories of unemployed, student, housewife and retired. This was considered a more sensitive tool for the classification of occupation in a chronic illness as compared with the more restrictive Registrar General's

Social class I-V. Also the interest was in the occupation that the respondent did rather than any social class classification.

8.9.6 Housing

Data had been collected about housing tenure. It was decided to use this data as an explanatory variable as it is known that housing tenure can be a sensitive indicator.

8.9.7 Religion

The religion of the patients may influence attitudes to genetic counselling. Some studies have suggested that the religion of the patient may influence their attitude to genetic counselling. For example Forbes and Markova (1979) found that religion did not influence the attitudes of female carriers of haemophilia to genetic counselling. Mastromaura et al (1987) found that religious affiliation strongly dictated the use of prenatal diagnosis in their study of attitudes towards prenatal diagnosis in Huntington's disease. Sujansky et al (1990) found that religious affiliation did not appear to influence the views of patients and at risk relatives. Our sample contained catholics, protestants and those who said that they had no religion.

8.9.8 Severity of illness

Some studies have indicated that the burden or severity of the illness as perceived by the patient may have a considerable influence on the patient's perception of the illness as well as their understanding of the illness and its wider implications. Little is known about the factors that may influence the patients' perception of the burden of the illness. For example Sujansky et al 1990 were surprised that the knowledge of the severity of the disorder in the family did not appear to influence the patients' desire for prenatal diagnosis

and termination of pregnancy. It is possible that the degree of illness or severity of illness in the individual patient may be an influencing factor. The severity of illness grading used in this analysis was based on the assessment of severity which reflected medical information taken from the patient's notes.

8.9.9 Family history

In a genetic disorder an influencing factor in the patient's perception of the burden of the disease may be the breadth or extent of the family history of APKD. In some cases the patient is a member of a family where there are several relatives with APKD as well as some whose death was attributed to APKD. It is possible that to be a member of a such family could be an important influence on the patient's perception of their illness or attitudes to other responses.

CHAPTER 9: DEMOGRAPHIC AND MEDICAL EXPLANATORY VARIABLES

9.1 Demographic information

Demographic, social, education and occupational information for each patient was gathered during the first interview. This information helped to establish the background of the population. Certain items from this information were selected as possible explanatory variables for the subsequent analysis of the answers to the questions of interest (the response variables). Details of the demographic items are described in this chapter, for each of the three populations as described in Chapter 7, i.e those who attended each of the three interviews. An analysis of the other demographic questions asked appears in Appendix B.

Medical information was gathered from the hospital records for 64 out of the 71 in the first population. On the basis of this information an assessment of the current severity of the disease for each patient was made; this is described in Section 9.11. The medical information is described in detail in Appendix C.

As each patient was interviewed a pedigree or family tree was drawn up. On the basis of this pedigree an assessment of the level of the family's experience of the disease, or family history was made; this is described in Section 9.12.

9.2 Sex

The numbers of males and females in each population are shown in Table 9.1. Nearly two thirds of the total were females (44 out of 71 in the first population or 62%) and about one third were males.

Table 9.1.

Distribution of each population by sex.

	Population 1		Population 2		Population 3	
Sex	Number	%	Number	%	Number	%
Females	44	62	40	62	32	68
Males	27	38	25	38	15	32
Total	71		65		47	

9.3 MARITAL STATUS

The marital status of all patients was identified and the numbers in each population of each marital status are shown in Table 9.2.

Table 9.2.

Distribution of each population by marital status.

	Population 1		Population 2		Population 3	
Marital status	Number	%	Number	%	Number	%
Single	15	21	15	23	13	28
Married	51	72	46	71	31	66
Widowed	3	4	2	3	2	4
Divorced	1	1	1	2	1	2
Separated	1	1	1	2	-	-
Total	71		65		47	

The distribution of the first population by sex and by marital status is shown in Table 9.3. Almost all the males were married (23 out of 27 or 85%), there being only one single, one divorced, one widowed and one separated. By contrast, almost one third of the females (14 out of 44 or 32%) were single, with two widowed and the rest (28) married.

Table 9.3.

Distribution of first population by sex and by marital status.

Marital status	Female	Male	Total
Single	14	1	15
Married	28	23	51
Widowed	2	1	3
Divorced	-	1	1
Separated	-	1	1
Total	44	27	71

The large groups are single females (14), married females (28) and married males (23). For subsequent analyses by sex and marital status it was found convenient to group all respondents into one of these three groups, including the two widows with the married females, and the four not married males (one of each status) with the married males. These groups are described as 'single females', 'married females' and 'males' in subsequent analyses. The numbers in each population are shown in Table 9.4.

Table 9.4.

Distribution of each population by sex and marital status.

	Population 1		Population 2		Population 3	
Sex and marital status	Number	%	Number	%	Number	%
Single females	14	20	14	22	12	26
Married females	30	42	26	40	20	43
All males	27	38	25	38	15	32
Total	71		65		47	

9.4 AGE

The age of each patient at the time of the first interview was recorded. The numbers in each population in each age group are shown in Table 9.5.

Table 9.5.

Distribution of each population by age group.

	Population 1		Population 2		Population 3	
Age group	Number	%	Number	%	Number	%
Up to 19	3	4	3	5	3	6
20-24	4	6	4	6	4	9
25-29	7	10	7	11	7	15
30-34	9	13	9	14	7	15
35-39	9	13	9	14	6	13
40-44	10	14	9	14	6	13
45-49	8	11	7	11	3	6
50-54	9	13	7	11	7	15
55-59	3	4	3	5	1	2
60-64	6	8	5	8	2	4
65-69	1	1	1	2	-	-
70 and over	2	3	1	2	1	2
Total	71		65		47	

The distribution of the first population by age group and by sex and marital status is shown in Table 9.6 and in Figure 9.1.

Table 9.6.

Distribution of first population by age group and by sex and marital status.

Age group	Single females	Married females	Males	Total
Up to 19	3	-	-	3
20-24	4	-	-	4
25-29	1	6	-	7
30-34	3	5	1	9
35-39	-	4	5	9
40-44	1	5	4	10
45-49	-	3	5	8
50-54	1	1	7	9
55-59	-	2	1	3
60-64	1	2	3	6
65-69	-	-	1	1
70 and over	-	2	-	2
Total	14	30	27	71

Figure 9.1.

First population: distribution by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	SSS	-	-
20-24	SSSS	-	-
25-29	S	MMMMMM	-
30-34	SSS	MMMMM	M
35-39	-	MMMM	MMMMA
40-44	S	MMMMM	MMMS
45-49	-	MMM	MMMMW
50-54	S	M	MMMMMMD
55-59	-	MM	M
60-64	S	MW	MMM
65-69	-	-	M
70 and over	-	MW	-

Note: S=Single M=Married W=Widowed D=Divorced A=Separated

The ages of the females in the population ranged from 17 to 72 (single females from 17 to 62, married females from 25 to 72), whereas for males it was 34 to 68. The average age of all females was 35.6 (standard deviation 14.2) and of males was 48.1 (standard deviation 9.1). The average age of single females was 30.0 (standard deviation 12.8) and of married females was 42.7 (standard deviation 12.9). The majority of patients of both sexes were in the age range 30 to 54 (see also Figure 9.1).

There was only one male aged less than 35 (who was 34), whereas there were 22 females below this age, 11 single and 11 married. These young females, of whom half were single, formed a separate group with a number of different characteristics from the others in the population; for example, they had many fewer symptoms of the disease (see Appendix C).

APKD is an autosomal dominant disorder which is governed by the principle that males and females are equally affected. The sample was collected from symptomatic patients who had been referred to the renal unit and in whom a diagnosis of APKD had subsequently been made. The larger number of females in the sample might be explained by the fact that, unlike men, women go to the doctor for contraceptive advice, prescription and antenatal care and on such a visit an abnormality such as hypertension may be discovered (Wilkie et al 1985). The larger number of younger females in the present sample is consistent with this hypothesis.

9.5 NUMBERS OF CHILDREN

The numbers of living children for those in each population are shown in Table 9.7.

Table 9.7.
Distribution of each population by number of living children.

	Population 1		Population 2		Population 3	
Number of children	Number	%	Number	%	Number	%
None	19	27	18	28	15	32
One	16	23	16	25	13	28
Two	18	25	16	25	8	17
Three	9	13	7	11	6	13
Four	8	11	7	11	4	9
Five or more	1	1	1	2	1	2
Total	71		65		47	

Three females had each had a child who had died but the cause of death of these children was not known. As APKD normally only affects adults, it is unlikely that the cause of death of these children could be attributed to APKD. Table 9.8 shows the same analysis as Table 9.7, but including the three children who had died.

Table 9.8
Distribution of each population by number of children, living or dead.

	Population 1		Population 2		Population 3	
Number of children	Number	%	Number	%	Number	%
None	19	27	18	28	15	32
One	15	21	15	23	12	26
Two	18	25	16	25	8	17
Three	10	14	8	12	7	15
Four	8	11	7	11	4	9
Five or more	1	1	1	2	1	2
Total	71		65		47	

The distribution of the first population by numbers of children, living or dead, is shown in Table 9.9 by sex and marital status, and in Figure 9.2 by sex and age group.

Table 9.9.

First population: numbers of children, living or dead, by sex and marital status.

Number of children	Single females	Married females	Males	Total
None	13	3	3	19
One	1	10	4	15
Two	-	8	10	18
Three	-	5	5	10
Four	-	3	5	8
Five or more	-	1	0	1
Total	14	30	27	71

Figure 9.2.

First population: numbers of children, living or dead, by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	000	-	-
20-24	1000	-	-
25-29	0	221111	-
30-34	000	32210	2
35-39	-	3211	22210
40-44	0	33211	4420
45-49	-	444	43210
50-54	0	5	4333211
55-59	-	21	2
60-64	0	32	432
65-69	-	-	2
70 and over	-	00	-

Note: the digit (0 to 5) represents the number of children, living or dead

Ever-married females had had on average 2.0 children (1.9 living and 0.1 dead) compared with 2.3 (all living) amongst ever-married males. However, the younger married females and the young single females might have further children in the future.

It was found during the subsequent analysis that the combination of age and number of children (including both living and dead children) was useful in explaining some of the results. These two factors were combined into one, splitting by age into those up to age 44 and those aged 45 and over, and splitting by number of children into those with up to two children and those with three or more.

The numbers in each category of age and number of children in each population are shown in Table 9.10, and the distribution of the first population by age and number of children is shown in Table 9.11 by sex and marital status.

Table 9.10

Distribution of each population by age and number of children combined.

Age and	Population 1		Population 2		Population 3	
number of children	Number	%	Number	%	Number	%
≤44, ≤2	36	51	35	54	28	60
≤44, ≥3	6	8	6	9	5	11
≥45, ≤2	16	23	14	22	7	15
≥45, ≥3	13	18	10	15	7	15
Total	71		65		47	

It can be seen that a higher proportion of those in the first group (age ≤44 and children ≤2) than of those in the other three groups persist up to the third interview (28 out of 36 or 78% as compared with 19 out of 35 or 54%). Fisher's exact test (see Everitt 1992) shows that the probability of the first number being 36 or more is 0.0323, so the result is significant at a 5%, but not at a 1% probability level.

Table 9.11.

First population: age and number of children, by sex and marital status.

Age and number of children	Single females	Married females	Males	Total
≤44, ≤2	12	16	8	36
≤44, ≥3	-	4	2	6
≥45, ≤2	2	5	9	16
≥45, ≥3	-	5	8	13
Total	14	30	27	71

9.6 POSSIBLE FUTURE CHILDREN

It seemed possible that the attitudes of respondents might be affected, not by the number of children that they had or had had, but by whether they might expect to have more in the future. Patients were not asked explicitly how many more children they intended to have, but an assessment was made, on a rather arbitrary basis, as follows.

Those aged 40 and over and all widows: none.

Those aged 30 to 39:

Single: none.

Two or more children already: none.

Others: one.

Those aged less than 30:

Two or more children already: none.

One child already: one.

No children so far: two.

The number of possible future children for those in each population are shown in Table 9.12.

Table 9.12

Distribution of each population by number of possible future children.

Number of possible future children	Population 1		Population 2		Population 3	
	Number	%	Number	%	Number	%
None	53	75	47	72	31	66
One	11	15	11	17	9	19
Two	7	10	7	11	7	15
Total	71		65		47	

The distribution of the first population by numbers of possible future children is shown in Table 9.13 subdivided by sex and marital status, and in Figure 9.3 by sex and marital status and by age group.

Table 9.13

First population: numbers of possible future children, by sex and marital status.

Number of possible future children	Single females	Married females	Males	Total
None	6	22	25	53
One	1	8	2	11
Two	7	-	-	7
Total	14	30	27	71

Figure 9.3

First population: numbers of possible future children, by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	222	-	-
20-24	2221	-	-
25-29	2	111100	-
30-34	000	11000	0
35-39	-	1100	11000
40-44	0	00000	0000
45-49	-	000	00000
50-54	0	0	0000000
55-59	-	00	0
60-64	0	00	000
65-69	-	-	0
70 and over	-	00	-

Note: the digit (0 to 2) represents the number of possible future children

9.7 EDUCATIONAL QUALIFICATIONS

Studies in other chronic illnesses such as haemophilia have pointed to the importance of good education which may lead to enhanced occupational opportunities and jobs that are more flexible and less physically demanding (Markova et al 1980).

Questions were asked about the age at leaving school, qualifications gained at school, and qualifications gained since leaving school. The results for the first population are summarised in Table 9.14, subdivided by sex and marital status. 42 out of the 71 (59%) had left school without any qualifications and gained none since. 8 (11%) had only school certificates, either Ordinary grade or Higher grade. A further 8 (11%) had left school with no qualifications but had gained later qualifications (typically City and Guild certificates but including 3 nurses). 6 (8%) had added later qualifications to school

certificates, and 7 (10%) had obtained degree level qualifications (4 with university degrees and 3 with Higher National Certificates).

Table 9.14

First population: educational qualifications, by sex and marital status.

Age at leaving school and qualifications	Single females	Married females	Males	Total
Age 14 no qualifications	2	4	8	14
Age 15 no qualifications	-	10	10	20
Age 16 no qualifications	4	3	1	8
Ages 14, 15 or 16 with school certificates	2	1	2	5
Ages 17 or 18 with school certificates	2	-	1	3
Ages 14, 15 or 16 with no school certificates but with later qualifications	1	5	2	8
Ages 15 or 16 with school and also later qualifications	2	4	-	6
Ages 15 or 16 with degree level qualifications	1	-	2	3
Ages 17 or 18 with degree level qualifications	-	3	1	4
Total	14	30	27	71

The age at leaving school was associated with the age of the respondent, almost necessarily so, since until 1947 the normal school leaving age in Scotland was 14; this was increased to 15 in 1947 and to 16 in 1976.

Those who are younger not only left school at a later age but also have gained more qualifications; this partially explains the greater number of females with more qualifications. Apart from the group of younger women, many with qualifications, there is little difference between the sexes in terms of educational level.

For the purpose of later analyses each patient was classified in a particular 'educational level' as follows:

1 those leaving school at ages 14, 15 or 16 and with no qualifications (42);

2 those leaving school with school certificates but with no later qualifications (8);

3 those with later qualifications not of degree level (14);

4 those with later qualifications of degree level (7).

Figure 9.4 shows the educational level for the first population subdivided by sex and marital status and by age group.

Figure 9.4

First population: educational level by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	122	-	-
20-24	1124	-	-
25-29	1	123334	-
30-34	233	13334	2
35-39	-	1113	11114
40-44	3	11113	1111
45-49	-	111	11144
50-54	1	1	1111233
55-59	-	11	1
60-64	1	14	112
65-69	-	-	1
70 and over	-	13	-

Note: the digit (0 to 4) represents the educational level

Table 9.15 shows the numbers in each educational level for each population.

Table 9.15.

Distribution of each population by educational level.

	Population 1		Population 2		Population 3	
	Number	%	Number	%	Number	%
Level 1	42	59	38	58	27	57
Level 2	8	11	7	11	5	11
Level 3	14	20	14	22	11	23
Level 4	7	10	6	9	4	9
Total	71		65		47	

9.8 Occupation

Each patient was asked questions about their current occupation, and also about their former occupations. Many were retired or were housewives and for these an occupation, styled their 'permanent' occupation, was derived from their occupation in their last period of employment. For those currently employed the 'permanent' occupation was taken as their current one.

Occupations were classified using an adaptation of the extended classification of occupations into socio-economic groups as used by the Registrar General for Scotland. This system gives a wide range of occupations as well as including the categories of unemployed, student, housewife and retired and it was considered a more sensitive tool for the classification of occupation in a chronic illness as compared with the more restrictive Registrar General's Social Classes I-V. In addition it was the occupation that the respondent did which was of interest rather than any social class classification.

The 'permanent occupation' of patients in the first population is shown in Table 9.16, subdivided by sex and marital status. The large numbers of females in clerical jobs is conspicuous and not unexpected, reflecting a pattern in the general population.

Table 9.16.

First population: permanent occupation, by sex and marital status

Occupation	Single females	Married females	Males	Total
Managerial	1	1	1	3
Professional	-	-	2	2
Lesser professions	1	5	3	9
Clerical	6	12	4	22
Service jobs	1	3	1	5
Skilled manual	-	-	5	5
Semi-skilled manual	2	3	7	12
Unskilled manual	1	4	1	6
Farmers	1	-	2	3
Agricultural workers	-	-	1	1
None	1	2	-	3
Total	14	30	27	71

The extent to which the occupation of respondents reflects their educational attainment is shown, for the first population, in Table 9.17. There is a clear tendency for those with higher educational qualifications to have corresponding occupations, in particular those in the professions, lesser professions and clerical jobs. There are, however, exceptions to this rule in both directions.

The tendency just noted can be tested by performing Fisher's exact test on a 2 by 2 table formed by grouping education Level 1 versus Levels 2, 3 and 4, and grouping managerial, professional, lesser professions and clerical jobs versus service, skilled, semi-skilled and unskilled manual, farmers and agricultural workers, omitting the 3 with no

occupation. The resulting table is shown in Table 9.18. Fisher's test shows that, if there were no connection between educational level and occupational group, the probability of obtaining by chance a value in the lower right corner of the table of 5 or less is as low as 0.00005, an extremely significant result.

Table 9.17.

First population: permanent occupation by educational level

Occupation	Level 1	Level 2	Level 3	Level 4	Total
Managerial	1	-	1	1	3
Professional	1	-	-	1	2
Lesser professions	1	1	3	4	9
Clerical	10	4	7	1	22
Service jobs	4	-	1	-	5
Skilled manual	3	1	1	-	5
Semi-skilled manual	12	-	-	-	12
Unskilled manual	5	-	1	-	6
Farmers	2	1	-	-	3
Agricultural workers	1	-	-	-	1
None	2	1	-	-	3
Total	42	8	14	7	71

Table 9.18.

First population: permanent occupation by educational level, grouped

Occupation	Level 1	Levels 2-4	Total
Managerial, professional, lesser professions and clerical	13	23	36
Service jobs, skilled, semi-skilled and unskilled manual, farmers and agricultural workers	27	5*	32
Total	40	28	68

$p(* \leq 5) = 0.00005$

Table 9.19 shows the numbers in each occupational category for each population.

Table 9.19.

Distribution of each population by permanent occupation.

	Population 1		Population 2		Population 3	
Occupation	Number	%	Number	%	Number	%
Managerial	3	4	2	3	1	2
Professional	2	3	2	3	1	2
Lesser professions	9	13	7	11	5	11
Clerical	22	31	22	34	18	38
Service jobs	5	7	5	8	5	11
Skilled manual	5	7	5	8	3	6
Semi-skilled manual	12	17	10	15	7	15
Unskilled manual	6	8	6	9	4	9
Farmers	3	4	2	3	1	2
Agricultural workers	1	1	1	2	-	-
None	3	4	3	5	2	4
Total	71		65		47	

9.9 Housing and type of accommodation

All patients were asked questions about their housing: for this purpose the only one of relevance is how the house was owned (owner-occupied, rented from local authority, ...). The results for the first population are shown in Table 9.20, subdivided by sex and marital status.

Table 9.20.

First population: ownership of house, by sex and marital status.

	Single females	Married females	Males	Total
Owner occupied	5	12	10	27
Local authority rented	9	17	16	42
Other	-	1	1	2
Total	14	30	27	71

Table 9.21 shows the numbers in each category of house ownership for each population.

Table 9.21.

Distribution of each population by house ownership.

	Population 1		Population 2		Population 3	
	Number	%	Number	%	Number	%
Owner occupier	27	38	24	37	17	36
Local authority rented	42	59	39	60	28	60
Other	2	3	2	3	2	4
Total	71		65		47	

In the West of Scotland there is a high incidence of local authority housing. The majority of patients in the first population rented from a local authority (42 out of the 71 or 59%). A smaller proportion were in owner-occupied houses (27 out of the 71 or 38%). Only two were in other forms of accommodation, both renting from private landlords. These numbers can be compared with the results from the 1981 Census of Scotland (Registrar General for Scotland 1982). The percentages of persons living in private households in Glasgow City and in Strathclyde Region, subdivided by the type of housing tenancy, are shown in Table 9.22, along with the numbers and percentages from the first study population. There was a slightly higher proportion in owner-occupied housing in the

study population than in either Glasgow or Strathclyde, and a lower proportion in 'other' tenancies. The difference between the study population and Strathclyde Region is not significant, but the difference between it and Glasgow City is significant at a 2% probability level.

Table 9.22.

Distribution first population and of persons in Glasgow City and in Strathclyde Region (Census 1981) by house ownership.

	Population 1		Glasgow City	Strathclyde Region
	Number	%	%	%
Owner occupier	27	38	26	32
Local authority rented	42	59	64	62
Other	2	3	10	6
Total	71		100	100

9.10 Religious affiliation

In this study questions were to be asked about prevention of APKD. Some patients might have had strong religious beliefs which would not have allowed them to consider the use of contraception or termination of pregnancy, although evidence from work in haemophilia suggests that religious affiliation did not play a significant part in the attitudes of patients to prevention of haemophilia.

The religious affiliation of those in the first population, subdivided by sex and marital status, is shown in Table 9.23. Fewer than half (31 out of 71 or 44%) had no religious affiliation; these included a majority of the males (16 out of 27 or 59%). Among those belonging to a church a rather greater proportion of female than male patients belonged to the Catholic church, though this difference is not significant. Such a

distinction could be of importance if women take the sole decision of whether or not to become pregnant.

Table 9.23.

First population: religious affiliation, by sex and marital status.

	Single females	Married females	Males	Total
Protestant	4	12	7	23
Catholic	4	9	4	17
No church	6	9	16	31
Total	14	30	27	71

Table 9.24 shows the numbers in each religious affiliation for each population.

Table 9.24

Distribution of each population by religious affiliation.

	Population 1		Population 2		Population 3	
Church	Number	%	Number	%	Number	%
Protestant	23	32	22	34	15	32
Catholic	17	24	15	23	10	21
No church	31	44	28	43	22	47
Total	71		65		47	

9.11 SEVERITY OF DISEASE

Each patient was classified as to the 'degree of severity' of his or her disease. This was done in the following way. The six who were found to be unaffected were given a severity grade of 0. The other patients were given severity grades of 1, 2 or 3 in increasing order of severity. The severity grade was assigned as follows.

Severity grade 3 (severe) was assigned to 30 patients:
- 10 who had received a successful transplant;
- 11 who were on dialysis;
- 5 who had had a cerebral haemorrhage;
- 4 whose creatinine level was 500 or more.

Severity grade 2 (moderate) was assigned to 21 patients:
- 12 whose loin pain had been classified as moderate, severe or very severe;
- 7 whose headaches had been classified as moderate, severe or very severe;
- 1 who had moderately severe gastro-intestinal trouble;
- 1 who had moderately severe chest pain.

Those assigned in this way to severity grade 2 included all those whose creatine level was 300 or more, which would also have been used as a criterion for level 2 severity.

Severity grade 1 (little affected) was assigned to the remaining 13 patients for whom medical records were available, and also to the one (a female in her 70s) who died between the first and second interviews for whom no medical records were available. Two of the 13 had mild loin pain; one had a creatinine level of 155; none had any other symptoms. All 13 were females under age 35.

The numbers of patients in each severity grade in the first population, subdivided by sex and marital status, are shown in Table 9.25 and by sex and marital status and by age group in Figure 9.5.

All but one of the 14 (20%) patients in grade 1 severity of disease were females under age 35. 21 out of 71 (29%) were in grade 2 severity and 30 out of 71 (42%) were in grade 3 severity. For the two higher levels there was little differences between the sexes and age groups.

Table 9.25

First population: severity of disease, by sex and marital status.

Severity grade	Single females	Married females	Males	Total
0 (unaffected)	-	3	3	6
1 (little affected)	7	7	-	14
2 (moderate)	3	7	11	21
3 (severe)	4	13	13	30
Total	14	30	27	71

Figure 9.5

First population: severity of disease, by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	123	-	-
20-24	1123	-	-
25-29	1	111122	-
30-34	111	11223	3
35-39	-	0233	22233
40-44	3	00233	2333
45-49	-	333	02233
50-54	2	3	2233333
55-59	-	33	2
60-64	3	33	022
65-69	-	-	0
70 and over	-	X2	-

Note: the digit (0-3) shows the severity grade of the disease;
X=no medical records, treated as 1.

Table 9.26 shows the numbers in each severity grade for each population.

Table 9.26

Distribution of each population by severity of disease.

	Population 1		Population 2		Population 3	
Severity grade	Number	%	Number	%	Number	%
Grade 0	6	8	5	8	-	-
Grade 1	14	20	13	20	12	26
Grade 2	21	30	20	31	15	32
Grade 3	30	42	27	42	20	43
Total	71		65		47	

9.12 FAMILY HISTORY

It is explained in Section MM.4.2 how family trees or pedigrees were drawn up during the interviews with the patients. The degree of involvement with APKD was assessed for each patient and a grading was assigned on the following criteria, so that the family history could be used as a variable in the analysis of the data.

Grade 0, no family history, where the patient was not affected by APKD.

Grade 1, weak family history, where the patient was the sole affected person or did not know of affected ancestors or other affected relatives.

Grade 2, moderate family history, where apart from the patient there were only two or three known affected relatives.

Grade 3, strong family history, where apart from the patient there were also affected sibs, cousins or uncles and aunts and offspring.

The numbers of patients in each family history grade in the first population, subdivided by sex and marital status, are shown in Table 9.27 and by sex and marital status and by age group in Figure 9.6.

Table 9.27

First population: family history grade, by sex and marital status.

Family history grade	Single females	Married females	Males	Total
0 (unaffected)	-	4	3	7
1 (weak)	2	5	4	11
2 (moderate)	4	13	12	29
3 (strong)	8	8	8	24
Total	14	30	27	71

Figure 9.6

First population: family history grade, by sex and marital status and by age group.

Age group	Single females	Married females	Males
Up to 19	233	-	-
20-24	1123	-	-
25-29	3	222333	-
30-34	333	22233	2
35-39	-	0222	12333
40-44	2	00123	2223
45-49	-	123	01223
50-54	2	2	2222233
55-59	-	12	3
60-64	3	13	011
65-69	-	-	0
70 and over	-	01	-

Note: the digit (0-3) shows the family history grade.

Table 9.28 shows the numbers in each family history grade for each population.

Table 9.28

Distribution of each population by family history grade

	Population 1		Population 2		Population 3	
Family history grade	Number	%	Number	%	Number	%
0	7	10	5	8	-	-
1	11	15	10	15	5	11
2	29	41	28	43	25	53
3	24	34	22	34	17	36
Total	71		65		47	

Note that none of those who were unaffected (grade 0) were asked back for the third interview.

Specimens of two family trees are shown in Figures 9.7 and 9.8. Figure 9.7 shows a simple family history, graded as 1, with a single male 'index' patient, an affected male, whose father and aunt were both affected and are both dead, and who has two children, one daughter affected and one son at risk but not yet tested. His father's grandparents are both dead; presumably one of them was affected, but which one is not known.

Figure 9.8 shows a much more complicated family tree. The male in the first generation was presumably affected, since children from both his marriages are affected. The surviving son from the second marriage has two affected daughters; all three are index patients, included in the study. From the first marriage there are two affected granddaughters, one of whom had seven children by three different men; two of these children are affected; all three affected are index patients. The status of many of the younger members of the family and of members of the lateral branches is not known. All six patients in the study were classified as having a strong family history, grade 3.

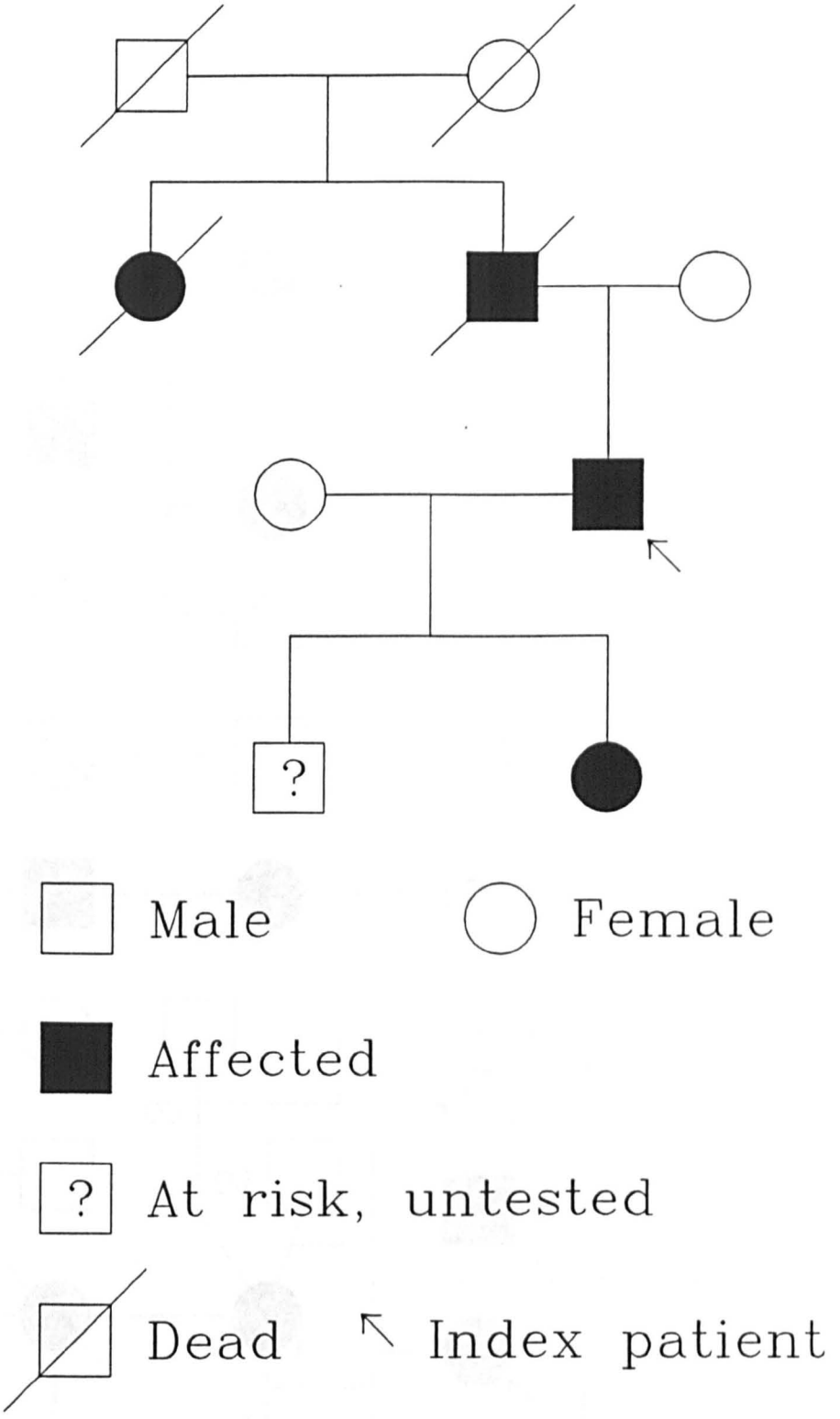

Figure 9.7. A specimen of a simple family history.

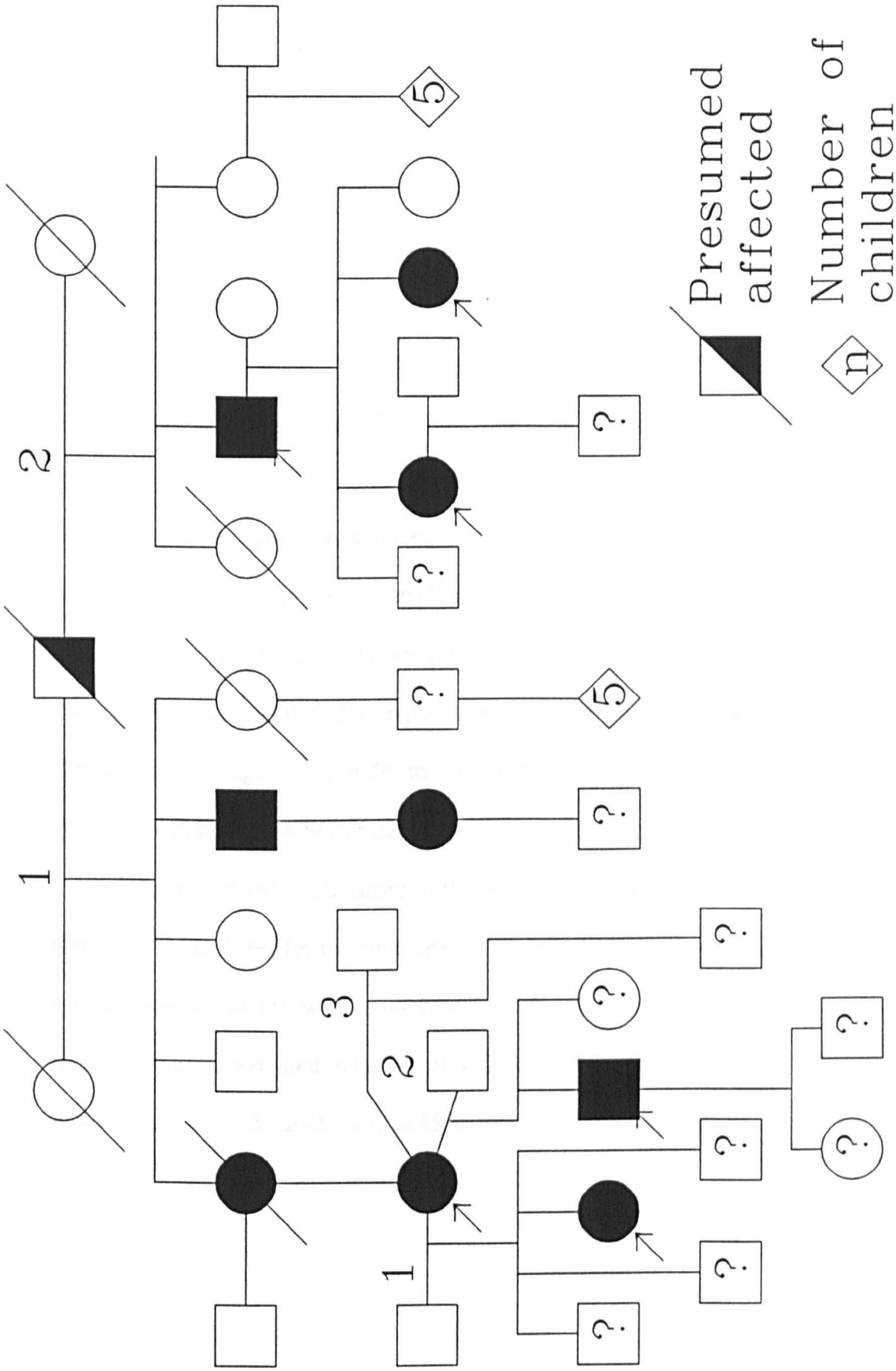

Figure 9.8. A specimen of a complicated family history.

9.13 USE OF EXPLANATORY VARIABLES IN SUBSEQUENT ANALYSES

In order to assist the analysis of areas of investigation — the 'response variables' described in Chapter 8 — the answers to certain groups of questions were turned into composite scores, which could be analysed numerically. Each score was used as the response variable in an analysis using the GLIM computer package (Aitkin et al 1987). This package is suitable for identifying complex interactions in the effects of possible explanatory variables. As it turned out, however, the analysis of the response variables in the present study showed that no very complex interactions needed to be included, and the results in subsequent chapters are therefore usually presented in a simple form as the mean scores for the appropriate explanatory variables.

All the possible explanatory variables were treated as categorical variables, rather than as numeric variables. The explanatory variables described above were grouped into slightly fewer categories, in order to avoid categories with too few observations, and they are listed, with the number of categories used in each, in Table 9.29.

Certain of the explanatory variables were grouped also in ways other than that shown in Table 9.29; for example age was grouped into a smaller number of categories; sex and marital status were combined into the three groups: single females, married females, males; age and number of children were combined into the four groups: $\leq 44, \leq 2$; $\leq 44, \geq 3$; $\geq 45, \leq 2$; $\geq 45, \geq 3$.

Table 9.29

Explanatory variables and number of categories used for each.

Explanatory variable	Categories
Sex	2
Age (in 10 year groups)	6
Marital status	3
Number of children	5
Number of possible future children	3
Housing	2
Occupation (in socio-economic groups)	11
Education	4
Church	3
Severity of disease	4
Family history	4

Each response variable was fitted to each possible explanatory variable in turn, and the amount of explanation, measured by the reduction in the residual sum of squares, was observed. The significance of the explanation was measured by testing the F-statistic. In general only explanatory variables whose effect was significant at a 1% probability level were accepted. It is appropriate to use a more stringent level such as 1% when a range of different explanatory variables is being considered. Where appropriate more than one explanatory variable was admitted, and in some cases, noted below, explanatory variables were admitted at a 5% probability level.

CHAPTER 10: ANALYSIS: EXPERIENCE OF GENETIC COUNSELLING

10.1 INTRODUCTION: THE SECOND INTERVIEW

The patients' experience of genetic counselling was explored during the second interview. In this chapter the patients' responses are analysed. Detailed results are presented in Appendix D.

As part of an investigation of patients' knowledge of genetic counselling, it was necessary to establish whether respondents had received any genetic counselling, who had given them genetic counselling and whether they had been counselled on their own, as well as what sort of information or content of genetic counselling the patient had received.

The questions asked were divided into two sections: the first section was concerned with the 'environment' of genetic counselling, i.e. whether the respondent had received genetic counselling, from whom they had received genetic counselling and where the counselling had taken place; the second section was concerned with the content of the counselling. The answers to some of the questions were used to construct scores, which were then used in the further analysis.

For this chapter each individual response and each constructed score was analysed by each of the demographic and medical variables described in Section 9.13. These are: sex, age, marital status, number of children, educational level, occupation, housing, religious affiliation, severity of disease and family history.

Before discussing the results of the analysis of the data, it is appropriate to comment on the factors that could have influenced the respondents' experience of genetic counselling. Severity of illness could influence experience in different ways. There is more opportunity to offer genetic counselling to patients who are more ill since these patients are seen by doctors frequently, and it may be thought important to ensure that the

more severely affected patients have been given genetic counselling so that they can inform their relatives while they are still able. On the other hand doctors may be concentrating on the medical management of those patients who are more ill rather than on giving them genetic information.

The sex of the respondent could influence the experience of genetic counselling, since much of it concerns whether or not to have children, and this may be seen as the woman's responsibility. However it was not known whether both the experience and the content of genetic counselling was the same for both sexes.

In the second section of the chapter the content of genetic counselling is discussed. Once again sex of respondent could be an important variable. Family history may also be important in this analysis. Those with a strong family history may be more familiar with the problems associated with APKD and, therefore, may remember more about the content of genetic counselling.

10.2 THE ENVIRONMENT OF GENETIC COUNSELLING

The first set of questions related to the environment within which patients had had genetic counselling, and the circumstances of it. The first point to establish was whether patients had had any genetic counselling at all. Respondents were therefore asked whether they had had any genetic counselling, which was described as 'a discussion about the inheritance of polycystic kidney disease, the effect on the patient and their children and what they could do about it'. The majority of respondents (49 out of 65 or 75%) had received information about the inheritance of APKD, but almost one quarter reported that they had not.

Patients were asked from whom they had received information about the inheritance of APKD. The majority of patients (40 out of 65 or 62%) had received it from doctors in the renal unit at Glasgow Royal Infirmary.

Respondents were also asked whether they had had any information about other problems associated with APKD. Only six of them (9%) said that they had.

Patients were asked how they had come to have genetic counselling. The most common route was that patients received genetic counselling during a routine medical consultation. Six patients were referred by their GP or by another specialist and five at the instigation of their spouse or another member of their family. Three patients said that it was their own idea to seek counselling.

Respondents were asked whether anyone else was present when the patient received genetic counselling, and, if so, whom. The spouse or partner was present when the patient received genetic counselling in 9 cases (14%). Other family members were present in 19 cases (29%) and these included sibs (12), children (4 — including one with the spouse), and other family members (2 — one mother and one nephew). This leaves 23 patients who received genetic counselling on their own (47% of the 49 who did receive it), including 11 out of the 17 males.

Respondents were asked whether they would have liked their spouse or partner to have been present. Just over half the respondents who did not have their spouse or partner present would have liked them to have been present (29 out of 56 or 52%); this preference was strong for married women (16 out of 26), half and half for men (11 out of 22) and, not surprisingly, weak for the single women (2 out of 12).

Most patients who had received information about the inheritance of APKD had received it on only one occasion (41 out of 49 or 84%), with 7 patients reporting that they had received information on two occasions and 1 patient on several occasions.

10.3 SCORE FOR ENVIRONMENT OF GENETIC COUNSELLING

A numeric score was constructed, denoted EGCS1, in order to measure the patients' experience of genetic counselling, based on the answers to some of these questions. The construction of this score is described in Appendix D. The maximum score was 7 points, and the average was 2.5 points. 15 respondents got no points, 13 got two points and 15 got three.

The score so constructed was then analysed using the GLIM system, as described in Section 9.13, in respect of all the possible explanatory variables described in Chapter 9. Analysis showed that severity of disease was the best explanatory variable, the only one significant at a 1% probability level. However, this only accounted for 21.3% of the original variance of the score ($R^2 = 0.213$), which is not a particularly high proportion. (The statistic R^2 in a GLIM analysis has the same meaning as in a multiple regression analysis; if it were a simple linear regression the value of 0.213 would correspond to a correlation coefficient of 0.46.)

The mean scores, subdivided by severity of disease, are shown in Table 10.1.

Table 10.1

Second population: mean scores for environment of genetic counselling (EGCS1), classified by severity of disease.

Severity of disease	Mean score
Grade 0	2.00
Grade 1	4.08
Grade 2	1.75
Grade 3	2.33

The scores fall into an irregular pattern. Those with severity Grade 1 (mildly affected) had the best experience of genetic counselling (average 4.08 points). The other

three Grades were not very different from one another, with mean scores ranging from 1.75 to 2.33.

10.4 INFORMATION GIVEN IN GENETIC COUNSELLING

Respondents were asked whether they had received information about 19 different topics that might have been included in a genetic counselling session. The results, subdivided by family history, are shown in Table 10.2.

The majority of respondents (45 out of 65 or 69%) had received information about the risk to children, 20 out of 65 (31%) had received information about the risk of inheritance. Fewer than one quarter of respondents had received information about having no more children (16 out of 65), sterilisation (14 out of 65), screening of the at risk (13 out of 65) and prevention of APKD (10 out of 65). Only a few respondents had received information about any other topic in the list.

Among the men, the only topic remembered by more than a few patients was the risk to children (14 out of 25 or 56%). For many of the topics none of the men had received information. The married women had in general had more information. The single women were in general no better informed than the men, except for two women (the same two, who were both in severity Grade 1 and family history Grade 2) who had received information about every topic on the list; they had received counselling from a specialist genetic counsellor.

The number of topics that each patient had had discussion about were counted. Apart from the two patients who had received information about every topic, no patient remembered receiving information about more than six topics, and the most common numbers were one (10 cases), two (10 cases) and four (13 cases).

Table 10.2

Second population: 'was discussion about the specified topic included in your genetic counselling?', subdivided by family history; the number responding 'yes' is shown.

		Grade 0	Grade 1	Grade 2	Grade 3	Total
	Maximum number	5	10	28	22	65
1	Risk of inheriting	3	1	8	8	20
2	Risk to children	3	4	23	15	45
3	Advantages of testing	-	1	5	2	8
4	Disadvantages of testing	-	-	3	-	3
5	How to tell	-	-	2	-	2
6	Screening of at risk	-	1	9	3	13
7	Adoption	-	-	3	-	3
8	Fostering	-	-	2	-	2
9	Voluntary childlessness	-	-	2	3	5
10	Having no more children	2	-	13	1	16
11	Family planning	-	-	3	-	3
12	Sterilisation	1	-	10	3	14
13	Vasectomy	2	-	3	-	5
14	A. I. D.	-	-	2	-	2
15	Prevention of APKD	1	1	5	3	10
16	Telling boy/girlfriend	-	-	2	-	2
17	Telling in-laws	-	-	2	-	2
18	Symptoms of APKD	-	-	4	-	4
19	Treatment available	-	1	3	1	5

10.5 SCORE FOR CONTENT OF GENETIC COUNSELLING

A numeric score was constructed, denoted EGCS2, based on the answers to the questions relating to the content in genetic counselling. The construction of this score is described in Appendix D. The maximum score was 10 points, and the average was 3.0

points. The most common scores were none (16 cases), three (11 cases) and five (11 cases).

Analysis using the GLIM system showed that of all the possible explanatory variables listed in Chapter 9, family history was the most useful factor, though significant only at a 5% probability level and not at a 1% level; the factor combining age and number of children was second, also significant at a 5% probability level. There was no significant interaction term. Family history by itself accounted for 15.1% of the original variance and the combined factor for age and number of children explained a further 13.4%, making 28.5% in all ($R^2 = 0.285$). The components for the two explanatory variables, relative to the mean score of 3.03, are shown in Table 10.3, and the expected scores for the two variables are shown in Table 10.4.

Table 10.3

Second population: components of mean scores for experience of genetic counselling (EGCS2).

Element	Component
Overall mean	3.03
Family history:	
Grade 0	+0.77
Grade 1	−1.47
Grade 2	+0.94
Grade 3	−0.70
Age and number of children:	
≤44, ≤2	+0.78
≤44, ≥3	−0.35
≥45, ≤2	−1.52
≥45, ≥3	−0.38

Table 10.4

Second population: mean scores for experience of genetic counselling (EGCS2), classified by family history and by age and number of children.

	Age and number of children			
Family history	≤44, ≤2	≤44, ≥3	≥45, ≤2	≥45, ≥3
Grade 0	4.58	3.45*	2.28	3.43*
Grade 1	2.33	1.20	0.03	1.18
Grade 2	4.74	3.61	2.44	3.59
Grade 3	3.11	1.98	0.81	1.96

There were no observations in the cells marked * and the mean scores are those implied by the model.

The mean scores again form an irregular pattern, those with Grades 0 (unaffected) and 2 (medium family history) being high, and those with Grade 1 (low family history) being low. There seem no obvious reasons for this. Those aged less than 45 and with fewer than three children scored more highly than those who were older or had more children.

The correlation coefficient between the two scores, EGCS1 and EGCS2, was calculated; its value is 0.73, very significantly different from zero.

10.6 DISCUSSION

This was a retrospective study. There had been no particular policy in the Renal Unit at GRI for routine genetic counselling to be given to patients with APKD. Yet 75% of respondents reported that they had received some genetic counselling. It was not easy to check from the medical records whether the patient had received information and if so what information had been given, as it was very seldom recorded in the patient's medical notes that the patient had received such information. In some cases it was possible to confirm with a particular consultant that information had been given to a patient, but

precise details of the content of the information were unknown. It is possible that some patients had in fact been given more information than they could remember.

It is good practice to record what information was discussed with the patient. This could be recorded in a letter sent both to the patient to refer to in the future and to remind them of what was discussed and also to the patient's GP (Hughes 1992).

Of the 25% of patients who reported that they had not received genetic counselling, the great majority were moderately or severely affected. It is possible that if they were uraemic they may not have remembered what they had been told. Another possible explanation is that, because they were more severely affected, the emphasis in the consultation would have been on the medical management of their symptoms. Since the great majority of respondents had received their genetic counselling from renal physicians it is possible that for many patients genetic counselling was simply not given.

Most counselling was given during a routine medical consultation and the majority of patients reported that they received information on one occasion only. This means that most patients received their genetic counselling along with any other information about the medical management of their condition.

More than half the patients had received their genetic counselling on their own. This is in keeping with the finding that most counselling had been given during a routine medical consultation. The very nature of a genetic disease such as APKD has implications not only for the affected person but also for their partner. And yet in this investigation in only nine cases was the partner or spouse present. Given a choice, the majority of respondents would have liked their partner to have been present.

The analysis of the first score relating to the environment of genetic counselling showed that severity of disease was the most significant explanatory variable. The mean scores for this variable, classified by severity of disease, are shown in Table 10.1. It can

be seen that there is little difference in the mean scores for severity of disease Grades 0, 2 and 3, but those in Grade 1 had a much higher mean score. Patients who are more severely affected may find it more difficult to assimilate the information that may be discussed in genetic counselling simply because they are more ill. In these circumstances the presence of a partner or other family member may assist in the transmission of information to the family unit.

Respondents in severity of disease Grade 1 who are only mildly affected may have had fewer immediate medical problems and this may explain their higher scores.

It can be seen from the analysis of the content of counselling that 69% of respondents had received information about the risk to children, and amongst the male respondents this was the only topic remembered by more than a few patients. Male patients reported receiving very little information in comparison with married women. A possible explanation is that less information was given to male patients. Alternatively male patients were given the information but they did not remember it as they did not think that such information was relevant to them.

It can be seen from Table 10.2 that some information was given about having no more children, and about sterilisation and vasectomy; but the majority of patients who received such information were married women (See Table D.21).

The analysis of the score for the content of genetic counselling showed that family history was the most useful explanatory variable, along with age and number of children. However, it can be seen from the contributions to the mean scores in Table 10.3 that the four grades of family history have very different scores which do not appear to follow an obvious pattern. It could be argued that those with little family history might have scored higher in this section. Since they do not have a family knowledge of the illness, they might have received more content in the genetic counselling. In this analysis those with

no family history, Grade 0, score highly while those with a low family history score very low. The respondents in Grade 0 had originally been diagnosed as having APKD and had been treated for symptoms similar to those of APKD as if they were caused by APKD for some time but, as a result of this study, had been found not to have APKD. I do not know whether the lack of family history in their case had influenced the amount of information given. It is possible that there was more concern about the diagnosis because of the absence of family history, so more information was given to them.

The effect for the combined factor for age and number of children is that those aged less than 45 and with fewer than three children were told more, or remembered more, of the possible topics than those who were older or had more children. This factor attains greater prominence when the results of questionnaire 3 are considered, and it will be discussed further there (Chapters 11 and 12).

CHAPTER 11: ANALYSIS:

KNOWLEDGE OF SYMPTOMS AND TREATMENT OF APKD

11.1 Introduction

Patients' knowledge of the symptoms of the illness as well as the risk of inheritance is frequently used as a measure of the effectiveness of genetic counselling as well as a means of trying to understand why patients followed certain courses of action following genetic counselling. It is appreciated that the patients' knowledge of the illness is needed as part of the evaluation of any genetic counselling service. However Beveridge (1989 p97), in her study of HIV and AIDS in Scottish Prisons, points to the importance of obtaining systematic baseline information about levels of knowledge, knowledge gaps and misconceptions about HIV and AIDS for the initial development and subsequent assessment of prison educational programmes. It seemed essential that, prior to establishing a genetic counselling service for APKD, a detailed investigation into the patient's knowledge of APKD, how the disease is transmitted and the treatments available was undertaken.

In this chapter the patients' knowledge of the disease and its treatments is discussed. Analysis of the basic results is presented in Appendix E. The patients' knowledge and understanding of the genetic inheritance and transmission of APKD are discussed in the next chapter.

The patients' knowledge of the symptoms and treatment of APKD was elucidated by questions in the first and the third interviews. Their responses are discussed below.

11.2 ANALYSIS OF RESPONSES

For this chapter each individual response and each constructed score was analysed by each of the demographic and medical variables described in Chapter 9. These are; sex, marital status, age, number of children, educational level, occupation, housing, religious affiliation, severity of disease, family history, and the combined factor for age and number of children. In addition each response and each score was analysed according to the two scores for the experience of genetic counselling described in Chapter 10 (EGCS1 and EGCS2); however, this could not be done for all the respondents in the first population, since the questions on the experience of genetic counselling came into the second interview.

It was anticipated that severity of illness, family history, educational level and possibly age of respondent could influence the respondent's knowledge of the symptoms of and treatments available for APKD. The subsequent GLIM analysis of the constructed scores showed that severity of illness and educational level were significant in explaining some of the variability of the score for knowledge of treatment in the first questionnaire.

11.3 KNOWLEDGE OF DISORDER AND TREATMENT: QUESTIONNAIRE 1, SECTION 6

11.3.1 Questions on knowledge of treatment

Respondents were asked in an open ended question in the first interview what they had been told about APKD. Respondents reported that they had been given information about the following topics: prognosis of APKD, inheritance of APKD, the risks to children and the association of cysts with APKD.

A majority of respondents (47 out of the 71 respondents or 66%) reported that they had been told about the presence of cysts. A minority of 12 respondents (17%) had been told about the inheritance of APKD and about the prognosis of APKD with the majority

of these respondents belonging to severity groups 2 and 3. Three respondents were told about the risk to children and one respondent reported that he had been told 'not to worry'.

The majority of patients (54 out of 71 or 70%) said that they were having some sort of treatment at the time of this interview, and these included almost all the patients in severity grades 2 and 3.

Just over half of patients were receiving antihypertensive drugs (39 out of 71 or 55%). The next most common treatment was dialysis (8 out of 71 or 11%).

Those who were having no treatment or 'other' treatment were asked whether they knew about what treatments were available. About half of those who were not having treatment (10 out of 21) knew about at least some forms of treatment.

All patients were asked what forms of treatment they knew about. The forms included: anti-hypertensive treatment, transplant, haemodialysis, CAPD and diet.

A majority of patients knew about each of the first three treatments (37, 38 and 39 out of 71 respectively), but fewer than half knew about CAPD (19 out of 71 or 27%) and diet (27 out of 71 or 38%). Those with the highest grades of severity of illness were much better informed than those with lower grades.

11.3.2 Score for knowledge of treatment in questionnaire 1

The answers to the questions in questionnaire 1 about the treatment of APKD were scored and a composite score of knowledge of treatment, denoted KDS1, was formed as described in Appendix E. The maximum score was 7. The distribution is distinctly bimodal, with 23 respondents getting only 1 point and 17 getting the full 7 points.

Analysis with GLIM using the replies from the respondents in the first population and the demographic and medical explanatory variables showed that both severity of

disease and education level were significant explanatory variables, both at a 1% level, and that the interaction between them was also significant at a 1% level.

Analysis of the responses for the second population using the scores for experience of genetic counselling as explanatory variables showed that there was no significant effect of these variables on this knowledge score.

The mean scores for each combination of severity grade and education level are shown in Table 11.1. The important point is best brought out by grouping the severity grades into 0-2 and 3, and the education levels into 1 and 2-4, and the mean scores are shown again in Table 11.2 with this grouping.

The percentages of the original variance explained by the different variables are shown in Table 11.3. It can be seen that the full 4 by 4 table explains 63.1% of the original variance, with the interaction term explaining more than education by itself; when the 2 by 2 table is used, the percentage of the original variance explained by the model falls to 43.9%.

Table 11.1

First population: mean scores for knowledge of treatment of APKD (KDS1), classified by severity of disease and education level.

	Education level			
Severity of disease	1	2	3	4
Grade 0	1.75	2.00	1.00	*
Grade 1	0.50	3.33	5.50	1.00
Grade 2	1.54	2.50	4.33	3.00
Grade 3	5.76	6.50	5.75	1.33

Note: there were no observations in the cell marked *.

Table 11.2

First population: mean scores for knowledge of treatment of APKD (KDS1), classified by severity of disease and education level.

	Education level	
Severity of disease	1	2-4
Grade 0-2	1.38	3.70
Grade 3	5.76	4.44

Table 11.3

First population: percentages of original variance of score for knowledge of treatment of APKD (KDS1) explained by successive factors.

Table:	4 by 4	2 by 2
	%	%
Original variance	100.0	100.0
Severity of disease	32.9	29.9
Education level	12.9	3.1
Interaction	17.3	10.9
Total explained	63.1	43.9
Residual	36.9	56.1

There is a significant contrast among those in education level 1 (low education) between those with high severity of disease (grade 3), whose average points are 5.76, and those with lower severities (0-2), whose average points are 1.38. In education level 1 respondents more severely affected by APKD have much better knowledge of the treatment for APKD than those less severely affected. On the other hand, among those with more educational qualifications (levels 2-4), there is much less difference in their knowledge of symptoms and treatment between those with greater severity of disease (grade 3), whose average points are 4.44, and those with lesser severity (grades 0-2), whose average points are 3.70.

11.4 KNOWLEDGE OF SYMPTOMS OF APKD: QUESTIONNAIRE 3, SECTION 6

11.4.1 Questions for knowledge of symptoms of APKD

In section 6 of questionnaire 3, respondents were asked to state which, if any, of a given list of symptoms might be associated with APKD. The results for all respondents in the third population are shown in Table 11.4. The total in each row is 47. A few respondents did not reply to any of this section, and others omitted certain items.

Table 11.4

Third population: 'are the symptoms listed associated with APKD?'.

Symptom	Yes	No	Sometimes	Don't know or no reply
Obesity	7	30	-	10
Headache	21	16	-	10
Kidney stones	11	25	-	11
Infection in urine	33	5	-	9
High blood pressure	37	2	-	11
Heartburn	15	22	-	10
Cloudy urine	32	6	-	9
Tiredness	33	4	-	10
Digestive problems	19	19	-	9
Pain	33	5	1	9
Itchy skin	23	14	-	10
Swollen ankles	23	13	-	11

Obesity and kidney stones are not symptoms normally associated with APKD, and a majority of respondents knew this. All the other symptoms can be associated with APKD, and for eight out of ten of these symptoms the majority of those who expressed a view knew this. But Heartburn was thought to be not a symptom by a majority (22 'no' against 15 'yes'), and the respondents were divided equally about Digestive problems (19

each). It is possible that respondents replied in respect of their own experience, rather than about what they knew in general, but there is no way of establishing whether this is the case.

11.4.2 Score for knowledge of symptoms of APKD

A composite score for each respondent's knowledge of the symptoms of APKD was formed, denoted KDS2, as described in Appendix E. The maximum score was 12 points. Although there were peaks in the distribution at 0 points and 10 points, the bimodality was less marked than the score for knowledge of treatment in questionnaire 1, KDS1.

Analysis using the GLIM system, and including all the explanatory variables described in Chapter 9 and also the scores for experience of genetic counselling, EGCS1 and EGCS2, showed that the most useful explanatory variable was the combined factor for age and number of children, which was significant at a 1% probability level. It explained 26.7% of the original variance.

The mean scores for each combination of age group and number of children group are shown in Table 11.5. The mean scores for those aged 45 and over are lower than those for younger ages, and the mean scores for those with 3 or more children are lower than the scores of those with fewer children.

Table 11.5

Third population: mean scores for knowledge of symptoms of APKD (KDS2), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	8.32	7.00
45 and over	4.43	3.57

11.5 KNOWLEDGE OF TREATMENT OF APKD: QUESTIONNAIRE 3, SECTION 6

11.5.1 Questions for knowledge of treatment of APKD

In the same section 6 of questionnaire 3, respondents were also asked to state which, if any, of a given list of treatments might be used to treat APKD. The answers, for all respondents in the third population, are shown in Table 11.6. The total in each row is 47. A few respondents did not reply to any of this section, and others omitted certain items.

Table 11.6

Third population: 'are the treatments listed used for treating APKD?'.

Treatment	Yes	No	Sometimes	Don't know or no reply
Water tablets	26	10	-	11
Blood pressure tablets	35	1	-	11
Kidney machine	35	3	-	9
Exercise	18	16	1	12
Diet	34	4	-	9
Kidney transplant	35	2	-	10
Rest	25	6	1	15

A large majority of respondents correctly said that Blood pressure tablets (anti-hypertensive drugs), Kidney machines (dialysis), Kidney transplants and Diet could be used to treat APKD. A smaller majority thought correctly that Water tablets could be so used, but about as many thought that Rest would be appropriate, when in fact doctors do not usually make any recommendation about this. Respondents were undecided about the benefits of Exercise, roughly half each of those who gave a reply saying 'yes' and 'no' (18 to 16). Again, doctors do not usually make any specific recommendations about this. It is again possible that respondents replied in respect of their own experience, rather than about what they knew in general.

11.5.2 Score for knowledge of treatment of APKD

A composite score for each respondent's knowledge of the treatments for APKD was formed, denoted KDS3, as described in Appendix E. The maximum score was 5. This score too showed some evidence of bimodality, with 9 respondents getting 0 points, and the rest getting 3 or more, with the largest number (20) getting the full 5 points.

Analysis using the GLIM system, and including all the explanatory variables described in Chapter 9 and also the scores for experience of genetic counselling, EGCS1 and EGCS2, again showed that the most useful explanatory variable was the combined age and number of children, which was again significant at a 1% probability level. This time it explained 29.2% of the original variance.

The mean scores for each combination of age group and number of children group are shown in Table 11.7. Again, the mean scores for those aged 45 and over are lower than those for younger ages, and the mean scores for those with 3 or more children are lower than the scores of those with fewer children.

Table 11.7

Third population: mean scores for knowledge of treatment of APKD (KDS3), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	4.32	2.60
45 and over	2.43	2.00

11.6 TOTAL SCORES FOR KNOWLEDGE OF SYMPTOMS AND TREATMENT OF APKD

Two further scores were formed as totals: the first was formed as the total score in questionnaire 3, the sum of the number of points for knowledge of symptoms and knowledge of treatments, i.e. KDS2 plus KDS3, denoted KDS4. The maximum score was

17 points. The second totals score was formed as the total score for knowledge of the symptoms and treatment for APKD in the two questionnaires combined, i.e. KDS1 plus KDS4, denoted KDS5. The maximum score was 24 points. Both of these scores are available only for the third population.

The first totals score, KDS4, like its component parts, showed evidence of bimodality, with a small peak at 0 points (7 respondents) and the rest of the distribution peaking at 15 points, though the peak is very flat.

This score is the sum of two scores which were highly correlated (correlation coefficient 0.82), and for both of which the variable combining age and number of children was the most useful explanatory one. It is not surprising that this variable provided the best explanation for this score, again significant at a 1% probability level, and explaining again 29.2% of the original variance.

The mean scores for each combination of age group and number of children group are shown in Table 11.8; they are simply the sum of the mean scores for the component parts, KDS2 and KDS3. The scores conform to the same pattern as before.

Table 11.8

Third population: mean scores for total score for knowledge of symptoms and treatment of APKD (KDS4), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	12.64	9.60
45 and over	6.86	5.57

The final score in this section, KDS5, is the grand total of the scores for knowledge of the symptoms and treatment of APKD, both in questionnaire 1 and questionnaire 3. The distribution has rather little evidence of bimodality, but is fairly flat.

This component parts of this score, KDS1 and KDS4, are not closely correlated (correlation coefficient 0.01), and these two scores were best explained by different variables, severity of disease and education for KDS1 and age and number of children for KDS4. In fact this latter variable explained more of the variance in this case, this time significant at a 5% but not at a 1% probability level, and explaining only 21.9% of the original variance.

The mean scores for each combination of age group and number of children group are shown in Table 11.9. The scores conform to the same pattern as before.

Table 11.9

Third population: mean scores for grand total score for knowledge of symptoms and treatment of APKD (KDS5), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	16.11	14.40
45 and over	11.29	8.86

11.7 CORRELATIONS BETWEEN SCORES

Correlation coefficients between the various scores for knowledge of the symptoms and treatment of APKD and between them and the scores for experience of genetic counselling described in Chapter 10 (EGCS1 and EGCS2) were calculated. The scores for knowledge of symptoms and of treatment in questionnaire 3 (KDS2 and KDS3) were closely correlated, the correlation coefficient being 0.82. The correlation coefficients of both these scores with the score for knowledge of treatment in questionnaire 1 (KDS1) were close to zero.

Five out of six of the correlation coefficients between the scores for knowledge of APKD (KDS1, KDS2 and KDS3) and the scores for experience of genetic counselling in

questionnaire 2 (EGCS1 and EGCS2) were in the range 0.21 to 0.31, significant at a (one-sided) 5% probability level, but not at a 1% level. The exception, the correlation coefficient between KDS1 and EGCS2, was close to zero.

11.8 FURTHER QUESTIONS ON KNOWLEDGE OF APKD: QUESTIONNAIRE 3, SECTION 1

Respondents to questionnaire 3 were asked what could be done to help someone suffering from APKD. 36 out of 47 offered a variety of answers including monitoring, control of blood pressure, drugs, dialysis and transplantation. 11 patients said that nothing could be done or they did not know of anything.

These patients were spread through the severity categories almost evenly. The majority of patients (8 out of 11) who suggested dialysis were in severity category 3, the group who would have most knowledge of dialysis. More patients in severity category 1 than 3 suggested monitoring. Patients in category 3 need treatment.

Patients were asked 'what are the medical problems associated with APKD?'. A variety of answers was given, the most common being 'raised blood pressure' (23 responses) and 'kidneys don't work' (10 responses), as shown in Table 11.10, though a number of single features or combinations of features were also given, such as renal failure (1 response). One patient (in severity category 3) did not know what the medical problems were and two married females (both in severity category 2) thought that there were no medical problems.

Table 11.10

Third population: 'what are the medical problems of APKD?', subdivided by sex and marital status.

	Single females	Married females	Males	Total
Blood pressure	5	10	8	23
Kidneys don't work	4	2	4	10
Other suggestions	1	2	-	3
Combinations of suggestions	2	4	2	8
Don't know or nothing	-	2	1	3
Total	12	20	15	47

Patients were asked whether they knew of other problems that might be associated with APKD. The list of problems given is shown in Table 11.11. Six patients, 2 from severity category 2 and 4 from severity category 3, explained that they were 'not whole people'. Eleven patients, spread evenly through the severity categories, reported that there were no problems.

Table 11.11

Third population: 'what other problems of APKD are there?', subdivided by sex and marital status.

	Single females	Married females	Males	Total
Pain	2	2	3	7
'Not a whole person'	-	2	4	6
Restricts children	1	3	-	4
Blood pressure	1	1	1	3
Infection	1	1	1	3
Assorted others	1	3	2	6
Don't know or none	6	8	4	18
Total	12	20	15	47

Respondents were asked whether APKD could be described as serious. 23 out of the 47 (49%) said that APKD is a serious illness and 13 of these 23 patients were in severity category 3 compared with four in severity category 1 and six in severity category 2. 12 out of the 47 patients said that it could be serious or was moderately serious but only 2 of these patients belonged to severity category 3.

These rather diverse questions were not consolidated into a single score.

11.9 DISCUSSION

APKD is not only an illness of variable age of onset, it is also an illness of several symptoms, and it may be that the absence of one major symptom could make it difficult for patients to have a totally accurate knowledge of the symptoms. 66% of the respondents had been told about the presence of cysts in APKD. The majority of patients knew about the availability of anti-hypertensive therapy, transplant and haemodialysis as possible treatments for APKD and in the first interview it was not surprising to find that those with the highest degree of severity of illness were much better informed.

Analysis of the results of knowledge of symptoms and treatment in the third interview showed that patients were really very well informed about symptoms and treatment of APKD with 26 out of 47 (55%) knowing about at least 8 out of the 12 symptoms, and more than half knowing about each individual symptom correctly. In addition 31 out of 47 (66%) knew about at least 4 of the 5 treatments and the majority of patients knew about each individual treatment.

From the results of the third questionnaire (Table 11.4) it can be seen that many patients were aware that hypertension, urinary tract infection and pain might all be associated with APKD. While half the patients said that blood pressure was a medical problem of APKD, fewer than half suggested diet as a possible means of controlling blood

pressure. This may reflect the lack of professional acceptance of the efficacy of the early introduction of diet to control hypertension in APKD, rather than simply lack of knowledge on the part of the patients. If diet is shown to be effective in the control of hypertension in APKD, then the use of diet may be helpful to the patient by giving them a feeling of some control over their illness. For this reason the relationship between diet and hypertension should be more widely understood by patients.

Diet is an important part of the treatment of patients in renal failure and for patients on haemodialysis (Gardner 1981). It is also a part of treatment that many patients in this study found difficult and restrictive.

Fewer than half the patients knew about CAPD. It is not surprising that CAPD as a method of dialysis, and often described by patients as the 'bag', is not so well known. It is a relatively new form of dialysis. Furthermore pictures of patients on dialysis usually show patients on haemodialysis and in this study patients tended to refer to 'going on the machine' when describing the principle of dialysis as a method of treatment for APKD. It would seem important for patients that wider publicity be given to all the different forms of dialysis.

Open ended questions about the medical problems associated with APKD and what can be done to help were asked of patients in the third questionnaire. It is interesting to note that there were as many respondents who said that nothing could be done as there were who suggested monitoring, dialysis and control of blood pressure. If this finding is a true reflection of what patients believe, it could affect whether patients were prepared to have presymptomatic diagnosis.

The respondents' knowledge of APKD was ascertained by examining their knowledge both of the symptoms of APKD and of the treatments that are available. Questions about this knowledge were asked in both interviews 1 and 3. The questions in

the two interviews were not, however, identical. In questionnaire 1 the questions were necessarily of a more exploratory nature in order to find out what the patient knew about the illness without raising anxiety whereas it was possible by the time of the third questionnaire to ask more detailed and specific questions.

The analysis of the knowledge of treatment in questionnaire 1 shows that severity of illness was a significant explanatory variable. This is not a surprising finding. It has already been stated that there had not been a special programme at the Renal Unit at GRI for genetic counselling for patients with APKD. Therefore the knowledge of patients is likely to have depended on their own experience. It might also have depended on the strength of their family history but the GLIM analysis did not show this to be a significant variable. Level of education was a statistically significant variable; but the important observation here was the interaction between the level of education and severity of illness. For those respondents with a low educational level, severity of illness was an important factor in their knowledge, whilst for respondents with a higher educational level severity of illness was a less important factor.

It would not have been unreasonable to have assumed that these same two variables would have been equally significant in the analysis of the patients' knowledge of the symptoms and treatment of APKD in questionnaire 3. However, this was not the case. In this second analysis of knowledge of symptoms and treatment two other variables were influential, expressed in the combined factor for age and number of children. It is not altogether obvious why these different factors should become important in the second part of this analysis. It is possible that by the time of the third interview the research project itself was having an influence on information given to patients. Medical, nursing and other ancillary staff were interested in the project, and the research worker had control only of information that she herself gave to patients. In the third population those who were

younger were more knowledgeable about the symptoms and treatment of APKD. This higher knowledge amongst younger people may reflect the possibility that they had been given information more recently, although there is no direct evidence of this; it may also be the case that younger people now have a greater general knowledge of biology; there may also be a general trend for greater knowledge in health matters amongst younger people.

Those who had fewer children were also more knowledgeable about the symptoms and treatments of APKD analysed in the third questionnaire. It is difficult to suggest reasons why this should be so.

CHAPTER 12: ANALYSIS:

KNOWLEDGE OF GENETIC INHERITANCE AND TRANSMISSION OF APKD

12.1 Introduction

The patients' understanding and knowledge of the genetic inheritance and transmission of APKD was elucidated by questions in the first and the third interviews. Their responses are reported in Appendix F and are discussed in this chapter.

12.2 Knowledge of inheritance in first questionnaire

12.2.1 Questions and basic results

Section 5 of the first questionnaire was concerned with what the patients knew about the inheritance and transmission of APKD. Ten questions were asked, but some of these questions were not relevant for some respondents.

Respondents were first asked whether they could describe how they got the condition. The word 'got' was used in order to allow respondents describe how they thought the illness was acquired, whether genetically or otherwise. More than half (38 out of 71 or 54%) knew correctly how they had got the condition. A higher proportion of females than of males (27 out of 44 or 61% as opposed to 11 out of 27 or 41%) knew correctly how they got the condition. Among the women were six who were aged under 35 and who had been screened for APKD, and two who had been diagnosed when they were pregnant. It is possible that these women were given information about APKD in the screening process. It is also possible that more information is given to women because they are the ones who have the children and that because women are the child bearers they are more interested in seeking information about problems that they or their child may have.

Respondents were next asked whether the disorder 'ran in the family'. 48 patients (68%, 32 females and 16 males) knew that the disorder ran in the family, compared with 12 (17%, 8 females and 4 males) who said that it did not run in the family. There were, however, 8 patients (4 females and 4 males) who said that the disorder 'did not seem to run in the family', 1 male who recorded that he did not know and 2 males who were not sure.

The fact that 48 patients (67%) knew that the disorder ran in the family compared with 38 who knew how they got the condition might be explained by a misunderstanding of the question by the respondents. It is also possible that patients knew that the disorder ran in the family but did not express their answer to 'how did you get the condition?' as an inherited or familial condition.

Every one of the 24 with a strong family history (Grade 3) said that APKD did run in the family, as did most of those (21 out of 29) in family history Grade 2.

The respondents were next asked whether APKD was inherited. 51 out of the 71 (72%) (33 females and 18 males) knew that APKD was inherited. In addition 8 patients (7 males and 1 female) answered that it seemed to be; 6 of these had no affected relatives, including 4 who had not been sure about whether APKD ran in the family; the other 2, however, had affected relatives and said that it ran in the family, so their answers were inconsistent.

All the 6 who said that it was not inherited also said that it did not run in the family and had no affected relatives. The 5 who did not know whether APKD was inherited included 1 who had no affected relatives, 1 who had affected sibs, but believed it not to run in the family, and 3 who had affected relatives and said that it did run in the family.

The patients were then asked how the condition was inherited. 29 out of the 71 (41%) (13 females and 16 males) did not know how APKD was inherited, and a further 22 (31%) (15 females and 7 males) were unsure. Only 6 (8%) (2 females and 4 males) got the answer almost correct. 2 patients thought that APKD skipped generations and 5 patients that it only affected members of the same sex.

Patients were then asked whether APKD could be passed on. 57 out of the 71 (80%) (34 females and 23 males) knew that APKD could be passed on, but 11 (15%) (7 females and 4 males) did not know; included in these 11 were 9 who had given uncertain answers to some of the previous questions. None asserted that it could not be passed on. 21 out of 24 in family history grade 3 and all the 29 in family history grade 2 said that it could be passed on.

Patients were then asked how APKD was passed on. Only 10 out of the total of 71 answered correctly (8 females and 2 males); 22 (9 females and 13 males) did not know how it was passed on; and 25 (17 females and 8 males) were unsure. 2 females stated that it was passed from mother to daughter (only one of these thought it was inherited in the same way), 1 female and 1 male thought that it skipped generations (neither of whom thought that it was inherited the same way), and 1 male reported that it was transmitted by a germ. This last was not a misunderstanding. The patient was quite emphatic that the condition was caused and passed on by a germ. It is clear from the results of this question that the great majority of patients did not understand the autosomal dominant transmission of APKD.

Different words including inherited, genetic and familial have been used to describe genetic disorders such as APKD. The next question for respondents was: 'is APKD a genetic disorder?'. 42 out of 71 (59%) (30 females and 11 males) knew that APKD is a genetic disorder compared with 24 (34%) (10 females and 14 males) who did

not. 3 patients (2 females and 1 male) were unsure. The one who believed that it was not genetic was quite consistent in her views: it did not run in her family, it was not inherited, it was not genetic; she was herself affected (severity grade 2), and the medical records showed that her father had died of APKD, though she claimed to have no affected relatives.

The question about whether the patient knew his or her own risk of inheriting APKD was not asked of 56 out of the 71 patients (79%) at this stage, since it was clear to the researcher that the method of transmission was problematic and potentially distressing to these patients.

For the same reasons 18 patients were not asked about whether they knew the risk to their children. Of the 53 patients who were asked about their knowledge of this, 36 (68%) (24 females and 12 males) did not know the risk compared with 17 (32%) (10 females and 7 males) who did know. Many more knew the risk for their (or any) children to inherit than knew the risk for themselves.

12.2.2 Score for knowledge of inheritance in questionnaire 1

Certain of the questions in questionnaire 1 about the genetic inheritance of APKD were used to form a composite score for the respondents' knowledge of genetics, denoted KIS1 and described in Appendix F. The maximum score was 5 points. A score of 4 or 5 represents good knowledge of the inheritable nature of APKD, even if the precise details were not known; a lower score indicates some uncertainty at least about the terminology used. The average score was 3.5 and 31 out of the 71 (44%) got the full 5 points, with a further 9 (13%) getting 4 points.

Analysis using the GLIM system of the score for knowledge of inheritance, KIS1, using all the possible explanatory variables described in Section 9.13 and including the

first population showed that the only factors to produce effects significant at a 1% probability level were family history and housing. Family history accounted for 41.7% of the original variance, and housing an extra 7.4%, making 49.1% in all, quite a substantial reduction in the original variance.

Further analysis using also the scores for experience of genetic counselling (EGCS1 and EGCS2) and including the second population showed that again family history and housing were significant at a 1% level, explaining 48.3% of the original variance, but score EGCS1 explained a further 4.5%, significant at a 5%, though not at a 1%, probability level. The correlation coefficient between scores KIS1 and EGCS1 was 0.44, so by itself it would explain 19.1% of the variance, but this is reduced when this factor is brought in after other and more powerful factors.

The components of the mean score for the two populations are shown in Table 12.1, and the mean scores for those with each combination of family history and housing, using the results from the first population, are shown in Table 12.2. Those with higher grades of family history (2 and 3) have better knowledge of the genetic inheritance of APKD than those with lower grades, to the extent of about 2.5 points more, and those who are owner occupiers have better knowledge than tenants to the extent of about one point.

Table 12.1

First and second populations: components of mean scores for knowledge of inheritance in questionnaire 1 (KIS1).

	Population	
Element	First	Second
Overall mean	3.46	3.55
Family history:		
Grade 0	−1.80	−1.28
Grade 1	−1.90	−1.78
Grade 2	+0.60	+0.54
Grade 3	+0.67	0.41
Housing:		
Owner-occupier	+0.60	+0.62
Tenant	−0.37	−0.36
Per unit of EGCS1	-	+0.21

Table 12.2

First population: mean scores for knowledge of inheritance in questionnaire 1 (KIS1), classified by family history and housing.

Family history	Owner occupier	Tenant
Grade 0	2.27	1.29
Grade 1	2.16	1.19
Grade 2	4.67	3.70
Grade 3	4.74	3.76

12.3 DISCUSSION OF KNOWLEDGE OF INHERITANCE IN QUESTIONNAIRE 1

Genetic counsellors often describe their work as a "communication process that deals with the human problems associated with the occurrence, or risk of recurrence, of a genetic disorder in the family" (Thomas 1986 p125). The patient's comprehension of the

risk of occurrence of a particular disease is often used as an outcome measure in genetic counselling studies as well as an indicator of possible reproductive behaviour (see Chapter 2). The fact that the patient may be able to repeat the risks correctly one month after counselling does not mean that he or she has comprehended the genetic information as it would concern their own situation. For example Evers-Kiebooms (1987) in her study of cystic fibrosis found that 3 out of 4 parents interviewed reported correctly that the risk of having a child with cystic fibrosis was 25%. However this author went on to say that "the knowledge of the autosomal recessive transmission seemed to be rather superficial in keeping with other studies" (p145).

It is not surprising that patients have difficulties in comprehending genetic risk. The language of genetics is unfamiliar and complicated. Different words such as 'genetic' and 'inherited' may be used by counsellors to describe the same concept. The words may also be rather randomly interchanged by counsellors and individual counsellors may not be consistent in their use of the words.

The focus in the section on knowledge of inheritance in questionnaire 1 was to assess what the respondents understood about the genetics of APKD. Genetic risk is discussed in Section 12.9 following the analysis of knowledge of inheritance from questionnaire 3.

The results of the analysis of this section show that there is some confusion amongst respondents in their knowledge of the genetics of APKD. While the majority of respondents (72%) knew that APKD was 'inherited' only 59% reported that APKD was 'genetic'. It is possible that the word 'inherited' is more familiar to the respondents than the word 'genetic' and this should be considered when giving information about the genetics of APKD. There may be a further confusion in the use of the expression 'ran in the family'. Although 48 out of 71 or 67% of respondents knew that the disorder ran in

the family, this does not mean that these respondents understand that the disease is genetically transmitted. It may simply mean that in the case of these patients the illness appeared to run in the family. If this assumption is correct then there may be a communication gap between the lay language of 'run in the family' and the language of the professionals which includes 'genetic'.

It would not be unreasonable to assume that, for those who are not familiar with Mendelian patterns of inheritance, it may not be initially obvious that if a disease is inherited then there is the possibility that it can be passed on to the next generation. However although analysis showed that 80% of respondents said that APKD could be passed on, only a small minority understood correctly how APKD is passed on. In this analysis, those respondents with a strong family history had better knowledge of the inheritance of APKD. While this result is possibly not surprising it would be important that counsellors do not assume that those with a strong family history always understood the correct pattern of inheritance. However, unless the pattern of inheritance is explained correctly, even in the presence of a strong family history patients are likely to base their knowledge on the experience in their own family, which may or may not be genetically correct.

12.4 KNOWLEDGE OF INHERITANCE OF APKD: QUESTIONNAIRE 3, SECTION 5

12.4.1 Questions and basic results

In Section 5 of questionnaire 3 five questions were asked about the patients' understanding of the genetics of APKD. These were of 'multiple choice' form, in that the respondent was asked to select one from a specified set of answers.

The first question was: 'how is APKD passed on?'. 34 out of the 47 respondents (72%) stated that APKD is passed from generation to generation (the only correct

statement in this question). The misconceptions about transmission were that APKD is passed from female to female (2 patients), that it is passed from female to male (1 patient) and that it is passed from male to female (2 patient).

The next two questions were: 'what is the risk of inheriting APKD?' and 'what is the risk of passing on APKD?'. To both these questions the greatest number of respondents (25 and 22 or 53% and 47% respectively) thought that the risk was a medium risk. 12 respondents thought that the risk of inheriting APKD was a big risk and 13 respondents thought the risk of passing on APKD was a big risk, of whom 9 were female.

Table 12.3 shows the results for these questions subdivided by severity of disease. There was a tendency for patients in severity groups 2 and 3 to say that the risk was a big risk.

Table 12.3

Third population: subdivided by severity of disease.

	Grade 1	Grade 2	Grade 3	Total
(a) 'what is the risk of inheriting APKD?'				
A big risk	2	3	7	12
A medium risk	9	8	8	25
A small risk	-	3	1	4
Don't know or no reply	1	1	4	6
(b) 'what is the risk of passing on APKD?'				
A big risk	2	5	6	13
A medium risk	8	7	7	22
A small risk	1	2	2	5
Don't know or no reply	1	1	5	7
Total	12	15	20	47

Respondents were then asked: 'when does APKD skip generations?'. Slightly more patients (21 out of 47 or 45%) said that APKD never skips a generation compared with

19 (40%) who thought that APKD sometimes skips a generation. Autosomal dominant disorders such as APKD do not normally 'skip' a generation. Each child of an affected parent has a 50-50 chance of inheriting the gene for APKD. A parent may die prematurely, for example from an accident, before they have either presented with or developed symptoms of APKD and in these circumstances an affected offspring of that person may think that the condition has 'skipped' a generation.

The final question in this section was: 'the risk of inheriting APKD is .. ?', and the possible replies were specific numbers. More than half of the respondents (29 out 47 or 62%) gave the answer as 50-50 with another 1 patient who said 1 in 2 and 1 patient who gave both these answers. Therefore 31 out of 47 patients (66%) gave the correct answer.

12.4.2 Score for knowledge of inheritance in questionnaire 3, section 5

A composite score was constructed from the answers to the questions in this Section, denoted KIS2 and described in Appendix F. The maximum score was 4 points. The average score was 2.8 points, with 16 respondents (34%) getting the full 4 points, and another 16 getting 3 points.

Analysis of this score using the GLIM system and considering all the possible explanatory variables described in Section 9.13 showed that the variable that had the most significant effect was the factor combining age and number of children, which was significant at a 1% probability level. Once this was taken into account no other factor had a significant effect. This factor accounted for 33.7% of the original variance of the score.

The mean scores for those in each combination of age and number of children are shown in Table 12.4. Those who have a larger number of children (3 or more) had less

knowledge of this aspect of genetic inheritance than those with fewer children or none. Those under 45 with fewer than 3 children had the best knowledge.

Table 12.4

Third population: mean scores for knowledge of inheritance of APKD (KIS2), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	3.36	1.60
45 and over	2.14	1.86

12.5 KNOWLEDGE OF TRANSMISSION OF APKD: QUESTIONNAIRE 3, SECTION 5

12.5.1 Questions and basic results

In Section 5 of questionnaire 3 six further questions were asked about the patients' understanding of the risks of transmitting APKD, with one question about the presence of symptoms. These too were of multiple choice form, in this case asking whether the given statements were true or false.

The first two statements were: 'all children of a person with APKD will develop the condition' and 'on average half the children of a person with APKD will develop the condition'. 27 out of 47 respondents (57%) knew that on average half the children of an affected parent with APKD will develop the illness. 4 patients (3 females and 1 male) thought that all the children of an affected parent would develop APKD.

The next two statements were: 'on average half the children of a person with APKD are at risk of developing the condition' and 'all children of a person with APKD are at risk of developing the condition'. Respondents were less sure when asked whether on average half the children of an affected person are at risk or all the children of an affected person are at risk. 14 respondents thought that on average half the children of an

affected parent are at risk of developing the problem and 20 out of 47 (43%) thought that all the children were at risk of developing the problem.

The next statement gave a choice of three mutually contradictory statements: 'a person with APKD sometimes (always/never) has a parent with APKD'. 29 out of 47 (62%) gave the correct answer, 'always', whereas 6 said 'sometimes', and 1 said 'never'; 3 respondents gave two contradictory replies as true.

The final statement in this section gave a choice of two mutually contradictory statements: 'APKD always (sometimes) has symptoms'. Replies were evenly divided between 'always' and 'sometimes', with 18 (34%) each; 2 respondents gave contradictory replies as true.

12.5.2 Score for knowledge of transmission in questionnaire 3, section 5

A composite score was constructed from the answers to the questions in this Section, as described in Appendix F, and denoted KIS3. The maximum score was 5 points. The average score was 3.0. 12 respondents (26%) got the full 5 points, 6 (13%) got 4, and 13 (28%) got 3 points, so well over half were reasonably well informed by the time of this third interview.

Analysis of this score using the GLIM system showed that the factor that had the most significant effect was again that combining age and number of children, which was significant at a 1% probability level. After this was taken into account the only other factor that had a significant effect was one of the scores for experience of genetic counselling, EGCS2; the correlation coefficient between KIS3 and EGCS2 was 0.44, significantly different from zero at a 1% level. The combined factor accounted for 42.5% of the original variance, and EGCS2 for a further 6.0%, making a total of 48.5%.

The components of the mean score for those in each combination of age and number of children and for each unit of EGCS2 are shown in Table 12.5. Those who were 45 or over had less knowledge of this aspect of genetic inheritance than those who were younger. Those under 45 with fewer than 3 children had the best knowledge.

Table 12.5

Third population: components of mean scores for knowledge of transmission of APKD (KIS3).

Element	Component
Age and number of children:	
≤44, ≤2	3.28
≤44, ≥3	2.41
≥45, ≤2	0.72
≥45, ≥3	1.43
Per unit of EGCS2	+0.16

12.6 KNOWLEDGE OF INHERITANCE OF APKD: QUESTIONNAIRE 3, SECTION 1

12.6.1 Questions and basic results

At the beginning of the third interview respondents were asked a variety of questions to ascertain their knowledge of APKD, the first of which was: 'how did you get APKD?'. The majority of patients (41 out of 47, 28 females and 13 males) said that they got the condition because it was a hereditary condition. 4 patients (3 females and 1 male) replied that they did not know how they got APKD. 1 female patient explained that she developed APKD as a result of pregnancy and 1 male patient said that he had become affected as a result of pain.

Respondents were asked how APKD is discovered in patients. The answers reflect the different ways in which APKD came to be diagnosed. 16 patients (15 females and 1

male) said that it is discovered through the hereditary nature of APKD. It is interesting that so many women answered the question in this way. It is possible that because women give birth they are more aware than men of hereditary illness. However it is also possible that doctors are more likely to give information about inherited illness to women. 5 males and 5 female patients gave blood pressure as the reason for discovering about APKD and 6 married women answered 'during pregnancy'.

Respondents were asked whether APKD could be caught. Almost all the patients (43 out of 47 or 91%) knew that APKD could not be caught. However 3 patients (2 married females aged 25-34 and 1 male aged 35-44) said that APKD could be caught and 1 male patient in the age group 45-54 and in severity group 3, did not know whether or not APKD could be caught.

Patients were asked whether APKD could be prevented. A majority (35 out of 47 or 74%) thought that APKD could not be prevented. 2 patients (1 female and 1 male) said that the condition could be prevented but were unable to specify how this could be done. 9 patients (3 single females, 3 married females and 3 males) said that APKD could be prevented by the affected person having no children.

12.6.2 Score for knowledge of inheritance in questionnaire 3, section 1

These questions also formed the basis of a composite score, as described in Appendix F and denoted KIS4. The maximum score was 3 points, the average was 2.0, and 28 out of the 47 (60%) got 2 points, with the rest splitting almost equally between 1 and 3 points (9 and 10 respectively).

Analysis of this score with the GLIM system showed not one explanatory variable that had any significant effect.

12.7 TOTAL SCORES FOR KNOWLEDGE OF GENETIC INHERITANCE

Two further scores were formed as totals: the first, denoted KIS5, was formed as the total score in questionnaire 3, the sum of the number of points for the three sections described above, KIS2, KIS3 and KIS4, combined. The maximum score was 12 points, and the average 7.7. The final total score, denoted KIS6, was formed as the total score in the two questionnaires combined, the sum of the score for questionnaire 1, KIS1, and the total score for questionnaire 3, KIS5. The maximum score was 17 points and the average was 11.6.

The average scores for the questionnaire 3 total, KIS5, and for the grand total, KIS6, subdivided by sex and marital status, by family history and by age and number of children, are shown in Tables 12.6, 12.7 and 12.8.

Table 12.6

Third population: average scores for questions on knowledge of inheritance of APKD (KIS5 and KIS6), subdivided by sex and marital status.

	Single females	Married females	Males	Total
Total score in questionnaire 3, KIS5	9.1	7.8	6.6	7.7
Total score in questionnaires 1 and 3, KIS6	12.7	12.1	10.1	11.6

Table 12.7

Third population: average scores for questions on knowledge of inheritance of APKD (KIS5 and KIS6), subdivided by family history.

	Grade 1	Grade 2	Grade 3	Total
Total score in questionnaire 3, KIS5	5.8	7.3	9.0	7.7
Total score in questionnaires 1 and 3, KIS6	7.0	11.3	13.5	11.6

Table 12.8

Third population: average scores for questions on knowledge of inheritance of APKD (KIS5 and KIS6), subdivided by age and number of children.

	≤44, ≤2	≤44, ≥3	≥45, ≤2	≥45, ≥3	Total
Total score in questionnaire 3, KIS5	9.2	6.4	5.4	5.1	7.7
Total score in questionnaires 1 and 3, KIS6	13.1	10.4	9.4	8.7	11.6

It would be reasonable to expect that a factor that had been relevant in explaining the variation in a part of any total score might contribute also to the explanation of the total. Analysis of the first total score, KIS5, showed that only one factor had a significant influence, again that combining age and number of children, which explained 61.5% of the original variance. No other variable made any significant contribution.

The mean scores are shown in Table 12.9. Again those under age 45 with fewer than 3 children have the highest score.

Table 12.9

Third population: mean scores for knowledge of inheritance of APKD in questionnaire 3 (KIS5), classified by age group and number of children.

	Number of children	
Age group	0-2	3 or more
up to 44	9.21	6.40
45 and over	5.43	5.14

Again it would be reasonable to expect that a factor that had been relevant in explaining the variation in a part of the total might contribute also to the total. Analysis of the final total score, KIS6, showed that the first two candidates were family history and the combined factor for age and number of children, both significant at a 1% probability level. No other factor had any significant effect; the experience score EGCS2 was next, but not at a 5% level.

The mean scores are shown in Table 12.10. (Note that there were no respondents with family history grade 0 (unaffected) in this population.) Those in the family history grade 3 have the highest mean score, the other grades having significantly lower scores.

The components for the two explanatory variables, relative to the mean score of 11.62, are shown in Table 12.10, and the expected scores for the two variables are shown in Table 12.11.

This analysis shows that family history is the strongest single factor overall and particularly of the larger first population in explaining variation in knowledge of genetic inheritance. Those with a stronger family history have a better appreciation of the genetics. Within the third population age and number of children were relevant. Those who were aged less than 45 and had fewer then 3 children had the best knowledge.

Table 12.10

Third population: components of mean scores for total knowledge of inheritance of APKD (KIS6).

Element	Component
Overall mean	11.62
Family history:	
Grade 1	−4.00
Grade 2	−0.11
Grade 3	+1.34
Age and number of children:	
≤44, ≤2	+1.20
≤44, ≥3	−1.69
≥45, ≤2	−1.73
≥45, ≥3	−1.89

Table 12.11

Third population: mean scores for total knowledge of inheritance of APKD (KIS6), classified by family history and by age and number of children.

	Age and number of children			
Family history	≤44, ≤2	≤44, ≥3	≥45, ≤2	≥45, ≥3
Grade 1	8.83	5.94	5.89	5.73
Grade 2	12.71	9.82	9.78	9.62
Grade 3	14.17	11.28	11.24	11.08

12.8 CORRELATIONS BETWEEN SCORES

Correlation coefficients were calculated for each of the scores for knowledge of inheritance with each other, and with the scores for experience of genetic counselling (EGCS1 and EGCS2) and the scores for knowledge of the symptoms and treatment of APKD (KIS1 to KIS6). There were only small coefficients between many of the scores,

but the scores for knowledge, both of symptoms and treatment and of the inheritance of APKD, in the third questionnaire, with the exception of KIS4, were reasonably highly correlated, as shown in Table 12.12.

Table 12.12

Third population: correlation coefficients for scores for knowledge of symptoms and treatment (KDS2 and KDS3) and of genetic inheritance (KIS2 to KIS4).

	KDS2	KDS3	KIS2	KIS3	KIS4
KDS2	1.00				
KDS3	0.82*	1.00			
KIS2	0.59*	0.52*	1.00		
KIS3	0.67*	0.62*	0.72*	1.00	
KIS4	0.13	0.01	0.17	0.18	1.00

Note: * indicates that the coefficient is significantly different from zero at a 1% probability level.

12.9 DISCUSSION OF KNOWLEDGE OF INHERITANCE IN QUESTIONNAIRE 3

There are three particular areas of interest in the questions on the knowledge of inheritance in the third interview. The first concerns the patient's understanding of whether the risk of inheriting APKD is a small, medium or big risk. The second area concerns the patient's understanding of the transmission of APKD and specifically whether this means that all the children of an affected person are at risk or whether half the children of an affected person are at risk. The third area of interest is concerned with the patient's understanding of whether APKD can be prevented.

Researchers have found that the interpretation of statistical probability is highly subjective (Pearn 1973). What one patient may think of as a high risk may be a medium risk for another patient or even a low risk. Wexler (1979), in her study of Huntington's chorea, an autosomal dominant illness that the author herself is at 50% risk of inheriting, emphasised

that a 50-50 risk of inheriting Huntington's chorea always means for an individual person a 100% certainty that the person will either develop or not develop the illness. The question being asked in this study concerned the size of the risk perceived by patients of inheriting APKD as I believe that it may be easier for people to understand and make sense of risk when described as small, medium or large.

The majority of respondents thought that both the risk of inheriting APKD as well as the risk of transmitting APKD was a medium risk. In addition 66% of respondents knew that the risk of inheriting APKD was 50-50. Within clinical genetics if the risk of transmission of a disease is greater than 1 in 10, the risk is generally considered to be a high risk and amongst professionals would be described as such. However, it is not illogical for patients to believe that a risk of 50-50 of inheriting APKD is a medium risk; the chances each way are the same. Patients were not asked in this study what size of risk they would consider a big risk. It may be that the risk of inheriting APKD would need to be nearer 100% before patients perceived the risk as a big risk. There is a danger that because many of those offering genetic counselling may themselves perceive a 50-50 risk as a high risk, they may assume that the patients' belief system is the same.

It can be seen from Table 12.3 that there was a tendency, not statistically significant, for the more severely affected patients to consider the risk to be high. It is possible that the assessment of probability by an individual patient may vary according to how they were feeling and according to their mood. In an optimistic state of mind the risk of transmitting APKD to their offspring may seem a medium risk to an affected person. However, when that patient is severely affected by APKD, the effect of the illness may make them perceive the risk more pessimistically. Wexler (1979) suggests that such perceptions may change depending upon the mental state of the patient and the change may be from moment to moment, day to day and month to month.

It is arguable that the difficulties inherent in the language of genetics are reflected in this study in the respondent's understanding of the risks of transmitting APKD, with considerable uncertainty about whether on average half the children of an affected person are at risk of developing APKD or all the children of an affected person are at risk. The questions asked of respondents in this section were quite complicated and it is possible that some respondents had become quite ill and had difficulty in concentrating. Older respondents had a poorer knowledge of inheritance and they were more likely to be more ill. However, if patients are to make informed choices on the basis of information given in genetic counselling, then it is essential that patients know that all the children of an affected person are at risk of inheriting APKD. These findings point to the need for great care to be taken by genetic counsellors in their choice of words used to explain genetic transmission.

Respondents were asked whether they thought that APKD could be prevented. 74% of respondents responded that APKD could not be prevented, with only 9 patients saying that APKD could be prevented by affected people not having children. It is perhaps not surprising that so few patients appeared to know that APKD can be prevented by the affected person not having children. This is a very radical form of prevention of an illness. It is possible that many people would consider prevention to include actions such as changing their diet, or giving up smoking or following a course of medication.

Finally, the importance of the strength of family history in patients understanding of inheritance and transmission of APKD should be noted. Patients may bring to genetic counselling an expertise of knowledge based on the experience in their family. This information may be quite correct. However, it is also possible that either because of the lack of total information within their family or because of the vagrancies of chance in that, for example, the illness had only affected one sex, the information is inaccurate. The task for the counsellor is to elicit this information and present it appropriately to the patient.

CHAPTER 13: ANALYSIS: PERCEPTION OF PROBLEMS

13.1 PERCEPTION OF PROBLEMS: FIRST QUESTIONNAIRE

Respondents to questionnaire 1 were asked to identify from a list of 28 topics which of these topics were problematic for the respondents and to indicate on a 6 point scale how problematic they were. The grades on the scale were:

1 Not applicable
2 Not important
3 Slight importance
4 Quite important
5 Very important
6 Extremely important

Of the 28 problems:

11 topics (1-11) were associated with the **physical symptoms** of kidney disease and kidney failure.
4 topics (12-14 and 22) were associated with **restriction on the patients physical activity.**
6 topics (16-21) related to **job, income and ability to remain a breadwinner.**
8 topics (15 and 23-29) were related to **relationships, marriage and tensions** that may be caused by having a chronic and a genetic illness.

The responses were scored by using 'ridit' analysis; according to Agresti (1984), ridits were originally suggested by Bross (1958) as appropriate for ordinal scales such as these. The methods described by Agresti have been followed for this analysis. The advantage of ridit analysis is that it avoids the otherwise arbitrary procedure of assigning scores such as 1 to 6 to the different grades of answer, which could imply that the respondents thought that, for example, a topic that was seen as 'extremely important' was precisely six times as important as one that was 'not applicable'. How ridits are calculated and used is explained below.

Table 13.1 shows the gradings for each topic for all respondents. Two respondents did not complete the questionnaire fully; their answers have been included as far as they went; the row totals are therefore variously 71 (topics 1 to 10), 70 (topics 11 to 26) and 69 (topics 27 and 28).

The totals of the numbers in each grade from Table 13.1 for all topics have been calculated and are shown in Table 13.2. There were 1,968 answers in total, of which 803 were at grade 1, 'not applicable'. The ridit for grade 1 is calculated by taking half of this number (803/2 = 401.5) and by dividing this by the total number of answers (1,968), giving a ridit for grade 1 of 0.204.

There were 625 answers in total in grade 2. The ridit for grade 2 is calculated by taking half the number in grade 2 (625/2 = 312.5) and adding all the number in grade 1 (803), giving a total of 1,115.5. This number is divided by the total (1,968) to give the ridit for grade 2 of 0.567.

The ridit for grade 3 is calculated by taking half the number in grade 3 (243/2 = 121.5) together with the total number in grades 1 and 2 (803 + 625 = 1,428), giving 1,549.5, and again diving by the grand total of 1,968 to give 0.787. The ridits for grades 4, 5 and 6 are calculated similarly.

The ridit is a measure of the empirical cumulative distribution of answers as at the mid-point of each grade. The mean ridit for each topic is then calculated. The average ridit for all topics is necessarily 0.5, so any topic with a ridit more than 0.5 is 'above average' and any topic with a ridit less than 0.5 is 'below average'.

Table 13.1

First population: numbers of patients who graded each topic in terms of how severe a problem it was.

	Grade	1	2	3	4	5	6
O	Topic	Not applicable	Not important	Slight	Quite	Very	Extremely
1	Lethargy	10	17	19	13	12	-
2	Headache	14	25	14	11	4	3
3	Abdominal pain	23	33	8	4	1	2
4	Itchiness	25	27	13	2	1	3
5	Nausea	24	28	10	8	-	1
6	Lack of concentration	20	30	11	5	4	1
7	Sleepiness	17	26	7	11	9	1
8	Sickness	28	33	7	3	-	-
9	Moodiness	18	28	11	4	8	2
10	Back pain	15	17	19	11	8	1
11	Other physical problems	46	6	6	11	-	2
12	Dependence on hospital	34	29	3	2	2	1
13	Restriction on eating	32	30	4	4	1	-
14	Restriction on drinking	35	27	7	-	2	-
15	Feeling different	32	30	7	1	1	-
16	Difficulty at work	46	18	5	-	1	1
17	Unable to continue job	41	16	5	3	5	1
18	Remain breadwinner	42	16	5	2	4	2
19	Loss of job	41	11	9	3	5	2
20	Loss of income	38	12	11	4	4	2
21	Reduction in standard of living	40	13	9	4	3	2
22	Restricts physical activity	17	18	17	7	10	2
23	Puts strain on marriage	34	16	8	8	4	1
24	Tension in family	30	23	8	6	3	1
25	Difficult to make plans	29	25	3	5	9	-
26	Difficult to keep friends	36	29	5	1	-	-
27	Difficulty with opposite sex	35	20	4	7	4	1
28	Family/genetic disorder	21	22	8	8	7	5

Table 13.2

First population: total numbers and calculated ridits.

Grade	1	2	3	4	5	6	Total
Numbers	803	625	243	148	112	37	1,968
Ridits	0.204	0.567	0.787	0.887	0.953	0.991	

The Kruskal-Wallis test (Agresti 1984 p182) was used to see whether the grading of topics could be assumed to have been picked at random by respondents from the same distribution of responses as the total numbers indicate, in which case the mean ridits for the topics would not have been significantly different from each other. The Kruskal-Wallis test statistic, W, is based on the weighted squares of the deviations of the mean ridits from 0.5, and it is distributed (asymptotically) as χ^2 with degrees of freedom equal to one less than the number of rows (in this case $27 = 28 - 1$). The value of W calculated for this table is 193.4, with 27 degrees of freedom, a very significant result.

Thus not all topics were graded equally by the respondents. The topics have been ranked in sequence by their mean ridit and are shown again in Table 13.3 in mean ridit sequence with the highest at the top. For each topic the numerical average of the scores (1 to 6) was also calculated, and these are also shown in Table 13.3. The rankings using the two measures are similar, but not identical. Most of the differences in ranks occur when the mean ridits for the topics and the average scores for the topics are both close together. The standard deviations of the scores are also given. These give an indication of the 'scatter' of the respondents gradings.

Table 13.3

First population: mean ridit, average score and standard deviation of score for each topic which might give problems.

Q1 seq	O	Topic	Mean ridit	Average score	Standard deviation
1	1	Lethargy	0.70	3.00	1.29
2	10	Back pain	0.65	2.76	1.33
3	22	Restricts physical activity	0.64	2.76	1.43
4	2	Headache	0.63	2.65	1.33
5	7	Sleepiness	0.61	2.61	1.40
6	28	Family/genetic disorder	0.60	2.67	1.58
7	9	Moodiness	0.58	2.46	1.37
8	6	Lack of concentration	0.55	2.24	1.18
9	5	Nausea	0.52	2.08	1.07
10	4	Itchiness	0.51	2.10	1.20
11	3	Abdominal pain	0.51	2.06	1.11
12	25	Difficult to make plans	0.50	2.17	1.36
13	24	Tension in family	0.49	2.06	1.22
14	23	Puts strain on marriage	0.49	2.10	1.33
15	27	Difficulty with opposite sex	0.47	2.01	1.30
16	20	Loss of income	0.46	2.03	1.37
17	8	Sickness	0.46	1.79	0.79
18	13	Restriction on eating	0.44	1.77	0.90
19	19	Loss of job	0.44	1.97	1.40
20	21	Reduction in standard of living	0.44	1.93	1.32
21	15	Feeling different	0.44	1.73	0.81
22	12	Dependence on hospital	0.43	1.77	1.03
23	14	Restriction on drinking	0.42	1.70	0.87
24	17	Unable to continue job	0.42	1.86	1.29
25	11	Other physical problems	0.41	1.87	1.34
26	18	Remain breadwinner	0.41	1.83	1.31
27	26	Difficult to keep friends	0.41	1.60	0.68
28	16	Difficulty at work	0.36	1.53	0.92

Note: column Q1 seq gives the sequence in this table; column O gives the original topic number as in Table 13.1.

The difference in level of importance for any two topics can be tested by using the Kruskal-Wallis test for the pair of rows, as described by Agresti (1984 pp183-184). For two rows this test is a discrete version of the Wilcoxon-Mann-Whitney test, allowing for tied ranks. Instead of using the overall ridits which have already been calculated, each pair of rows is treated in isolation and pooled ridits are calculated using the numbers in each grade for the two rows combined.

Mean ridits are calculated for each of the two rows, and these necessarily sum to unity. The difference of either mean ridit from 0.5 is then compared with the standard deviation of this difference, to give a test statistic, z, which has (asymptotically) a unit normal distribution.

Since there is a large number of different pairwise comparisons, Agresti suggests that it is appropriate to choose a significance level corresponding to p/d where p is the normally desired significance level and d is the number of comparisons. In this case there are 378 (= 28 × 27 / 2) different pairwise comparisons. A normal significance level of 5% therefore corresponds to one of 0.013% (= 5%/378), or to a normally distributed z of about 3.1. A 1% significance level corresponds to one of 0.0026% or a z of about 3.8.

The value of z for the difference between the highest and the lowest mean ridits (topics 1 and 16 in the original list) is 6.9, which is very significant. Using a test value of z of 3.8 it is observed that topic 1 (Lethargy), ranked 1st, is not significantly different from any topic down to and including topic 6 (Lack of concentration) ranked 8th; topic 16 (Difficulty at work), ranked 28th, is not significantly different from any topic up to and including topic 4 (Itchiness) ranked 10th; and the middle pair, topics 23 (Puts strain on marriage) and 27 (Difficulty with opposite sex), ranked 14th and 15th respectively, are not significantly different from any other topic except number 1. The extreme topics are

therefore ranked differently by respondents, but many in the middle are ranked at about the same level.

In order to compare the 'concordance' of two topics, i.e. the extent to which respondents give similarly ranked grades of importance to the two topics (not necessarily at the same overall level), the *gamma* measure of Goodman and Kruskal (1954) was used, following the method described by Agresti (1984 p160 for the calculation and p180 for the significance test). The *gamma* measure is defined in terms of C, the number of concordant pairs, and D, the number of discordant pairs, taking each pair of respondents in the sample and treating them as concordant if one respondent gives higher grades on both topics than the other, discordant if the ranking is reversed, and not counting the pair if the grades they allocate to either topic are the same. Then:

$$gamma = (C - D) / (C + D).$$

For large samples the difference $(C - D)$ is normally distributed, and the formula for the variance is given by Agresti, quoting Kendall (1970).

The concordance for each pair of topics was calculated, and the value of z, which in this case represents the value of the difference $(C - D)$ divided by its standard deviation. A significance level for z of 3.8 was considered interesting, and this corresponded in general with a value of *gamma* of about 0.5. A high level of *gamma* represents close concordance between the gradings given by the respondents. If identical grades had been given, the value of *gamma* would be 1.0.

The relationship between topics with a high level of concordance can be mapped in a diagram, as described for example by Gordon (1981). Figure 13.1 shows such a diagram. Each topic is represented by a square box, in which is shown the number of the topic as listed in Table 13.1. The outline of the box indicates the mean ridit for the topic, those with higher mean ridits having more lines round the box, and those with the lowest

mean ridits having dotted lines round the box. The boxes representing pairs of topics that have a high concordance are joined by lines, and the value of *gamma*, multiplied by 100, is shown alongside the line. All concordances with a value of *gamma* at least as great as 0.5 ($100gamma \geq 50$) are shown, and the strength of the concordance is indicated by the heaviness of the line. If a topic, or group of topics, is not sufficiently concordant with any other, so that it would remain detached from the other topics, then a dotted line is drawn indicating the highest available value of *gamma*.

It can be seen that the six topics relating to job, income and ability to remain a breadwinner are all closely concordant with each other, and are detached from the other topics except for a medium concordance of 0.44 with topic 7 (Sleepiness). Partly this is because respondents divided into those still at work, for whom these topics were important, with varying degrees, and those who were not in work and not likely to be, for whom these topics were not applicable.

The topics in the top left part of the diagram, Moodiness, Sleepiness, Lethargy, Headache, Back pain and Restricts physical activity, are all physical problems that tend to occur in the earlier stages of APKD (but not restricted to the earlier stage). Below them is a group of problems that are mainly concerned with the social implications of chronic illness. To the bottom right is a group of problems that are concerned with physical activity (note that the reference to Drinking means problems with restricting fluid intake, not alcohol), and also physical symptoms, Itchiness, Sickness, Nausea, and Abdominal pain, that tend to occur in the later stages of APKD. The diagram thus reveals certain logical connections between topics.

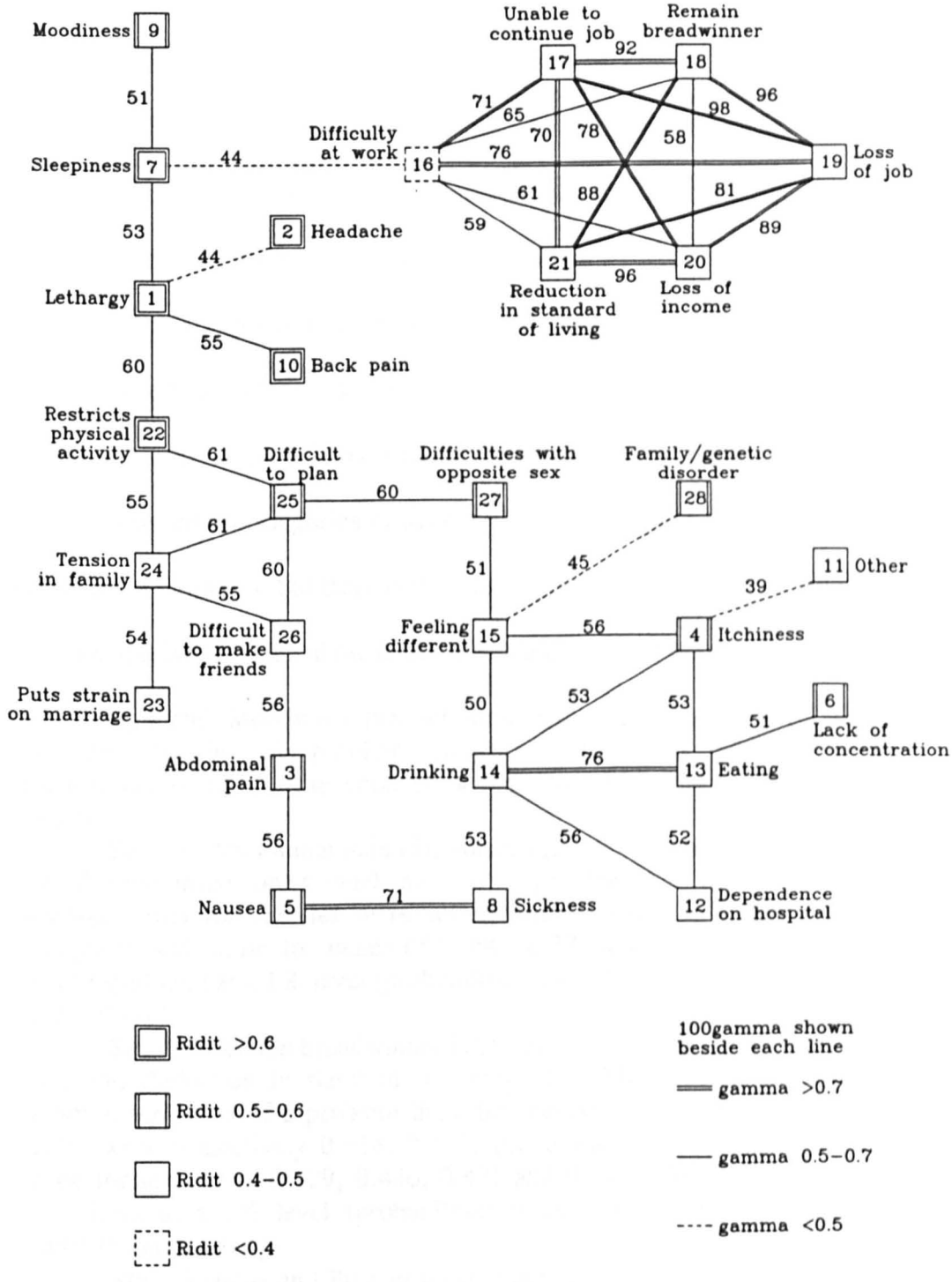

Figure 13.1. Relationships between problems of APKD.

13.2 EFFECT OF EXPLANATORY VARIABLES

The effect of different explanatory variables on the gradings given to the topics can also be compared. Each topic was assessed first in relation to each of 10 possible explanatory variables (sex, age, marital status, number of children, education level, occupation, housing, religious affiliation, severity of disease, family history), using a Kruskal-Wallis test. This gives 280 comparisons. Using a 2% probability level, one would expect about 6 such comparisons to show apparent significance, even if the grades had been allocated wholly at random. There were in fact 11 comparisons significant at a 2% level, of which 8 were at a 1% level (denoted * below). There is thus some evidence of differences in how certain categories of patient view the problems of APKD, as indicated by the explanatory variables, but there is still considerable homogeneity in the population.

The comparisons which show a significance at a 2% level are noted below.

Age and Moodiness (9): all those over age 44 had lower than average ridits for this problem, generally reducing as they got older (probability 0.0051*); the younger patients saw Moodiness as a greater problem.

Sex and Abdominal pain (3), Nausea (5) and Sickness (8): Females found these three topics much more of a problem than did males. The average ridits for females were respectively 0.567, 0.579 and 0.598, compared with those for males of 0.390, 0.372 and 0.340. All of these were significant at a 1% level (probabilities respectively 0.0075*, 0.0021* and 0.0001*).

Sex and Remain breadwinner (18), Loss of job (19), Loss of income (20) and Reduction in standard of living (21): Males found these four topics much more of a problem than did females. The average ridits for males were respectively 0.614, 0.617, 0.626 and 0.595, compared with those for females of 0.429, 0.426, 0.421 and 0.440. Three of these were significant at a 1% level (probabilities respectively 0.0034*, 0.0029*, 0.0017* and 0.0164).

Marital status and Puts strain on marriage (23): it is not surprising that those who were single found this much less of a problem (average ridit 0.294) than did those who were married (a.r. 0.573) (probability 0.0007*).

Number of children and Puts strain on marriage (23): it is also not surprising that those who had no children, many of whom were single,

found this much less of a problem (average ridit 0.355) than did those who had children (probability 0.0149).

Occupation and Loss of income (20): those who were managers, skilled manual, semiskilled manual or agricultural workers had mean ridits all above 0.6, (probability 0.0164). The significance is not very strong, but possibly those who were or had been in these sort of jobs had greater fear of redundancy or poorer ill-health pension provision than those in professional or clerical jobs who thought this less of a problem.

Comparisons were also made of the mean ridits for all topics combined within each category of the chosen explanatory variables. There were certain interesting tendencies, but none that was significant at a 5% probability level. Each explanatory variable is considered below.

Sex: there was a negligible difference between males and females.

Age: those 65 and over had a low average ridit (0.335); those 35-54 had above average ones.

Marital status: the single (a.r. 0.520) were slightly higher than the married (a.r. 0.496).

Number of children: negligible differences.

Educational level: those with the highest education level had the lowest average ridit (0.435); the others were much the same.

Occupation: professionals (a.r. 0.327) and farmers (a.r. 0.371) had lower figures than others.

Housing: tenants (a.r. 0.517) had slightly higher figures than owner-occupiers (a.r. 0.473).

Church: catholics (a.r. 0.537) were above average; those with no church (a.r. 0.472) were below.

Severity of disease: those with higher severity grades had higher average ridits; for grades 0 to 3 they were 0.445, 0.486, 0.506 and 0.513 respectively.

Family history: those with higher family history grades had generally higher average ridits; for grades 0 to 3 they were 0.449, 0.487, 0.511 and 0.507 respectively.

It should be repeated, however, that none of these differences was significant even at a 5% probability level.

It is perhaps surprising that although those with a higher grade of severity of disease had rather higher mean ridits in respect of some topics, and also taking all topics into account, none of the differences for individual topics, nor for all topics, was significant. The same is true for those with different grades of family history.

Each topic was then assessed in relation to each of the 11 independent scores described in Chapters 10, 11, 12 and 14, namely EGCS1, EGCS2, KDS1 to KDS3, KIS1 to KIS4, ATCS and OGCS, thus omitting the four scores formed as totals. The connections between the problems and these scores were compared by using ordinary (Pearson product-moment) correlation coefficients (as an alternative to the *gamma* measure) and measuring (two-sided) significance by the t-statistic, calculated as the correlation coefficient divided by $\sqrt{(n-2)}$, where n is the number of observations (respondents). Counting all the 11 independent scores and the 28 topics, there are 308 comparisons. Using a 2% probability level ($|t| \geq 2.4$), one would expect again about 6 such comparisons to show apparent significance. There were in fact 6 comparisons significant at a 2% level, of which only one was at a 1% level ($|t| \geq 2.7$, denoted * below). There is thus also some evidence of dependence of how some patients view the problems of APKD on the scores, but again there is still considerable homogeneity in the population.

The comparisons which show a significance at a 2% level are noted below.

Environment of genetic counselling (EGCS1) and Lethargy (1): correlation coefficient (*c.c.*) = −0.33, $t = -2.69$; there was thus a negative correlation between these factors, those with a better experience of genetic counselling finding Lethargy less of a problem.

Knowledge of disease (KDS1) and Back pain (10): *c.c.* = −0.37, $t = -3.15$*; those who knew more about the treatment for APKD in questionnaire 1 found Back pain less of a problem.

Knowledge of disease (KDS1) and Tension in family (24): *c.c.* = 0.32, $t = 2.59$; those who knew more about the treatment for APKD in questionnaire 1 found Tension in family more of a problem.

Knowledge of symptoms (KDS2) and Moodiness (9): *c.c.* = 0.37, $t = 2.52$; those who know more about the symptoms of APKD found Moodiness more of a problem.

Knowledge of inheritance (KIS4) and Headache (2): *c.c.* = 0.35, $t = 2.43$; those who know more about the inheritance of APKD in Section 1 of questionnaire 3 found Headache more of a problem.

Attitude to having fewer children (ATCS) and Itchiness (4): *c.c.* = 0.31, $t = 2.51$; those who would favoured considering fewer children found Itchiness more of a problem.

It must be said that these correlations look as if they were the result of chance; they do not have any great rationale for their existence, and to rationalise them might look rather like 'data-mining' after the event.

13.3 REPEAT IN THIRD QUESTIONNAIRE

In the third questionnaire the same question was asked with the same list of topics. Respondents were asked to complete the questionnaire themselves. Two respondents failed to do so. The responses of the 45 respondents who did are shown in Table 13.4.

Table 13.4

Third population: numbers of patients who graded each topic in terms of how severe a problem it was.

	Grade	1	2	3	4	5	6
O	Topic	Not applicable	Not important	Slight	Quite	Very	Extremely
1	Lethargy	8	2	4	10	9	12
2	Headache	10	15	7	6	4	3
3	Abdominal pain	12	12	6	5	6	4
4	Itchiness	14	12	63	3	5	5
5	Nausea	14	9	5	8	8	1
6	Lack of concentration	13	10	6	7	6	3
7	Sleepiness	11	8	6	9	7	4
8	Sickness	16	17	2	4	3	3
9	Moodiness	11	9	9	6	5	5
10	Back pain	13	1	10	6	8	7
11	Other physical problems	29	4	4	-	4	4
12	Dependence on hospital	12	16	6	4	4	3
13	Restriction on eating	26	12	-	2	2	3
14	Restriction on drinking	26	12	1	2	1	3
15	Feeling different	20	12	1	8	2	2
16	Difficulty at work	30	9	2	2	1	1
17	Unable to continue job	28	6	1	6	2	2
18	Remain breadwinner	28	6	1	5	2	3
19	Loss of job	28	6	1	6	2	2
20	Loss of income	26	6	1	6	3	3
21	Reduction in standard of living	26	6	1	7	1	4
22	Restricts physical activity	9	9	8	8	5	6
23	Puts strain on marriage	22	14	6	-	-	3
24	Tension in family	21	15	2	3	1	3
25	Difficult to make plans	20	12	7	1	2	3
26	Difficult to keep friends	26	19	-	-	-	-
27	Difficulty with opposite sex	21	17	6	-	-	1
28	Family/genetic disorder	6	13	8	4	6	8

The totals of the numbers in each grade from Table 13.4 for all topics were calculated and are shown in Table 13.5. There were 1,260 answers in total. The ridits were calculated as described above.

Table 13.5

Third population: total numbers and calculated ridits.

Grade	1	2	3	4	5	6	Total
Numbers	526	289	117	128	99	101	1,260
Ridits	0.209	0.532	0.693	0.790	0.881	0.960	

The Kruskal-Wallis test was again used to see whether the mean ridits for the topics were significantly different from each other. The value of the test statistic, W, for this table was 177.96, which compared with χ^2 with 27 degrees of freedom, is an extremely significant result.

Again not all topics were graded equally by the respondents. The topics have again been ranked in sequence by their mean ridit and are shown in Table 13.6 in mean ridit (Q3 m.r.) sequence with the highest at the top. Also shown are the averages of the scores in questionnaire 3 (Q3 a.s.), the standard deviations of the scores (Q3 s.d.), and the mean ridit (Q1 m.r.) and sequence (Q1 seq) for the responses in questionnaire 1.

The sequence in this questionnaire is not the same as in questionnaire 1, though the same group of topics is at the top and the same group at the bottom. Since many of the topics were ranked close together in both questionnaires the shuffling is in general of no significance. However, it is worth noting that Dependence on hospital has moved up from 22nd to 12th, and Feeling different has moved up from 21st to 15th. It is possible that the respondents had progressed further in their illness since the first questionnaire, were in fact more dependent on the hospital, and did feel more different by this time.

Table 13.6.

Third population: mean ridit, average score and standard deviation of score for each topic which might give problems.

Q3 seq	O	Topic	Q3 m.r.	Q3 a.s.	Q3 s.d.	Q1 m.r.	Q1 seq
1	1	Lethargy	0.73	4.02	1.77	0.70	1
2	28	Family/genetic disorder	0.66	3.33	1.71	0.60	6
3	22	Restricts physical activity	0.64	3.20	1.67	0.64	3
4	10	Back pain	0.64	3.36	1.82	0.65	2
5	7	Sleepiness	0.62	3.11	1.66	0.61	5
6	9	Moodiness	0.61	3.00	1.66	0.58	7
7	3	Abdominal pain	0.58	2.84	1.66	0.51	11
8	2	Headache	0.58	2.73	1.50	0.63	4
9	6	Lack of concentration	0.58	2.82	1.62	0.55	8
10	5	Nausea	0.57	2.78	1.58	0.52	9
11	4	Itchiness	0.56	2.73	1.72	0.51	10
12	12	Dependence on hospital	0.55	2.58	1.51	0.43	22
13	8	Sickness	0.50	2.33	1.52	0.46	17
14	15	Feeling different	0.47	2.24	1.49	0.44	21
15	25	Difficult to make plans	0.46	2.16	1.46	0.50	12
16	24	Tension in family	0.44	2.04	1.43	0.49	13
17	20	Loss of income	0.44	2.18	1.66	0.46	16
18	21	Reduction in standard of living	0.44	2.18	1.68	0.44	20
19	23	Puts strain on marriage	0.42	1.91	1.30	0.49	14
20	27	Difficulty with opposite sex	0.41	1.76	0.95	0.47	15
21	11	Other physical problems	0.41	2.07	1.72	0.41	25
22	18	Remain breadwinner	0.41	2.02	1.60	0.41	26
23	17	Unable to continue job	0.40	1.98	1.51	0.42	24
24	19	Loss of job	0.40	1.98	1.51	0.44	19
25	13	Restriction on eating	0.40	1.91	1.49	0.44	18
26	14	Restriction on drinking	0.40	1.87	1.42	0.42	23
27	16	Difficulty at work	0.35	1.62	1.14	0.36	28
28	26	Difficult to keep friends	0.34	1.42	0.49	0.41	27

Note: column Q3 seq gives the sequence in this table; column Q1 seq gives the sequence in Table 13.3 relating to questionnaire 1; column O gives the original sequence as in Table 13.1.

13.4 COMPARISON OF FIRST AND THIRD QUESTIONNAIRES

The responses of the 45 patients who replied to questionnaire 3 were compared with the responses of the same 45 patients to questionnaire 1. First, the average level of assessment of severity of each problem was compared by an analysis of the mean ridits, where the ridits were calculated using just the two responses from each respondent for the same topic. Secondly, the concordance between the replies of the respondents to each topic on the two occasions was compared using the *gamma* statistic. Table 13.7 lists the topics again, in the same order as in Table 13.3, the sequence according to mean ridit on the first occasion, and shows the difference (diff) between the individual mean ridits on the two occasions (+ for those where the assessment was higher in questionnaire 3, − for those where the assessment was lower in questionnaire 3), the probability (prob) that this difference occurs by chance (using the Kruskal-Wallis test), and the value of *gamma* when the two sets of responses for each topic are compared.

Table 13.7.

First and third populations: comparisons of responses for each topic which may be a problem for those with APKD.

Q1 seq	Q3 seq	Topic	Q1 m.r.	diff	prob	*gamma*
1	1	Lethargy	0.70	+0.163	0.0067	0.52
2	4	Back pain	0.65	+0.077	0.20	0.39
3	3	Restricts physical activity	0.64	+0.063	0.29	0.53
4	8	Headache	0.63	+0.000	0.99	0.58
5	5	Sleepiness	0.61	+0.074	0.22	0.31
6	2	Family/genetic disorder	0.60	+0.090	0.13	0.19
7	6	Moodiness	0.58	+0.064	0.28	0.35
8	9	Lack of concentration	0.55	+0.105	0.076	0.36
9	10	Nausea	0.52	+0.073	0.22	0.25
10	11	Itchiness	0.51	+0.061	0.30	0.37
11	7	Abdominal pain	0.51	+0.115	0.049	0.27
12	15	Difficult to make plans	0.50	+0.020	0.72	0.40
13	16	Tension in family	0.49	−0.035	0.54	0.26
14	19	Puts strain on marriage	0.49	+0.020	0.73	0.69
15	20	Difficulty with opposite sex	0.47	−0.020	0.72	0.11
16	17	Loss of income	0.46	+0.007	0.90	0.70
17	13	Sickness	0.46	+0.054	0.35	0.12
18	25	Restriction on eating	0.44	−0.034	0.54	0.33
19	24	Loss of job	0.44	−0.003	0.95	0.50
20	18	Reduction in standard of living	0.44	+0.008	0.88	0.71
21	14	Feeling different	0.44	+0.054	0.34	0.30
22	12	Dependence on hospital	0.43	+0.179	0.0019	0.40
23	26	Restriction on drinking	0.42	−0.024	0.67	−0.03
24	23	Unable to continue job	0.42	−0.016	0.77	0.74
25	21	Other physical problems	0.41	−0.034	0.53	0.24
26	22	Remain breadwinner	0.41	−0.003	0.96	0.78
27	28	Difficult to keep friends	0.41	−0.068	0.21	0.10
28	27	Difficulty at work	0.36	−0.015	0.78	0.50

Note: column Q1 seq gives the sequence in Table 13.3, relating to questionnaire 1, and column Q3 seq gives the sequence in Table 13.6, relating to questionnaire 3.

The top 12 topics, those which were the more important ones in questionnaire 1 and many of which relate to physical problems, have gone up in importance since the first interview, and the bottom six, the less important, have gone down. Only Lethargy and Dependence on hospital are significantly up, and none is significantly down. Overall, the topics have become more problematic for the respondents.

The concordances between the responses of individuals are surprisingly low. One is negative (Restriction on drinking). There is quite strong agreement only among those topics relating to employment and income. Although the individual respondents may have changed their views, the collective response is remarkably uniform.

13.5 Effect of explanatory variables in third questionnaire

As for questionnaire 1, comparisons were made between the average ridits for each of the categories in the 11 explanatory variables considered. Of the 280 comparisons only 5 showed differences significant at a 2% probability level, which is fewer than might reasonably have been expected, and 3 of these (denoted * below) were significant at a 1% probability level. The five were:

Sex and Lethargy (1): males (average ridit 0.668) found lethargy to be more of a problem than did females (a.r. 0.432) (probability 0.0117).

Sex and Remain breadwinner (18): males (a.r. 0.664) found this more of a problem than did females (a.r. 0.433) (probability 0.0057*).

Sex and Restricts physical activity (22): males (a.r. 0.710) found this much more of a problem than did females (a.r. 0.415) (probability 0.0018*).

Severity of disease and Lethargy (1): those with more severe grades of disease found this more of a problem than did those with lower grades (a.r. for grades 1, 2 and 3: 0.303, 0.530, 0.602 respectively) (probability 0.0155).

Severity of disease and Restricts physical activity (22): the same is true for this topic as for the last; those with more severe grades of disease found this more of a problem than did those with lower grades (a.r. for grades 1, 2 and 3: 0.248, 0.585, 0.596 respectively) (probability 0.0019*).

The connections that were found for the first population had weakened or even been reversed in this population. This might suggest that they may really have been the result of chance, but it would also be the case that in a smaller total population they are less likely to show up as significant.

Each topic was also assessed in relation to each of the scores as described in relation to questionnaire 1, the connections being compared as before by using correlation coefficients. Of the 308 comparisons 8 were significant at a (two-sided) 2% level ($|t| \geq 2.4$), of which only one was at a 1% level ($|t| \geq 2.7$, denoted * below). There is again some evidence of dependence of how some patients view the problems of APKD on the scores, but there is still considerable homogeneity in the population.

The comparisons which show a significance at a 2% level are noted below.

Environment of genetic counselling (EGCS2) and Puts strain on marriage (23): correlation coefficient *c.c.* = 0.38, $t = 2.57$; those who received more content in their genetic counselling found strain on marriage more of a problem.

Knowledge of disease (KDS1) and Puts strain on marriage (23): *c.c.* = 0.37, $t = 2.46$.

Knowledge of disease (KDS1) and Difficult to make plans (25): *c.c.* = 0.37, $t = 2.52$.

Attitude to having fewer children (ATCS) was associated positively with five problems:

Restriction on eating (13): *c.c.* = 0.37, $t = 2.48$;
Restriction on drinking (14): *c.c.* = 0.37, $t = 2.46$;
Restricts physical activity (22): *c.c.* = 0.37, $t = 2.47$;
Puts strain on marriage (23): *c.c.* = 0.39, $t = 2.62$;
Tension in family (24): *c.c.* = 0.42, $t = 2.78$*;

this cluster suggests that, at least among those in this population, those who favoured considering fewer children found some of the restrictions of APKD irksome, found that it caused difficulties in the family, and were therefore more in favour of not having children, who might seem more of a burden to them.

None of these relationships showed significant correlations for the responses in the first questionnaire, and none of those found significant for the first questionnaire remained significant here. This supports the idea that most of these correlations are the result of

chance. Only the last cluster, those in relation to the attitudes to having children, seems to have a good rationale.

13.6 COMPARISON OF INDIVIDUAL RESPONSES IN FIRST AND THIRD QUESTIONNAIRES

The responses of each individual to the 28 topics in the first and the third questionnaires were compared in order to see how consistent was their ranking of the problems. This required constructing a 6 by 6 table for each respondent, showing how their 28 pairs of responses fell into grades. The concordances between the responses in the first and third questionnaires were then calculated, using the *gamma* measure described above.

The values of *gamma* theoretically range from −1.0 to 1.0, and the actual range observed was indeed from −1.0 (1 case) to +1.0 (3 cases). The distribution of values of *gamma* for the third population is shown in Table 13.8. There is a considerable number of cases with quite high concordance (say $gamma \geq 0.6$), but a fair number with low concordance.

Table 13.8

Third population: values of *gamma* for each individual, subdivided by sex and marital status.

	Single females	Married females	Males	Total
Not calculated	-	-	2	2
−1.0 to −0.0	-	1	2	3
+0.0 to +0.2	1	1	-	2
+0.2 to +0.4	3	1	2	6
+0.4 to +0.6	-	4	1	5
+0.6 to +0.8	4	6	6	16
+0.8 to +1.0	4	7	2	13
Total	12	20	15	47

Correlation coefficients were calculated for the average ridits for each individual in the two questionnaires, the *gamma* measure of concordance described above, all the constructed scores described in Chapters 10, 11, 12 and 14, and also severity of disease and family history. The values of the coefficients ranged from −0.23 to +0.24, not remotely significant, except for the following:

> the ridits for the first questionnaire and the third questionnaire, correlation coefficient 0.52, easily significant at a 1% level;
>
> the ridit for the third questionnaire and severity of disease, *c.c* = 0.36, significant at a (two-sided) 2% level;
>
> the concordance measure, *gamma*, and attitude to having no more children (ATCS), *c.c.* = −0.33, just significant at a (two-sided) 2% level; those with a high score for attitude to having no more children have a low concordance between their answers to these parts of the questionnaires.

The first of these is not surprising; those with a relatively high assessment of their problems at the time of the first interview might well also assess their problems highly by the time of the third interview.

The second is also not surprising, though it did not appear as significant by the Kruskal-Wallis test; those more severely affected have more problems overall,

The third is not readily explained, and may just be a random result; on the other hand, those with a strong attitude to having no more children were seen above to have problems of an irksome kind, and they may have found it difficult to be consistent in their responses to the questions, or may have found them irritating, and so answered them without careful consideration.

13.7 DISCUSSION: ANALYSIS OF PROBLEMS

The patient's perception of the burden of an illness is often given as an explanation for patient's reproductive decisions following genetic counselling, as well as by researchers investigating the demand for prenatal diagnosis (Chapter 2).

However, in these studies there is very little discussion about what are the factors that are used in the development of the patient's concept of the burden of APKD. In this study respondents were asked twice, in questionnaires 1 and 3, to rate the importance of factors that could influence their perception of the burden of the illness.

There are two particular results of this analysis that deserve comment. The first concerns the groupings of the problems and the second concerns the position of certain individual problems.

The four groupings concerned physical symptoms associated with APKD, restrictions on activities, questions related to job and income and questions relating to personal relationships.

It is notable that there is very considerable agreement between the two interviews in the emphasis that is placed on the different items and on the different groups of topics.

Patients placed the greatest importance on what could be described as the physical symptoms associated with APKD. The next group of questions seen as most problematic were those relating to relationships, with those relating to restrictions on activities and jobs and income coming third and fourth. There were, however, exceptions: Restricts physical activity was rated as a serious problem, as was the fact that APKD is a Family/genetic disorder.

It is interesting that respondents perceive the physical problems associated with APKD, rather than the genetic nature of the disease, as the most problematic. It is arguable that, as long as the treatments for APKD continue to improve and remain available, the burden of the disease will not be perceived as serious.

Importance is placed by respondents on the social relationships and these become more problematic by the time of the third interview when patients had become more ill.

The psychological stress caused by chronic renal failure, described by Long (1989), is often ignored by medical and nursing staff in renal units.

Patients may feel that they are no longer sexually attractive, perhaps because of the changes in physical appearance due to uraemia. In this study some patients said that they did not feel 'a whole person'.

The importance placed on income-related questions received less importance than might have been expected. By the time of the third questionnaire some patients may have been too ill to be any more concerned about being able to remain in employment.

The item Lethargy was seen as the most important problem in both interviews. This is interesting as lethargy is not a symptom of APKD that is normally described in the medical textbooks. It was included because of the frequency it was mentioned as a problem by patients in a small pilot study carried out before the main investigation. During the course of the research several patients made another observation about lethargy in relation to their as yet untested offspring. These patients commented that a particular offspring was 'always tired and lethargic' and that that child 'would possibly be the one with APKD'.

In questionnaire 3 the importance of the physical problems became greater. This is possibly because the patients were then more ill. For example in this interview males found Lethargy more problematic as did those more severely affected. It is difficult to believe that female respondents did not also experience lethargy. Culturally women may be more accepting of tiredness as a way of life. Two items, Restrictions on physical activities and the Family/genetic nature of the disorder, became more problematic in the third questionnaire. A likely explanation for this is that patients were more ill by the third questionnaire. Furthermore as the study was about genetic counselling, it is possible that

by the time of the third interview there was more awareness of the genetic nature of the illness.

Many of the interactions with explanatory variables appears to be a result of chance. However it is worth commenting on some of the results which were significant at a 1% or 2% level. In the first interview female patients found Abdominal pain, Nausea and Sickness significantly more problematic than did male patients. It is not known whether there would be a physiological or other medical explanation for this finding.

Male patients were more concerned than females with Remaining a breadwinner, Loss of job, Loss of income and Reduction in standard of living. This finding was also significant at the 1% level in the third interview. This makes sense particularly in a part of the world, the west of Scotland, where the man has traditionally been the major breadwinner. One of the major problems for patients with another chronic illness, haemophilia, is to obtain a job and then hold on to it (Markova et al 1977), and this finding was confirmed for APKD by Wilkie et al (1985). These authors show that the ability of the patients with APKD to remain in employment is affected by their illness and they suggest that "patients should be encouraged to seek the appropriate training for non-manual employment" (p80). It is important that counsellors are aware of the considerable concerns that male patients in particular may have about their ability to obtain work and remain the breadwinner and the psychological distress and loss of identity that may be suffered when patients lose their job.

In the third interview male patients perceived restriction on their physical activity significantly more problematic than female patients. Again this may be relevant information for counsellors to give to male patients. The study did not ask what specific activities the patient felt restricted in doing although one moderately severely affected patient explained that 'he did not even have the energy to go to a football match'. This

comments supports the finding also from the third interview that those patients more severely affected found Restriction on physical activity more problematic than those more mildly affected.

It is disappointing that so few of the specific problems of APKD were associated with the possible explanatory variables or with the composite scores at a significant level. There were few comparisons significant at a 1% level and only a few more at a 2% level. These are described in Sections 13.2 and 13.5. It is worth commenting in particular on the score concerning the attitude to having fewer children. Patients who would consider favourably restricting the number of children had found the restrictions concerning diet, fluid intake and physical activity caused by APKD very problematic, as well as finding that APKD puts a strain on the marriage and causes tension in the family.

Although so few of the possible associations were 'significant', and many of these may have been the results of chance, they are nevertheless indicative of possible associations that would be worth investigating in other or larger studies.

CHAPTER 14: ANALYSIS: RESULTS OF GENETIC COUNSELLING

14.1 Introduction

In this chapter the results of the following topics of interest in genetic counselling are discussed; the detailed results are presented in Appendix G.

attitudes to having children;

attitudes to screening and testing at risk relatives;

attitudes to testing children;

outcomes of genetic counselling;

who should do genetic counselling.

14.2 Respondents' attitudes to having children

14.2.1 Numbers of children and influence of APKD thereon

Respondents were asked how many children they had had, and then how many children would like or would have liked to have had; the two answers were compared.

There were 20 respondents who had two children, 14 who had more than two, and 31 who had fewer than two. Nevertheless 36 respondents would like to have two children; these included 10 single females and 13 married females.

Only one person would have liked fewer children than she (a married woman) already had. 29 respondents (out of 65 or 44%) were happy with the number of children they had, and 33 (out of 65 or 51%) would have liked more. In a few cases it was not appropriate to ask the respondent this question.

There is no evidence that those with a higher grade of severity of disease either have had fewer children, or would like to have fewer children, than those with a lower severity.

Among the 14 respondents with more than two children, all but one had obtained no school qualifications (education level 1).

Respondents were asked whether their knowledge of APKD had affected their views about how many children they would like. 42 out of the 65 (65%) respondents said that knowledge of APKD had not affected their decision about the number of children they would like, as opposed to 23 (35%) who said that it had. 17 out of the 40 female respondents (42%) said that the decision about the number of children they would like had been affected by the knowledge of APKD, as opposed to only 6 out of 24 (25%) among the men. However the contrast, although suggestive, is not statistically significant.

Respondents were asked to describe the effect that their knowledge of APKD had had on the number of children they had had or would have liked. Among the 23 who said that it had had an effect, 8 had been sterilised (including the wife of one affected male) or had had a vasectomy, 3 had had fewer children, 2 had altered the spacing of their children, 1 had decided not to have any children, and another not to marry; 7 knew that knowledge of APKD would affect their decisions, 4 of these not yet having made any plans about children and 3 not having decided what to do.

14.2.2 Attitudes to voluntary childlessness, sterilisation, vasectomy and A.I.D.

Respondents were asked whether they would be prepared to consider various forms of action to limit their families: 'having no children', sterilisation or vasectomy (of themselves or their partner as appropriate), or A. I. D. (strictly appropriate only if the male partner is affected).

The majority of respondents (40 out of 65 or 61%, comprising 29 females and 11 males) would not consider or would not have considered having no children. Of the 29 females in this category 25 were aged under 35. However 18 respondents (9 females and

9 males), would consider having no children and 2 respondents would possibly consider such a possibility. Six of the females and 4 of the males who said that they would consider having no children were under 35. There was a tendency for the more severely affected patients to say that they would consider having no children.

27 respondents (22 females and 5 males) said that they would consider sterilisation. 10 of the female patients were aged less than 35. In addition 2 female patients said that they would consider sterilisation and 1 single female patient aged 19 said that she would consider the possibility of sterilisation after she had had a child. 22 patients (14 females and 8 males) would not consider sterilisation. 9 of the females and none of the males were under the age of 35. The numbers of patients who would consider sterilisation and vasectomy increased according to the severity of their disease.

19 patients (8 females and 11 males), would consider vasectomy, 2 patients (1 female and 1 male) would think about it and 1 male patient was unsure. 32 patients (21 female and 11 males) would not consider vasectomy. The 7 female patients who would consider vasectomy for their partner were in the age range 25-44 while 13 of the 21 women who would not consider vasectomy for their partner were under the age of 35.

The majority of patients (41 out of 65 or 63%) would not consider A. I. D. Only three patients were in favour, with an additional 6 patients unsure. One female patient was in favour of A. I. D. and one was unsure. Otherwise none of the female patients would consider the use of A. I. D.

In each case there was a clear tendency for the more severely affected patients to say that they would consider limiting their family in the way suggested, though in no single case is the result statistically significant.

14.2.3 Score for attitude to having no more children

A composite score, denoted ATCS, was formed to represent each respondent's attitude to having no more children, constructed as described in Appendix G. A high score represented a favourable attitude to not having more children. The maximum score was 8 and the mean was 2.3, with 25 respondents getting 0 points.

Analysis of this score showed that no explanatory variable had any significant bearing on this score representing the respondent's attitude to having no children. Nor had any of the previously constructed scores, representing experience of genetic counselling and knowledge of various aspects of APKD.

14.3 ATTITUDE TO SCREENING AND TESTING AT RISK RELATIVES

14.3.1 Attitudes to screening at risk

Respondents were asked a number of questions that related to their attitude to the screening and testing of those at risk of APKD. The first question was whether those at risk should be told of their situation. The great majority (59 out of 65 or 91%) thought that those at risk should be told. Only one (a male) thought that they should not, though 5 respondents (4 males and one female) were unsure.

Respondents were asked why they thought that those at risk should be told of their risk. There was a variety of answers given being, the most frequent being 'so that they can be screened' (24 respondents or 37%), and 'so that they can have choices' (17 or 26%), and also including 'so that they can plan their lives' (6), 'so that they are prepared' (4), 'they have to know' (3), 'because it is sensible' (2), etc.

14.3.2 Attitudes to testing at risk

Respondents were asked whether they thought that those at risk should be tested for APKD. Almost all (62 out of 65 or 95%) thought that they should be tested. One male and one married female were unsure and one married female felt strongly that testing was the choice of the individual concerned and she could herself give an opinion.

The reasons that respondents gave to explain why they thought that those at risk should be tested included 'so that they know' (18 replies), 'so that they can plan their lives' (13), 'so that they can be treated' (8), and 'so that they are aware' (6).

14.4 ATTITUDES TO TESTING CHILDREN

14.4.1 Testing children at risk

Most respondents were asked whether they thought that their children should be tested for APKD; 10 respondents were not asked because they were either younger or older and the question was inappropriate. 51 out of the 55 asked (93%) thought that they should be, although for 8 of these the question was inapplicable currently, mainly because they were single. The other 4 had views that reflected uncertainty rather than opposition.

The most frequent reasons given by respondents for having their own children tested were so that the child, if found to be affected, could be looked after (12 respondents or 18%), and so that the child(ren) could plan their lives (10 or 15%). Five respondents gave as the reason 'so that the parent would know and could therefore initiate treatment'.

Respondents were asked whether or not to have their child tested was a difficult decision. 11 respondents (17%) said that it was, but 35 (54%) said that it was not. The more severely affected were rather more likely to respond that this was a difficult decision.

14.4.2 Informing children at risk

Respondents were asked at what age they thought that children of an affected parent should be told of their risk. The majority of respondents (36 out of 65 or 55%) were in favour of children being told between the ages of 16 and 18, with these two ages being particularly popular.

Most respondents (54 out of 65 or 83%) thought that the at risk child should be tested between the ages of 16 and 20; the ages of 16 and 18 were the most favoured. One male patient thought that they should be tested prenatally, and another male patient thought that they should be tested at birth.

14.4.3 Dependency on other factors

It would have been interesting to investigate whether the attitudes of respondents to the screening and testing of those at risk and of children differed by any of the possible factors that could have been considered. However, when there is almost complete unanimity in the responses, almost all being in favour of informing, testing and screening, no further analysis is possible.

14.5 OUTCOMES OF GENETIC COUNSELLING

14.5.1 Consequences of genetic counselling

Respondents were asked five questions about whether genetic counselling had helped them in specific ways, whether it had informed them about risk, helped them to decide on their family, informed them about APKD, relieved stress, or informed them about treatment.

A majority of patients (40 out of 65 or 61%) had received information about the risk of inheritance. No other feature of genetic counselling had been noted by more than

25% of respondents. 14 patients had found that genetic counselling had helped them in deciding whether or not to have a family, 9 patients reported having received information about (the symptoms of) APKD, and 5 patients about the treatment available for APKD.

Five patients (all females) reported that the genetic counselling had helped to relieve stress and anxiety; of these 5 who had found that genetic counselling had relieved stress 3 were in severity grade 1 and 2 were in severity grade 2, so none of the most severely affected patients had found that the genetic counselling they received had relieved stress.

In addition to the responses to questions reported in Appendix G, respondents offered the information that genetic counselling had given them information which helped them to consider the number of children they had, whether to get married and whether those at risk should be screened. One male patient reported that he had found his experience of genetic counselling 'very upsetting' and one female patient said that she had 'hesitated' about having a family after she had had genetic counselling.

14.5.2 Score for outcomes of genetic counselling

A composite score, denoted OGCS, was formed from the questions relating to the outcome of genetic counselling, as described in Appendix G. The maximum score was 5 points.

Analysis of this score using the GLIM system showed that, of the possible explanatory variables described in Section 9.13, the only factor with any significance was that combining age and number of children, which was significant only at a 5% probability level. However, when the scores for the experience of genetic counselling, EGCS1 and EGCS2, are introduced as possible factors, each is very significant by itself, but adding the other provides little improvement. The correlation coefficients of OGCS

with these two scores are 0.60 and 0.65 respectively. The higher of the two is that with EGCS2, which therefore gives the better fit. The model then takes the form of a simple linear regression, accounting for 42.5% of the original variance. The parameters are shown in Table 14.1.

Table 14.1

Parameters for score on outcome of genetic counselling (OGCS).

Element	Score
Constant	0.09
Per unit of EGCS1	+0.34

14.5.3 Decisions taken as a result of genetic counselling

Patients were asked whether they had taken decisions as a result of the information they had received in genetic counselling. Out of the 49 patients who had received genetic counselling, only 16 or 33% had taken decisions as a result of genetic counselling information compared with 33 (67%) who had not. Most of those who had taken decisions were married women (13 out of 16), or a majority of the married women counselled (13 out of 22 or 59%). By contrast, only one male (out of 17) and 2 single females (out of 10) had taken decisions. In a 2 by 2 contingency table, setting single females plus males versus married females and 'yes' versus 'no' among those who had taken decisions Fisher's exact test shows that the difference is strongly significant ($p=0.0005$).

Of the 16 patients who had taken decisions following genetic counselling 8 were in severity grade 3 (out of 19 who had received genetic counselling); but 2 out of the 4 unaffected also had taken decisions.

The decisions taken by patients included the following: 8 had opted for sterilisation (including one single female and one male who had had a vasectomy; two had decided to

have no more children; one had decided to have no children; and two had decided to have a smaller family than they otherwise might have done (including the other single female who had taken a decision) (these two were both in the higher education level); one patient had told their child; and one patient had suggested that her child should be screened.

Five of the married women who had been sterilised were in severity grade 3.

14.6 WHO SHOULD GIVE GENETIC COUNSELLING?

14.6.1 Who should give genetic counselling?

Patients were asked what kind (or kinds) of person they would like to see giving genetic counselling. The two most popular were a specialist genetic counsellor (47 out of 65 or 72%) and doctors in the renal unit (44 out of 65 or 68%).

17 out of the 65 thought that the GP should give genetic counselling, with single women being least in favour of the GP's involvement.

Two thought that nurses should, and one that a social worker should. The one patient in favour of a social worker was a married female, who was severely affected and who had had considerable professional help from social workers.

Nurses in a renal unit are highly specialised. They have considerable responsibility in, for example, the running of a haemodialysis unit and in the training of patients for dialysis and are therefore in close contact with the patients and are an obvious source of information for the patients. Nevertheless only two patients thought that the nurse should give genetic counselling.

Respondents were also asked to name any other person or category of person who could give genetic counselling. This question did not yield many suggestions; only 15 out of 65 made a suggestion. One patient suggested a parent or cousin, 4 patients suggested another affected patient, and 10 patients (8 female and 2 male) suggested 'someone like

you', ie like the research worker. 6 of these 10 patients belonged to severity grade 3 and may well have seen the research worker more often than those less severely affected; all 10 patients belonged to the lower educational levels 1 and 2.

Patients were also asked whether they thought that no genetic counselling should be given. Not one patient out of the 65 believed that no genetic counselling should be given.

Respondents were asked about the sort of information that they would like in a genetic counselling service if it were to become available, or about the features that should characterise it. Respondents were unable to offer suggestions about the precise sort of information that they would like in genetic counselling, but comments were offered about the need for information (19 responses), the need for quiet (3) and time (1), the use of a specialist counsellor (2), or someone non-clinical (1) or a good listener (1); 3 patients suggested that the GP should be involved, and one suggested a group discussion.

14.6.2 Who should inform children?

Almost all the patients (63 out of 65 or 97%) thought that the parents should tell their children that they were at risk. One younger female patient thought that the doctor and the parents together should tell the child, and one male was not asked this question.

Respondents were asked how the child should be told. The most frequent response was 'in the normal course of conversation'. This was expressed by one patient as 'as an opportunity arises at home and certainly always by the parents, as they know the child and how to put things over to him'.

14.7 Discussion

In this chapter five topics relating to genetic counselling were analysed. These were: attitudes to having children, attitudes to screening and testing at risk relatives, attitudes to testing children, what was called the outcomes of genetic counselling, which included decisions that patients may have taken as a result of genetic counselling, and finally who should carry out genetic counselling. These five topics are discussed below.

The first comment to make concerns attitudes to having children. It was not unreasonable to assume that among the explanatory variables, sex of patient, severity of illness, family history and religion might have an influence on the patients' attitudes to having children. The GLIM analysis showed that not one of the explanatory variables had any bearing at all on the patients' attitudes to having children. Furthermore it is arguable that the patients' knowledge of APKD could influence their attitudes to having children, on the assumption that the more knowledge that they had about the illness and its wider implications the more likely they would be to restrict the number of children they had. This was one of the principles within paradigm 2 described in Section 2.4. The focus in this paradigm was on prevention. Patients are given information about the illness in the hope that they will then have no or no more children. The GLIM analysis showed that knowledge of the symptoms, treatment and inheritance of APKD had no bearing on the patients' attitudes to having children. Furthermore nor had the experience of genetic counselling any influence on attitudes to having children.

There are comments concerning attitudes to having children although not statistically significant that are worth discussing. The majority of respondents (61%) would not or would not have considered having no children and that includes 25 females under the age of 35 who might still have children or more children. However there were 18 respondents who would consider having no children and of these 10 patients, 6 females

and 4 males were under the age of 35. There was a tendency, but not statistically significant, for those patients more severely affected to say that they would consider having no children. A feature, however, of APKD is that it is an illness of variable age of onset with the result that it is highly likely that patients will have had their children by the time they become more ill.

With regard to the screening and testing of those at risk for APKD, the very great majority of respondents thought that those at risk should be told of their risk and that they should be tested. As there was such consensus in the responses to this question, no further analysis was worth carrying out.

Almost all respondents also thought that their children should be tested, with the majority suggesting that children should be tested between the ages of 16 and 20. Respondents were asked why should children be tested. This was an open ended question and the answers are those offered by the respondents. Only 5 patients gave the reason 'so that they as parents would know'. This was quite surprising, as in discussion with parents during the course of the study it became evident that parents would certainly like to be reassured that their child did not have APKD and so one reason for agreeing to have a child tested would be so that the parent knew.

There were 11 patients who said that it was a difficult decision whether or not to have their child tested. Once again I was surprised that so few patients reported that this was a problem as it had appeared from their comments during the course of the research that this was an area of concern. One male patient reported that this subject had been a source of considerable tension between himself and his wife. His wife had wished that their son be told of his risk of inheriting APKD when he was in primary school. His father, who had APKD, had disagreed. When the patient eventually got round to discussing the illness with his son, by then a student at university, he was surprised to

discover that his son already knew, having sought information from a public library some years previously.

There were rather varied answers to how genetic counselling might have helped patients. A majority of respondents (61%) reported that they had received information about the inheritance of APKD, but only nine respondents reported that they had received information about the symptoms and treatment and yet it was here that patients were really quite well informed (see Chapter 11).

One of the aims of genetic counselling, as described by the Ad Hoc Committee on Human Genetics in 1974 (p23), is to relieve stress and anxiety and yet only five patients had reported that genetic counselling had helped to relieve stress and anxiety for them. None of these patients were the most severely affected although the may have been the patients most concerned.

Approximately one third of the respondents had taken decisions as a result of genetic counselling with most of those who had taken decisions being married women. By contrast only one male and two single females had taken decisions and this was statistically significant ($p=0.0005$). It is possible that genetic counselling was aimed at the married women. Doctors giving the counselling may also have been concerned for the health of female patients should they become pregnant particularly if their renal function was impaired. However APKD affects the sexes equally and it would seem important that genetic counselling is given to both sexes.

The majority of decisions taken as a result of genetic counselling were concerned with control of fertility and reflect an emphasis on prevention which would appear to have been the objective of the genetic counselling given to these patients.

Finally patients were asked which category of person should give genetic counselling. The majority of respondents favoured either a specialist genetic counsellor

or a doctor in the renal unit with less than a third of patients favouring the GP. Before answering this question patients asked whether a specialist genetic counsellor would be like 'the research worker'. Thus the answer to this question and the comment of ten respondents who, in answer to the next question, suggested that someone like the research worker would be appropriate, are examples of the effect of the research on responses to questions.

CHAPTER 15: ANALYSIS: PERCEPTIONS OF THE ELEMENTS IN GENETIC COUNSELLING

15.1 CONTENT OF GENETIC COUNSELLING: SECOND QUESTIONNAIRE

Respondents to questionnaire 2 were asked to identify from a list of 19 topics which of these topics it was important should be included as an element of genetic counselling, and to indicate on a 6 point scale how important they thought they were. The grades on the scale were:

1 Not applicable
2 Not important
3 Slight importance
4 Quite important
5 Very important
6 Extremely important

The topics that were included in the list of elements of genetic counselling were selected following an extensive literature review as well as from previous experience on the Acceptability Study. These topics can be grouped into the following areas: information about risk, information about family planning and voluntary childlessness and information about the symptoms of and treatment for APKD. Information about the risk of inheriting and transmitting a disease is considered by genetic counsellors to be an extremely important aspect of genetic counselling (See chapter 2). It can be argued that unless patients are also told about the advantages and disadvantages of testing those at risk patients may be unable to reach an informed decision. If prevention is seen as an aim of genetic counselling, then information about family planning and the possibility of adoption or fostering could be included in a counselling session. If patients are to understand what are the problems associated with a particular illness they may need to be given information about the symptoms of the illness as well as the treatments that are available.

The responses of patients obtained in the second interview were scored by using ridit analysis as described in Chapter 13 in relation to the perception of problems associated with APKD.

Table 15.1 shows the gradings for each topic for all respondents to questionnaire 2. All respondents replied to all topics, so the total for each row is 65.

Table 15.1

Second population: numbers of patients who graded each topic in terms of how important it was for genetic counselling.

	Grade	1	2	3	4	5	6
O	Topic	Not applicable	Not important	Slight	Quite	Very	Extremely
1	Risk to you	43	-	1	1	16	4
2	Risk to children	2	-	4	12	33	14
3	Advantages of testing	-	-	8	17	34	6
4	Disadvantages of testing	-	1	12	19	28	5
5	How to tell the at risk	-	4	15	26	18	2
6	Screening of sibs, etc	1	15	25	21	2	1
7	Possibility of adoption	4	4	22	26	8	1
8	Possibility of fostering	3	11	25	22	4	-
9	Voluntary childlessness	8	16	14	15	9	3
10	Having no more children	6	9	10	23	15	2
11	Family planning	3	5	14	24	16	3
12	Sterilisation	7	15	13	18	11	1
13	Vasectomy	9	14	14	15	12	1
14	A.I.D.	21	21	13	8	3	-
15	Prevention of APKD	10	16	14	13	9	3
16	Telling boy/girlfriends	5	8	27	14	11	-
17	Telling in-laws	7	24	25	5	3	1
18	Information about symptoms of APKD	1	1	1	7	28	27
19	Information about treatment of APKD	1	-	2	6	26	30

The totals of the numbers in each grade from Table 15.1 for all topics were calculated and are shown in Table 15.2. There were 1,235 answers in total. The ridits were calculated as described in Section 13.1.

Table 15.2

Second population: total numbers and calculated ridits.

Grade	1	2	3	4	5	6	Total
Numbers	130	150	249	296	305	105	1,235
Ridits	0.053	0.166	0.328	0.548	0.791	0.957	

The Kruskal-Wallis test (see Section 13.1) was used to see whether the grading of topics could be assumed to have been picked at random by respondents from the same distribution of responses as the total numbers indicate, in which case the mean ridits for the topics would not have been significantly different from each other. The value of the test statistic, W, for this table is 429.7, which compared with χ^2 with 18 degrees of freedom (one less than the number of rows) is an extremely significant result.

Thus not all topics were graded equally by the respondents. The topics have been ranked in sequence by their mean ridit and are shown again in Table 15.3 in mean ridit sequence with the highest at the top. For each topic the average of the numerical scores (1 to 6) was also calculated, and these are also shown in Table 15.3. The rankings using the two measures are very close, but not identical.

The standard deviations of the numerical score were also calculated and are shown in Table 15.3. They give an indication of the relative scatter of the gradings. One value of the standard deviation is particularly high, that for topic 1 (Risk to you). This shows a bimodal distribution with 43 in grade 1 (not applicable) and the rest in grades 3 to 6. Presumably many of those who knew they were already affected considered that the risk

of APKD to themselves was now a certainty and so not relevant to future genetic counselling.

Table 15.3

Second population: mean ridit, average score and standard deviation of score for each topic which may be of importance in genetic counselling.

Q2 seq	O	Topic	Mean ridit	Average score	Standard deviation
1	19	Information about treatment for APKD	0.82	5.25	0.93
2	18	Information about symptoms of APKD	0.81	5.17	0.97
3	2	Risk to children	0.73	4.78	1.04
4	3	Advantages of testing	0.69	4.58	0.82
5	4	Disadvantages of testing	0.64	4.37	0.92
6	6	Screening of sibs, etc	0.58	4.08	0.93
7	5	How to tell at risk	0.55	3.98	0.94
8	11	Family planning	0.53	3.83	1.16
9	10	Having no more children	0.48	3.58	1.31
10	7	Possibility of adoption	0.46	3.51	1.04
11	16	Telling boy/girlfriends	0.41	3.28	1.12
12	12	Sterilisation	0.41	3.22	1.31
13	13	Vasectomy	0.40	3.15	1.36
14	9	Voluntary childlessness	0.40	3.15	1.38
15	8	Possibility of fostering	0.39	3.20	0.95
16	15	Prevention of APKD	0.38	3.06	1.42
17	1	Risk to you	0.30	2.37	1.95
18	17	Telling in-laws	0.29	2.63	1.03
19	14	A.I.D.	0.24	2.28	1.16

Note: column Q2 seq gives the sequence in this table; column O gives the original topic number as in Table 15.1.

The difference in level of importance for any two topics can be tested by using the Kruskal-Wallis test for the pair of rows, as described in Section 13.1. Since in this case there are 171 (= 19 × 18 / 2) different pairwise comparisons, it is appropriate to use

adjusted significance levels as described in Section 13.1. A normal significance level of 5% therefore corresponds to one of 0.029% (= 5%/171), or to a normally distributed z of about 3.4. A 1% significance level corresponds to one of 0.0586% or a z of about 3.9.

The value of z for the difference between the highest and the lowest mean ridits (topics 19 and 14 in the original list) is 9.2, which is very significant. Using a test value of z of 3.9 it was found that topic 19 (Information about treatment for APKD), ranked 1st, is significantly different from the topics ranked 4th and below; topic 14 (A.I.D.), ranked 19th, is significantly different from the topics ranked 12th and above. The extreme topics are therefore ranked very differently by respondents, but many in the middle are ranked at about the same level.

The concordance of each pair of topics was also calculated using the *gamma* measure described in Section 13.1, and the test statistic z. A significance level for z of 3.4 was considered interesting, and this corresponded in general with a value of *gamma* of about 0.5. A high level of *gamma* represents close concordance between the gradings given by the respondents. If identical grades had been given, the value of *gamma* would be 1.0.

The relationship between topics with a high level of concordance can be mapped in a diagram, as was done for the importance of certain problems of APKD in Chapter 13. Figure 15.1 shows such a mapping, on the same lines as Figure 13.1.

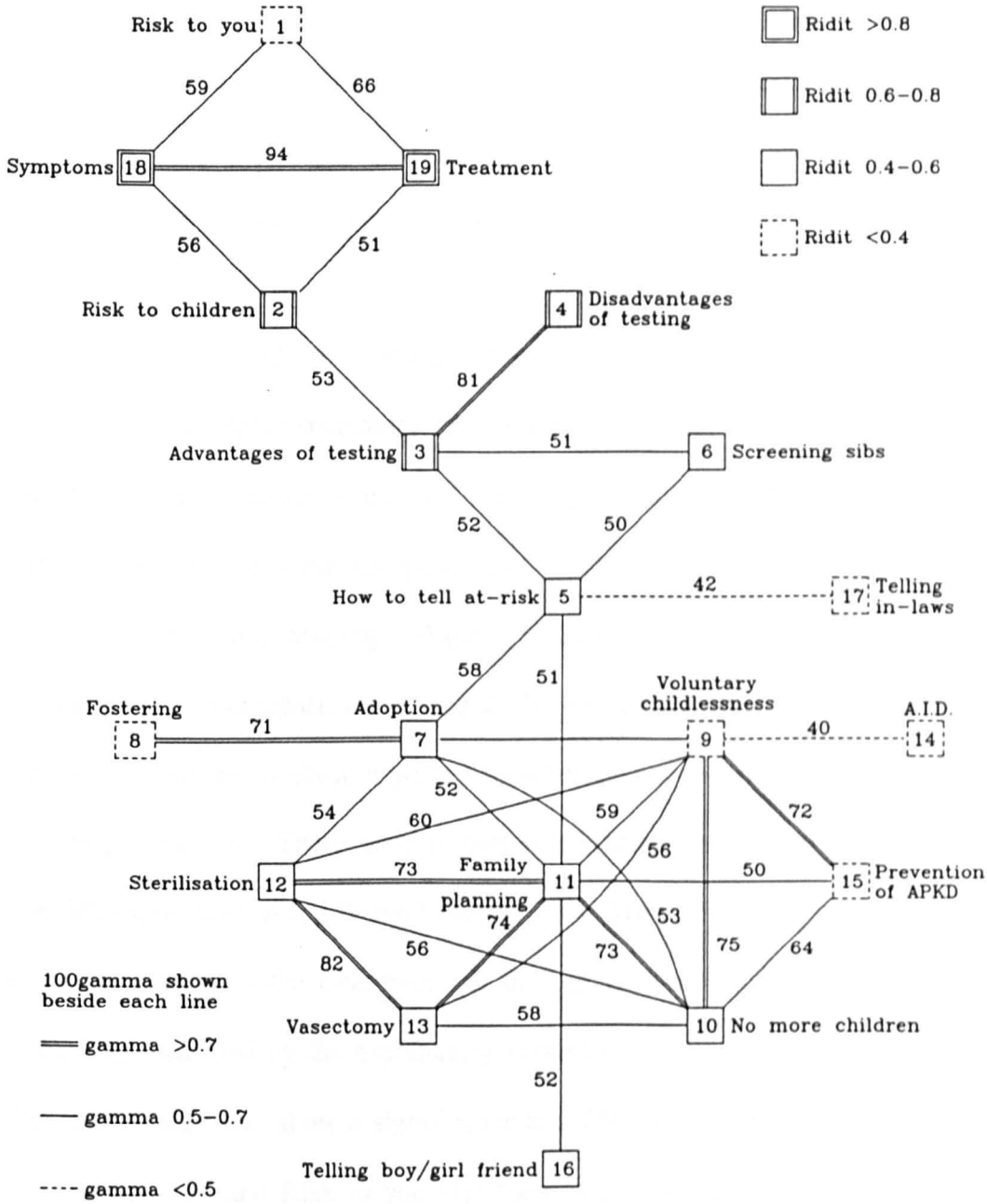

Figure 15.1. Relationships between elements that might be included in genetic counselling.

It can be seen that Information about symptoms and Information about treatment, near the top of the diagram, have a very strong concordance, with a value of *gamma* of 0.94. Risk to you and Risk to children are linked with these two, and a number of other topics are thinly connected in this region. At the foot of the diagram is a 'spider's web' of connections between a group of topics mostly related to Family planning, which itself is at the centre of the web. A few topics, such as A.I.D., Fostering and Telling in-laws are distributed around the edge of the main part of the diagram.

15.2 Effect of explanatory variables

The effect of different explanatory variables on the gradings given to the topics can also be compared with a Kruskal-Wallis test. Each topic was assessed in relation to each of 10 possible explanatory variables (sex, age, marital status, number of children, education level, occupation, housing, religious affiliation, severity of disease, family history). This gives 190 comparisons. Using a 2% probability level, one would expect about 4 such comparisons to show apparent significance, even if the grades had been allocated wholly at random. There were in fact seven comparisons significant at a 5% level, of which three were at a 1% level (denoted * below). There is thus evidence of remarkable homogeneity in the assessment of the topics of respondents with different characteristics, as measured by the explanatory variables.

The comparisons that show a significance at a 2% level are noted below.

> Education and Risk to you (1): those with education grade 1 (no qualifications) thought this less important (average ridit - a.r. - 0.416) than the others (probability 0.0090*). This is mentioned because it is statistically significant but this finding is possibly due to chance.
>
> Education and A.I.D. (14): those with education grade 1 (no qualifications) thought this more important (a.r. 0.593) than the others (probability 0.0152).

Education and Information about treatment for APKD (18): those with education grade 1 (no qualifications) thought this less important (a.r. 0.418) than the others (probability 0.0158).

Church and Voluntary childlessness (9): those with no church thought this more important (a.r. 0.611) than those who had; for catholics (a.r. 0.392) this was particularly unimportant (probability 0.0113).

Church and Family planning (10): for catholics (a.r. 0.315) this was particularly unimportant (probability 0.0123).

Number of children and Risk to children (2): those with no children (a.r. 0.518), one child (a.r. 0.653) and those with five or more children (a.r. 0.892) thought this more important than those with two, three or four children (probability 0.0062*).

Number of possible future children and Risk to children (2): those with no likely future children (a.r. 0.434), thought this less important than those with one (a.r. 0.729) or two (a.r. 0.585) future children (probability 0.0031*); this is of course associated with the preceding factor.

The three findings above relating to the explanatory variable educational level are possibly due to chance and is not considered in the discussion at the end of the chapter.

Each topic was assessed in relation to each of the 11 independent scores described in Chapters 10, 11, 12 and 14, namely EGCS1, EGCS2, KDS1 to KDS3, KIS1 to KIS4, ATCS and OGCS, thus omitting the four scores formed as totals. The connections between the problems and these scores were compared by using ordinary (Pearson product-moment) correlation coefficients (as an alternative to the *gamma* measure) and measuring (two-sided) significance by the t-statistic, as described in Section 13.2. Counting all the 11 independent scores and the 19 topics, there are 209 comparisons. Using a 2% probability level ($|t| \geq 2.4$), one would expect about 4 such comparisons to show apparent significance. There were in fact 10 comparisons significant at a 2% level, of which 6 were at a 1% level ($|t| \geq 2.7$, denoted * below). There is thus evidence of some dependence of how patients view the importance of various elements of genetic counselling on the scores, although there is still considerable homogeneity in the population in general.

The comparisons which show a significance at a 2% level are noted below.

Environment of genetic counselling (EGCS1) and Risk to children (2): correlation coefficient (*c.c.*) = 0.48, $t = 3.90$*; those who had had a better experience of genetic counselling thought it more important that Risk to children should be included.

Content of genetic counselling (EGCS2) and Risk to children (2): correlation coefficient (*c.c.*) = 0.44, $t = 3.52$*; those who had had more content in their genetic counselling also thought it more important that Risk to children should be included.

Knowledge of symptoms (KDS2) and Prevention of APKD (15): *c.c.* = −0.35, $t = -2.41$; those who knew more about the symptoms of APKD thought it less important that Prevention of APKD should be included.

Knowledge of treatment (KDS3) and Risk to you (1): *c.c.* = 0.39, $t = 2.66$; those who knew more about the treatments for APKD thought it more important that Risk to you should be included.

Knowledge of inheritance (KIS3) and Risk to children (2): *c.c.* = 0.36, $t = 2.45$; those who knew more about the transmission of APKD thought it more important that Risk to children should be included.

Attitude to having fewer children (ATCS) was associated positively with four elements:

No more children (10): *c.c.* = 0.30, $t = 2.40$;
Sterilisation (12): *c.c.* = 0.34, $t = 2.73$*;
Vasectomy (13): *c.c.* = 0.35, $t = 2.83$*;
Prevention of APKD (15): *c.c.* = 0.45, $t = 3.63$*;

and a fifth associated element was almost significant:

Family planning (11): *c.c.* = 0.29, $t = 2.36$;

it is not surprising that those who favoured considering fewer children thought that information about aspects of family planning should be included in genetic counselling.

Consequences of genetic counselling (OGCS) and Risk to children (2): *c.c.* = 0.44, $t = 3.52$*; those who felt that genetic counselling had had a beneficial effect for them thought it important that Risk to children should be included.

Although some of these correlations might be the result of chance, there is a good rationale for some of them, and indeed several are statistically very significant.

15.3 Repeat in third questionnaire

In questionnaire 3 the same question was asked with the same list of topics. Respondents were asked to complete the questionnaire themselves. Two respondents failed to do so. The responses of the 45 respondents who did are shown in Table 15.4.

Table 15.4

Third population: numbers of patients who graded each topic in terms of how important it was for genetic counselling.

	Grade	1	2	3	4	5	6
O	Topic	Not applicable	Not important	Slight	Quite	Very	Extremely
1	Risk to you	34	-	1	1	3	6
2	Risk to children	-	2	2	5	21	15
3	Advantages of testing	-	3	2	4	21	15
4	Disadvantages of testing	1	4	3	6	18	13
5	How to tell the at risk	1	4	4	10	15	11
6	Screening of sibs, etc	-	3	3	8	24	7
7	Possibility of adoption	5	15	7	10	7	1
8	Possibility of fostering	6	15	8	10	6	-
9	Voluntary childlessness	8	14	3	9	10	1
10	Having no more children	2	4	7	12	13	7
11	Family planning	3	6	3	13	14	6
12	Sterilisation	5	9	4	10	12	5
13	Vasectomy	6	10	3	10	10	6
14	A.I.D.	20	19	3	2	-	1
15	Prevention of APKD	4	6	6	8	13	8
16	Telling boy/girlfriends	2	5	6	12	16	4
17	Telling in-laws	10	22	6	2	3	2
18	Information about symptoms of APKD	-	-	1	-	8	36
19	Information about treatment of APKD	-	-	1	-	8	36

The totals of the numbers in each grade from Table 15.4 for all topics were calculated and are shown in Table 15.5. There were 855 answers in total. The ridits were calculated as described above.

Table 15.5

Third population: total numbers and calculated ridits.

Grade	1	2	3	4	5	6	Total
Numbers	107	141	73	132	222	180	855
Ridits	0.063	0.208	0.333	0.453	0.660	0.895	

The Kruskal-Wallis test was again used to see whether the mean ridits for the topics were significantly different from each other. The value of the test statistic, W, for this table was 360.67, which compared with χ^2 with 18 degrees of freedom, is an extremely significant result.

Again not all topics were graded equally by the respondents. The topics have again been ranked in sequence by their mean ridit and are shown in Table 15.6 in mean ridit (Q3 m.r.) sequence with the highest at the top. Also shown are the averages of the scores in questionnaire 3 (Q3 a.s.), the standard deviations of the scores (Q3 s.d.), and the mean ridit (Q2 m.r.) and sequence (Q2 seq) for the responses in questionnaire 2.

As in questionnaire 2, one value of the standard deviation is particularly high, that for topic 1 (Risk to you). This again shows a bimodal distribution with 34 in grade 1 (not applicable) and the rest in grades 3 to 6.

The sequence in this questionnaire is almost the same as in questionnaire 2, except that Prevention of APKD has moved up from 16th to 10th, and Possibility of adoption has moved down from 10th to 15th.

Table 15.6

Third population: mean ridit, average score and standard deviation of score for each topic which may be of importance in genetic counselling.

Q3 seq	O	Topic	Q3 m.r.	Q3 a.s.	Q3 s.d.	Q2 m.r.	Q2 seq
1	19	Information about treatment for APKD	0.84	5.76	0.56	0.82	1
2	18	Information about symptoms of APKD	0.84	5.76	0.56	0.81	2
3	2	Risk to children	0.68	5.00	1.01	0.73	3
4	3	Advantages of testing	0.68	4.96	1.10	0.69	4
5	4	Disadvantages of testing	0.62	4.67	1.31	0.64	5
6	6	Screening of sibs, etc	0.61	4.64	1.04	0.58	6
7	5	How to tell at risk	0.59	4.49	1.31	0.55	7
8	10	Having no more children	0.52	4.13	1.34	0.48	9
9	11	Family planning	0.51	4.04	1.43	0.53	8
10	15	Prevention of APKD	0.51	3.98	1.57	0.38	16
11	16	Telling boy/girlfriends	0.50	4.04	1.30	0.41	11
12	12	Sterilisation	0.45	3.67	1.58	0.41	12
13	13	Vasectomy	0.44	3.58	1.65	0.40	13
14	9	Voluntary childlessness	0.36	3.04	1.52	0.40	14
15	7	Possibility of adoption	0.35	3.04	1.35	0.46	10
16	8	Possibility of fostering	0.32	2.89	1.27	0.39	15
17	17	Telling in-laws	0.26	2.38	1.30	0.29	18
18	1	Risk to you	0.23	2.04	1.90	0.30	17
19	14	A.I.D.	0.18	1.80	1.00	0.24	19

Note: column Q3 seq gives the sequence in this table; column Q2 seq gives the sequence in Table 15.3 relating to questionnaire 2; column O gives the original sequence as in Table 15.1.

15.4 COMPARISON OF SECOND AND THIRD QUESTIONNAIRES

The responses of the 45 patients who replied to questionnaire 3 were compared with the responses of the same 45 patients to questionnaire 2. First, the average level of

assessment of severity of each problem was compared by an analysis of the mean ridits, where the ridits were calculated using just the two responses from each respondent for the same topic. Secondly, the concordance between the replies from each respondent to each topic on the two occasions was compared using the *gamma* statistic. Table 15.7 lists the topics again, in the same order as in Table 15.3, the sequence according to mean ridit on the first occasion, and shows the difference (diff) between the mean ridits on the two occasions (+ for those where the assessment was higher in questionnaire 3, − for those where the assessment was lower in questionnaire 3), the probability (prob) that this difference occurs by chance (using the Kruskal-Wallis test), and the value of *gamma* when the two sets of responses for each topic are compared.

The top few items, those which were the more important ones on the first occasion, have increased in importance, and the bottom few, which were the less important, have gone down. Information about treatment, Information about symptoms, Screening of sibs, and Telling boy/girlfriends are all significantly up at a 1% probability level, and no topic is significantly down. However, the relative positions have polarised.

It should be noted that the concordances between the responses of patients in questionnaire 2 and questionnaire 3 are low; four are negative and the largest is 0.52. While individual patients changed their views about the importances of the different elements, the view of the collective population remained almost unchanged on the two occasions.

Table 15.7

Second and third populations: comparisons of responses for each topic which may be of importance in genetic counselling.

Q2 seq	Q3 seq		Q2 m.r.	diff	prob	*gamma*
1	1	Information about treatment for APKD	0.82	+0.195	0.0002	0.16
2	2	Information about symptoms of APKD	0.81	+0.208	0.0001	0.27
3	3	Risk to children	0.73	+0.047	0.41	0.52
4	4	Advantages of testing	0.69	+0.123	0.027	0.41
5	5	Disadvantages of testing	0.64	+0.090	0.12	0.00
6	6	Screening of sibs, etc	0.58	+0.161	0.0050	−0.09
7	7	How to tell at risk	0.55	+0.123	0.036	0.29
8	9	Family planning	0.53	+0.037	0.53	0.47
9	8	Having no more children	0.48	+0.066	0.27	0.42
10	15	Possibility of adoption	0.46	−0.131	0.030	0.25
11	11	Telling boy/girlfriends	0.41	+0.186	0.0018	−0.05
12	12	Sterilisation	0.41	+0.060	0.31	0.28
13	13	Vasectomy	0.40	+0.058	0.33	0.19
14	14	Voluntary childlessness	0.40	−0.060	0.31	0.25
15	16	Possibility of fostering	0.39	−0.082	0.16	−0.06
16	10	Prevention of APKD	0.38	+0.149	0.013	0.44
17	18	Risk to you	0.30	−0.032	0.52	0.13
18	17	Telling in-laws	0.29	−0.082	0.15	−0.01
19	19	A.I.D.	0.24	−0.127	0.027	0.41

Note: column Q2 seq gives the sequence in Table 15.3, relating to questionnaire 2; column Q3 seq gives the sequence in Table 15.6 relating to questionnaire 3.

15.5 EFFECT OF EXPLANATORY VARIABLES IN THIRD QUESTIONNAIRE

The effect of the different explanatory variables on the gradings given to the topics was examined. Out of 190 independent comparisons made, not one was significant at a 2% probability level. The chance of this event occurring if the gradings had been allocated

to topics at random is as low as 0.0215, or not much more than 2%. While chance results like this do occur sometimes, it is further evidence of the remarkably homogeneity of this population in its attitudes.

Each topic was also assessed in relation to each of the scores as described in relation to questionnaire 2, the connections being compared as before by using correlation coefficients. Of the 209 comparisons only three were significant at a (two-sided) 2% level ($|t| \geq 2.4$), and not one at a 1% level ($|t| \geq 2.7$). This is further evidence of the remarkable homogeneity of these answers from this population.

The comparisons which do show a significance at a 2% level are noted below.

Environment of genetic counselling (EGCS2) and How to tell the at risk (5): correlation coefficient *c.c.* = 0.36, $t = 2.44$.

Knowledge of inheritance (KIS1) and Having no more children (10): *c.c.* = 0.38, $t = 2.54$.

Attitude to having fewer children (ATCS) and Sterilisation (12): *c.c.* = 0.34, $t = 2.46$.

Only the last of these relationships, for which there is good rationale, showed significant correlation for the responses in the second questionnaire, and no others of those found significant for the second questionnaire remained significant here. This supports the idea that most of these correlations are the result of chance.

15.6 COMPARISON OF INDIVIDUAL RESPONSES IN SECOND AND THIRD QUESTIONNAIRES

The views of each individual about the 19 topics in the second and the third questionnaires were compared in order to see how consistent was their ranking of the importance of the topics. This required constructing a 6 by 6 table for each respondent, as described in Section 13.6, showing how their 19 pairs of responses fell into grades. The concordances between the responses in the second and third questionnaires were then calculated, using the *gamma* measure described previously.

The values of *gamma* theoretically range from −1.0 to 1.0, and the actual range observed was from −0.12 (2 cases) to +0.98 (3 cases). The distribution of values of *gamma* for the third population is shown in Table 15.8. It is fairly similar to the distribution for the importance of different problems as shown in Table 13.8; a considerable number of cases have quite high concordance (say *gamma* ≥ 0.6), but a fair number have low concordance.

Table 15.8

Third population: values of *gamma* for each individual, subdivided by sex and marital status.

	Single females	Married females	Males	Total
Not calculated	-	-	2	2
−1.0 to −0.0	1	1	1	3
+0.0 to +0.2	1	-	1	2
+0.2 to +0.4	1	5	1	7
+0.4 to +0.6	3	4	-	7
+0.6 to +0.8	4	3	2	9
+0.8 to +1.0	2	7	8	17
Total	12	20	15	47

Correlation coefficients were calculated for the average ridits for each individual in the two questionnaires, the *gamma* measure of concordance described above, all the constructed scores described in Chapters 10, 11, 12 and 14, severity of disease and family history and also the ridits and the *gamma* measure for the problems discussed in Chapter 13. The values of the coefficients ranged from −0.21 to +0.30, not significant, except for the following:

> the ridits for the importance of elements in the second questionnaire and in the third questionnaire, correlation coefficient 0.42, significant at a 1% level;

the ridit for the second questionnaire and the score for attitudes to having further children (ATCS), $c.c = 0.38$, significant at a 1% level.

The first of these is not surprising. The second is also not surprising, considering the fact that those with a positive attitude to having no further children identified several topics that they thought particularly important to have included in genetic counselling.

15.7 DISCUSSION OF SECOND QUESTIONNAIRE

In Table 15.3 the mean ridit and average crude score for each topic which may be of importance in genetic counselling is shown. It is quite clear that information about the treatment for and symptoms of APKD are perceived by respondents as the two most important elements to be included in genetic counselling and are seen as more important than giving information about the risk to children of inheriting APKD. This is an important finding as there is considerable emphasis in the literature on genetic counselling in giving information about the risk of inheritance and transmission of the particular disease and little reference to the importance of information about the treatment and the symptoms of the illness. It is possible that the patient's perception of the burden of the illness is in part based on their knowledge of the symptoms of the illness and the treatments available. All respondents had APKD and it could be that this emphasis on the importance of information about the treatment and the symptoms also reflects what is a common request from patients generally ie the need for more information.

The next four items in importance all concerned information about testing and screening. Presymptomatic diagnosis of APKD by ultrasound was already available and while patients agreed in principle with presymptomatic diagnosis of APKD, some patients reported to the research worker that it was difficult to know what they should do and say when it was suggested that their at risk relatives could be offered presymptomatic testing

for APKD. There is evidence in the genetic counselling literature of the reluctance of the affected person to inform their at risk relatives of their possibility of inheriting the particular illness and this behaviour is frequently attributed to denial (Lynch 1969). While not underestimating the importance of denial in this context, it is also possible that patients have not had the opportunity to talk about the advantages and the disadvantages of testing those at risk and may simply not know what to do about it.

Eight out of the next 9 items, with mean ridits of 0.53 to 0.38, are concerned with the control or prevention of APKD. The exception is information about the telling of boyfriends or girlfriends with a mean ridit of 0.40. It would be relevant to consider including any of these 8 topics in genetic counselling where prevention of the illness is emphasised. It is interesting to note that respondents perceive these elements only of moderate importance.

Artificial Insemination by Donor (A.I.D.) was strongly viewed as an unimportant topic. It could be that a population from a different part of the United Kingdom may not be so dismissive of A.I.D. Several respondents did not know what this procedure involved. When this was explained to them a frequent comment was 'disgusting'. This West of Scotland population may not be representative, but on the other hand these views may reflect the general population.

The effect of different explanatory variables on the gradings given to topics in genetic counselling is described in Section 15.2. The first comment to be made concerns the influence of the explanatory variable of church or religious affiliation. Many authors in studies of genetic counselling have sought a link between religious affiliation and attitudes to genetic counselling and most studies have reported that they have not found an association between religious affiliation and attitudes to genetic counselling. For all authors this has appeared a surprising finding. In this analysis there are two statistically

significant findings associated with religious affiliation. Catholics did not think either voluntary childlessness or family planning were important topics to be included in genetic counselling. Respondents in this study may have answered the questions in relation only to APKD although they were asked to consider the questions more generally. And for these respondents APKD may not be considered sufficiently serious to merit preventing the birth of a child who may develop APKD.

Respondents who had no children, respondents who had one child and those with five or more children compared with those who had two, three and four children thought it important to include a discussion about the risk to children. For those who have no children or one child, such a discussion may be important as these respondents may consider having children or more children in the future. It is likely that those respondents who have two, three and four children may have completed their families and therefore for them this item is of less importance as it is for those with no likely future children. There were not many respondents with five or more children. Although the probability of having a child with APKD is 50-50 at each conception, the more children a person has the greater the chance there is that there will be an affected offspring. These respondents with very large families may simply have thought about the situation very carefully.

15.8 DISCUSSION OF THIRD QUESTIONNAIRE

In questionnaire 3 respondents were asked to complete the same section as in questionnaire 2 on the list of topics that could be important in genetic counselling.

The first observation is to note the very great consistency in answers between the two interviews and therefore over a period of time. The time between the second and the third interviews was between 6 and 12 months and respondents completed this section of the questionnaire themselves so it is very unlikely that there was any collusion.

Information about the treatment for and symptoms of APKD remain by far the two most important elements and A.I.D. still remains the least important item. Prevention of APKD becomes the 10th most important item in this section compared with 15th in the analysis of questionnaire 2. This result could be by chance. But between interviews 2 and 3 some of the respondents had become ill or more ill and this could influence the priority they gave to this topic.

CHAPTER 16: THE SECONDARY STUDY

16.1 PRENATAL DIAGNOSIS AND A GENE MARKER

A secondary study was also carried out. The background and methodology of the study is described in this chapter. The results of the study are described in Chapter 17.

The purpose of this study was to explore the views of patients with APKD to prenatal diagnosis and termination of pregnancy. The discovery of a gene marker for APKD on chromosome 4 in 1986 by Reeders et al before the completion of this study and the use of chorion villus sampling in prenatal diagnosis (see Section 2.7.4) meant that it could become increasingly possible to offer prenatal diagnosis to some families with APKD followed by termination of an affected fetus if they so wished. If the knowledge of the gene marker had been available at the beginning of the study, questions about prenatal diagnosis would have been included as part of the content of genetic counselling.

At the time of this study there were no known published investigations into the views of APKD patients to prenatal diagnosis for APKD. It was not known whether patients would be interested in using prenatal diagnosis for APKD nor whether the timing of the procedure in the first or second trimester of pregnancy would influence their views. Moreover it was not known what the views of this group of patients would be to termination of pregnancy for APKD.

Because of the delicate nature of this particular question, an interview would normally have been required in order to collect data. However, as many of the respondents were already well known to the research worker, it was not considered inappropriate to give patients a self-administered questionnaire to complete. This was sent to patients between 1986 and 1987.

16.2 STUDY POPULATION

It is likely that a decision about whether or not to take prenatal diagnosis would often be taken by both parents. It seemed important therefore to seek the views of the partners of the patients for this section of the study. It also seemed relevant to ascertain the views of patients with APKD in different stages of the illness from the asymptomatic to those with more severe symptoms as well as those at risk for APKD. The main study did not include those at risk for APKD.

It was decided to include subjects of another investigation that was being carried out by Dr Keith Simpson and the research worker in conjunction with the Department of Human Genetics, Yorkhill Hospital, Glasgow and to seek the views of the subjects of this investigation to prenatal diagnosis. This investigation involved following up families with members known to have APKD in order to collect blood samples which would be used to ascertain the accuracy of a gene marker for APKD. This population included those at risk for APKD and their partners and the research worker had already met all the proposed sample.

16.3 METHOD OF INVESTIGATION

It is appreciated that the subject matter under investigation, prenatal diagnosis and termination of pregnancy, could be distressing for some people to consider. However as all the proposed subjects for this part of the study had already met the researcher worker, it was decided that it was not inappropriate for the questionnaire to be sent out by post. The main reason for using a postal questionnaire was that there was insufficient time to interview all subjects.

Some of the known disadvantages of postal questionnaires include a possible low response rate, acquiring less detailed information than in interview, and the possibility that

the respondent will either omit or misunderstand some of the questions. It was hoped that there would be a moderate response rate as many of the respondents particularly those in the APKD sample were known to the researcher. The questionnaire was kept as short as possible to make it easier for respondents and to encourage a higher response rate. There was only one topic per page and no more than 6 questions per topic. The language used was clear and unambiguous.

200 self-administered questionnaires and a prepaid reply envelope were sent to the first 200 participants in the gene marker investigation. In the event 194 were returned, an exceptionally high response rate of 97%.

The questionnaires were numbered sequentially and anonymised making it impossible to trace respondents.

16.4 CONTENT OF PRENATAL QUESTIONNAIRE

In Section A four demographic questions were asked. These were sex, age range, marital status and relationship to the disease.

Section B asked questions about the number of children and grandchildren that the respondent had had.

Section C was concerned with screening for APKD. Four questions were asked about the testing of children and grandchildren for APKD and the appropriate age for this and whether extended family members should be told of their risk and offered screening for APKD.

Section D was concerned with prenatal screening. Questions were asked about whether patients would consider using prenatal diagnosis to diagnose APKD in a fetus and whether they would prefer this to be done in the first or second three months of pregnancy. There is some evidence that patients prefer termination to be carried out in the

first rather than the second trimester of pregnancy (Report of the Royal College of Physicians 1989). It is appreciated that the available technology for prenatal diagnosis of APKD in 1986 could not detect APKD in the fetus with 100% accuracy. Therefore, questions were phrased 'whether in the future it becomes possible to tell during pregnancy whether or not a baby has APKD'. The questions were appropriate given the state of knowledge at the time.

Section E was concerned with termination of pregnancy. One of the choices that becomes open to parents as a result of prenatal diagnosis is termination of an affected fetus. Respondents were therefore asked whether they would consider termination of pregnancy of a fetus shown to have APKD. Termination of pregnancy is an emotive subject. Three questions were asked in this section to assess in what circumstances and with which illnesses the respondent would consider termination of pregnancy.

Sections F and G of the questionnaire were concerned with questions about how the respondent ranked APKD in terms of other illnesses. How someone perceives the burden of an illness may be one reason why that person would decide to terminate a pregnancy. In Section F respondents were asked to rank on a five-point scale the degree of impairment likely to be caused to an individual by ten conditions chosen because of the frequency with which patients with these conditions were referred to the out-patient clinics at GRI. It was assumed that these conditions would be well known to respondents in the study. APKD was included in this list of ten conditions.

In Section G the respondents were asked to answer the same questions as if the respondent were the manager of a life insurance company and that the people with the ten conditions had applied for insurance. The question was asked in this manner in order to explore how the respondent thought that others perceived the seriousness of APKD.

16.5 HAEMOPHILIA AND PRENATAL DIAGNOSIS

It was not known to what extent the views of respondents about prenatal diagnosis of APKD would be representative of views of prenatal diagnosis in other illnesses. The research worker was already working in the Haemophilia Unit, GRI, where there was considerable staff interest in prenatal diagnosis. Since 1984 it has been possible to detect haemophilia A in families with a clear history of haemophilia as well as to identify carriers. In families with a clear history of haemophilia A it was also possible to offer prenatal diagnosis by chorion villus sampling in the twelfth week of pregnancy.

Haemophilia is transmitted in a sex linked recessive fashion. Carrier women have a 50-50 chance of producing a son with haemophilia. All daughters born to an affected male will be carriers but their sons will be unaffected. This is in contrast to the autosomal dominant inheritance of APKD where each child, regardless of sex, of an affected person has a 50-50 chance of inheriting the gene and subsequently of developing symptoms of the disease. In recent years improvements in the treatment for haemophilia had resulted in considerable optimism in the haemophilia world. The expectation of life was approaching that of normal and a new generation of haemophiliacs were able to anticipate living a 'normal life', attending school on a regular basis and obtaining employment appropriate to their ability (Wilkie 1992).

However, in 1982 in the USA a person with haemophilia was diagnosed with what was to become known as the human immunodeficiency virus (HIV) and since then many patients worldwide with haemophilia have died of HIV. Since all blood donors in the United Kingdom are now tested for HIV, and since the blood products used in the treatment of haemophilia have been heat treated since 1985, there should be no new cases of HIV transmitted to people with haemophilia through their treatment by blood products.

There are other differences between these two illnesses. APKD is a disease of variable age of onset affecting both sexes, whereas haemophilia affects baby boys from birth and haemophilia affects only the males.

It was considered that it would be useful to assess the views on prenatal diagnosis of another study group and that it was inappropriate to use a sample from the general population because of the complexity of the subject and the lack of involvement of such a sample. While there were other groups that could have been sampled, it was considered appropriate to use a sample from haemophilia patients, their partners and female carriers of haemophilia. This sample were easily accessible, some of the patients were already known to the research worker and prenatal diagnosis was a subject of interest to this group.

Permission was sought from the West of Scotland Haemophilia Reference Centre Director, Dr Gordon Lowe, to send the prenatal diagnosis questionnaire, adapted for haemophilia, to a sample of haemophilia patients, their partners and carrier women. Assistance was offered by staff of the haemophilia unit to distribute the questionnaires to carrier women when they came to the unit as well as to haemophilia patients and their partners. It was hoped that it would be possible to accrue 200 respondents. In the event 90 questionnaires were returned, but it is not known how many were actually sent out by the staff of the Haemophilia Unit.

CHAPTER 17. ANALYSIS:

PRENATAL DIAGNOSIS AND TERMINATION OF PREGNANCY

17.1 Introduction

In this chapter the results of the analysis of the responses to questionnaire 4, which was sent to the two populations described in Chapter 16, are discussed. Section 17.2 contains an analysis of the results from the APKD respondents. In Section 17.3 the results from the haemophilia respondents are examined and compared with the results from the APKD population. In Section 17.4 certain results from the two populations are discussed together. Section 17.5 contains a general discussion of the results.

17.2 The APKD population

17.2.1 Characteristics of the population

Out of the 200 questionnaires distributed 194 were returned satisfactorily completed. This is a response rate of 97%. One was returned with so little completed that it could not be used, and five were not returned. As the questionnaires were anonymised it is not possible to comment on the characteristics of the non-respondents.

Responses were received from 119 females (61.3%) and 75 males (38.7%). Besides their sex, respondents were asked to state their marital status, age (in bands mostly of five years) and their 'relationship to the disease', and also the number of children and grandchildren that they had. The distribution of the population by each of these characteristics, subdivided by sex, is shown in Tables 17.2.1 to 17.2.5.

Table 17.2.1

APKD population: subdivided by marital status and sex.

	Female	Male	Total	%
Single	31	27	58	29.9
Married	68	40	108	55.7
Widowed	12	2	14	7.2
Divorced or separated	7	4	11	5.7
Other	1	2	3	1.5
Total	119	75	194	100.0

Table 17.2.2

APKD population: subdivided by age group and sex.

	Female	Male	Total	%
15-19	14	12	26	13.4
20-24	15	9	24	12.4
25-29	19	8	27	13.9
30-34	16	11	27	13.9
35-39	14	12	26	13.4
40-44	8	4	12	6.2
45-49	8	7	15	7.7
50-59	11	8	19	9.8
60 and over	14	4	18	9.3
Total	119	75	194	100.0

Table 17.2.3

APKD population: subdivided by 'relationship to disease' and sex.

	Female	Male	Total	%
Affected	61	26	87	44.8
Screened and unaffected	23	14	37	19.1
At risk (unscreened)	13	12	25	12.9
Unaffected *	3	4	7	3.6
Spouse of affected	12	12	24	12.4
Spouse of screened unaffected	5	2	7	3.6
Spouse of at risk	2	3	5	2.6
Spouse of unaffected	-	2	2	1.0
Total	119	75	194	100.0

Note: * these comprise those who might have been at risk, but are now established as unaffected, for example because their at risk parent has been screened and found to be unaffected.

Table 17.2.4

APKD population: subdivided by number of children and sex.

	Female	Male	Total	%
None	41	35	76	39.2
One	24	11	35	18.0
Two	28	17	45	23.2
Three	15	7	22	11.3
Four	6	3	9	4.6
Five or more	5	2	7	3.6
Total	119	75	194	100.0

Table 17.2.5

APKD population: subdivided by number of grandchildren and sex.

	Female	Male	Total	%
None	97	69	166	85.6
One	5	4	9	4.6
Two	6	-	6	3.1
Three	3	1	4	2.1
Four	2	-	2	1.0
Five or more	6	1	7	3.6
Total	119	75	194	100.0

17.2.2 Testing of children for APKD

Respondents were asked whether they thought that their children (or grandchildren) should be tested for APKD. Some 79% of them (154 out of 194) said that they thought that their children should be tested for APKD. The percentages among males and females were almost the same (94 out of 119 females or 79% and 60 out of 75 males or 80%). Only 14 (7%) thought that their children should not be tested; the remainder gave various intermediate responses, such as 'children already tested' (9), 'don't know' (11) and 'not applicable' (6) (see Table 17.2.6).

Table 17.2.6

APKD population: responses to 'should your children be tested for APKD', subdivided by sex.

	Female	Male	Total	%
Yes	94	60	154	79.4
No	10	4	14	7.2
Already tested	7	2	9	4.6
Not applicable	3	3	6	3.1
Don't know	5	6	11	5.7
Total	119	75	194	100.0

Respondents were asked at what age (of the child) they would like to know whether their child had inherited APKD. The responses, subdivided by sex, are shown in Table 17.2.7. A majority favoured early testing, 66 (34%) wanting to know prenatally and 48 (25%) choosing the ages of 0-4. A second group favoured the ages of 15-19 (17) or 20 and over (14). Rather few favoured the intermediate ages of 5-9 (10) and 10-14 (9), while 30 (16%) did not know.

Table 17.2.7

APKD population: responses to 'at what age would you like to know whether your child had APKD', subdivided by sex.

	Female	Male	Total	%
Prenatally	39	27	66	34.0
0-4 years	29	19	48	24.7
5-9 years	6	4	10	5.2
10-14 years	7	2	9	4.6
15-19 years	12	5	17	8.8
20 years & over	9	5	14	7.2
Don't know	17	13	30	15.5
Total	119	75	194	100.0

17.2.3 Screening of relatives for APKD

In answer to the question whether other members of the family (e.g. brothers, sisters, cousins) who may be at risk for APKD should be told of their risk, a large majority (179 or 92%) were in favour. Only 5 thought that relatives should not be told. See Table 17.2.8.

Table 17.2.8

APKD population: responses to 'should your relatives be told of their risk of APKD', subdivided by sex.

	Female	Male	Total	%
Yes	109	70	179	92.3
No	2	3	5	2.6
Don't know	8	2	10	5.2
Total	119	75	194	100.0

When asked whether these same relatives should be tested for APKD a few changed their answers to 'no'; many replied that their relatives had already been tested, and a few that the question was not applicable (perhaps because they had no such relatives). See Table 17.2.9.

Table 17.2.9

APKD population: responses to 'should your relatives be tested for APKD', subdivided by sex.

	Female	Male	Total	%
Yes	85	48	133	68.6
Already tested	23	19	42	21.6
No	4	3	7	3.6
Not applicable	1	2	3	1.5
Don't know	6	3	9	4.6
Total	119	75	194	100.0

17.2.4 Prenatal screening and termination of pregnancy

Respondents were asked whether they thought couples should take a test, if such a test were to become available, to test for APKD prenatally. A majority (134 or 69%) thought that couples should take such a test. See Table 17.2.10.

Table 17.2.10

APKD population: responses to 'should couples take a test for APKD during pregnancy?', subdivided by sex.

	Female	Male	Total	%
Yes	78	56	134	69.1
No	25	11	36	18.6
Don't know	16	8	24	12.4
Total	119	75	194	100.0

Almost the same number (135 or 69%) reported that they personally would take such a test to see whether the baby had APKD. See Table 17.2.11.

Table 17.2.11

APKD population: responses to 'would you consider taking a test for APKD during pregnancy?', subdivided by sex.

	Female	Male	Total	%
Yes	77	58	135	69.6
No	32	10	42	21.6
Don't know	10	7	17	8.8
Total	119	75	194	100.0

Respondents were then asked whether they would take such a test if it were to be followed by termination of pregnancy if it were shown that the baby had APKD. A considerable majority (120 or 62%) replied that they would not. See Table 17.2.12. The proportion of females who would not take such a test (77 out of 119 or 65%) was rather greater than

the proportion of males who took the same view (43 out of 75 or 57%). This is an interesting but not statistically significant result.

Table 17.2.12

APKD population: responses to 'would you consider taking a test followed by termination if the baby had APKD?', subdivided by sex.

	Female	Male	Total	%
Yes	16	13	29	14.9
No	77	43	120	61.9
Don't know	26	19	45	23.2
Total	119	75	194	100.0

The last two questions in this part of the questionnaire concerned respondents views on prenatal diagnosis followed by termination of pregnancy in the first or the second trimester of pregnancy. The responses to these questions were similar to those for the previous question, all but 30 (15.5%) giving the same answers to all three questions (22 'yes' to all three; 108 'no' to all three; 34 'don't know' to all three). The results, subdivided by sex, are shown in Tables 17.2.13 and 17.2.14. Only 25 respondents (13%) would consider termination for APKD in the second trimester. A few more (36 or 18%) would consider termination of pregnancy for APKD in the first trimester.

Table 17.2.13

APKD population: responses to 'would you consider testing followed by termination in the second trimester?', subdivided by sex.

	Female	Male	Total	%
Yes	13	12	25	12.9
No	80	44	124	63.9
Don't know	26	19	45	23.2
Total	119	75	194	100.0

Table 17.2.14

APKD population: responses to 'would you consider testing followed by termination in the first trimester?', subdivided by sex.

	Female	Male	Total	%
Yes	20	16	36	18.6
No	71	41	112	57.7
Don't know	28	18	46	23.7
Total	119	75	194	100.0

17.2.5 Termination of pregnancy

Respondents were asked which of three statements best reflected their views on termination of pregnancy. The greatest number of respondents (129 or 66%) believed that termination should be available sometimes; 36 (19%) believed that termination of pregnancy should be available on request; only 28 (14%) said that they were totally against termination. See Table 17.2.15.

Table 17.2.15

APKD population: responses to 'which best represents your views on termination of pregnancy?', subdivided by sex.

	Female	Male	Total	%
Available on request	18	18	36	18.6
Available sometimes	83	46	129	66.5
Totally against	17	11	28	14.4
Total	119	75	194	100.0

Respondents were asked under which of seven circumstances, all relating to the situation of the parents, they would consider termination of pregnancy. The results are shown in Table 17.2.16, in which the circumstances are listed in order of the proportion of respondents who replied 'yes'.

Table 17.2.16

APKD population: numbers replying 'yes' to 'would you consider termination of pregnancy in the circumstances described?', subdivided by sex.

	Female	Male	Total	%
One parent has AIDS	80	46	126	64.9
Mother's physical health	73	52	125	64.4
Mother's mental health	54	38	92	47.4
Mother a young teenager	14	11	25	12.9
Mother over 40	11	8	19	9.8
Family too large	4	5	9	4.6
Mother unmarried	2	4	6	3.1
Maximum	119	75	194	100.0

The third question in this part sought the views of respondents on termination early in pregnancy for ten specific conditions from which the baby might suffer. The results are shown in Table 17.2.17, in which the conditions are listed in order of the proportion of respondents who replied 'yes'.

Table 17.2.17

APKD population: numbers replying 'yes' to 'would you favour termination of pregnancy if it could be determined early in the pregnancy that the baby would definitely have the condition described?', subdivided by sex.

	Female	Male	Total	%
AIDS	84	49	133	68.6
Severe mental handicap	80	48	128	66.0
Severe physical handicap	76	41	117	60.3
Disease likely to cause death before age 5	43	33	76	39.2
Disease likely to cause death aged 6-10	38	22	60	30.9
Disease likely to cause death aged 11-15	30	19	49	25.3
Haemophilia	29	16	45	23.2
APKD	17	13	30	15.5
Mild mental handicap	17	8	25	12.9
Slight physical handicap	9	6	15	7.7
Maximum	119	75	194	100.0

17.2.6 Analysis by sub-groups

So far, 27 questions had been asked about testing, screening and termination. The responses to each of these questions were analysed by each of the six possible explanatory variables, sex, age, marital status, relationship to the disease, number of children or number of grandchildren to see whether there were any significant differences in the responses. For this, the categories of both the responses and the explanatory variables were grouped somewhat so as to avoid too many cells with too few observations, and then the Pearson statistic $X^2 = \Sigma(O-E)^2/E$ was calculated and compared with χ^2 for the appropriate number of degrees of freedom.

With 162 (27 x 6) tests in all it is reasonable to expect that, by chance, one or two of the tests would be apparently significant at a 1% probability level. In fact six of the tests showed probabilities less than 0.01, four of them less than 0.001. These are noted below. but the main conclusion to be drawn is that there was little difference in the attitude of the respondents to testing, screening or termination, according to any of the explanatory variables recorded.

The six explanatory variables were themselves strongly interconnected in a number of obvious ways: for example, older people had more children and grandchildren, widows were more likely to be older, and younger people were more likely to be single and to have fewer children. There were, however, two groups with a particular relationship to the disease worth noting: the older respondents were much more likely to be the spouses of those who were affected, some of them being widows; and those who were at risk but unscreened were much more likely to be younger.

The significant results were:

Testing of relatives and relationship to disease: those who were affected were much more likely to have relatives that had already been tested than were the other groups (probability 0.0001); but when these are combined with those who answered 'yes' to the question about relatives being tested the differences disappear.

All the other significant tests related to the attitudes to termination:

Age: those aged 20-24 were more likely to favour termination if the baby would suffer from mild mental handicap (probability 0.0043); but even then only 37.5% (9 out of 24) were in favour, as compared with 12.9% overall.

Relationship with disease: those who were at risk but unscreened were more likely to favour termination if the mother were over 40 (probability 0.0007), but this still meant that only 32% (8 out of 25) were in favour as compared with 9.8% overall. The same group were also more likely to favour termination if the baby was likely to die at ages 6-10 or 11-15 (probabilities 0.0010 and 0.0005), and in each case there was a majority in favour of 56% (14 out of 25 in both cases), as compared with 30.9% and 25.3% overall.

Number of grandchildren: those with 4 or more grandchildren were more likely to be against termination on the grounds of the mother's physical health, 8 out of 9 being against, as compared with 35.6% overall (probability 0.0025).

The fact that so few of the factors analysed show any significance demonstrates that the views of respondents on all the topics investigated are extremely consistent across all categories of respondents.

17.2.7 Perception of severity of illness

The final two sets of questions in the questionnaire asked respondents to rate on a five point scale firstly how they perceived the degree of impairment that might be caused to individuals by ten different conditions including APKD and secondly how others, for example the manager of a life insurance company, might view these conditions. The descriptions used in the two sets of questions were different, the first using: very mild: mild; moderate; severe; very severe, and the second using: normal; slight increase; moderate increase; high increase; unacceptable, all with reference to the extent to which the hypothetical manager of a life insurance company might increase the cost of insurance above the normal level.

The responses are shown in Tables 17.2.18 and 17.2.19, in the approximate order of severity as assessed by the respondents. Further analysis of these results appears in Section 17.3, after the results for the haemophilia population have been discussed.

Table 17.2.18

APKD population: numbers assessing each degree of impairment for each condition shown.

	Very mild	Mild	Moderate	Severe	Very severe
AIDS	-	1	15	13	165
Cancer	2	-	22	63	107
Previous heart attack	4	14	98	65	13
Chronic bronchitis	4	22	78	75	15
APKD	10	23	82	57	22
Epilepsy	19	27	113	27	8
Diabetes	17	52	96	25	4
High blood pressure	19	53	93	26	3
Stomach ulcer	27	58	92	15	2
Overweight	50	66	73	4	1
Total	152	316	762	370	340
% out of 1,940	7.8	16.3	39.3	19.1	17.5

Table 17.2.19

APKD population: numbers assessing how others might assess each degree of impairment for each condition shown.

	Normal	Slight	Moderate	High	Unacc-eptable
AIDS	2	1	9	11	171
Cancer	3	3	13	65	110
Previous heart attack	4	26	61	90	13
Chronic bronchitis	13	37	82	54	8
APKD	19	38	55	61	21
Epilepsy	25	49	90	26	4
Diabetes	50	66	56	20	2
High blood pressure	46	69	54	20	5
Stomach ulcer	76	70	44	4	-
Overweight	88	66	30	9	1
Total	326	425	494	360	335
% out of 1,940	16.8	21.9	25.5	18.6	17.3

17.3 THE HAEMOPHILIA POPULATION

17.3.1 Characteristics of the population

Only 90 respondents were accrued to the study in the time available. The questions asked were almost the same as those that the APKD population was asked, modified only as necessary. There were 51 females (56.7%) and 39 males (43.3%). All but one of the males had haemophilia; 32 females were known carriers of haemophilia; 4 females had von Willebrand's disease, which is a bleeding disorder similar to haemophilia that can also affect women. Tables 17.3.1 to 17.3.5 show the demographic details of the population on the same lines as for the APKD population, including, where appropriate, the percentage distribution in the APKD population. In most cases the two populations were similar.

Table 17.3.1

Haemophilia population: subdivided by marital status and sex.

	Female	Male	Total	%	% APKD
Single	4	24	28	31.1	29.9
Married	38	13	51	56.7	55.7
Widowed	2	-	2	2.2	7.2
Divorced or separated	7	-	7	7.8	5.7
Other	-	2	2	2.2	1.5
Total	51	39	90	100.0	100.0

Table 17.3.2

Haemophilia population: subdivided by age group and sex.

	Female	Male	Total	%	% APKD
15-19	1	2	3	3.3	13.4
20-24	4	11	15	16.7	12.4
25-29	5	7	12	13.3	13.9
30-34	13	5	18	20.0	13.9
35-39	12	3	15	16.7	13.4
40-44	7	4	11	12.2	6.2
45-49	4	4	8	8.9	7.7
50-59	3	3	6	6.7	9.8
60 and over	2	-	2	2.2	9.3
Total	51	39	90	100.0	100.0

Table 17.3.3

Haemophilia population: subdivided by 'relationship to disease' and sex.

	Female	Male	Total	%
Affected male	-	38	38	42.2
von Willebrand's	4	-	4	4.4
Female carrier	32	-	32	35.6
Female, not carrier	3	-	3	3.3
Female, carrier status not known	3	-	3	3.3
Spouse of affected male	9	-	9	10.0
Spouse of female carrier	-	1	1	1.1
Total	51	39	90	100.0

Table 17.3.4

Haemophilia population: subdivided by number of children and sex.

	Female	Male	Total	%	% APKD
None	5	26	31	34.4	39.2
One	11	2	13	14.4	18.0
Two	21	5	26	28.9	23.2
Three	8	5	13	14.4	11.3
Four	3	1	4	4.4	4.6
Five or more	3	-	3	3.3	3.6
Total	51	39	90	100.0	100.0

Table 17.3.5

Haemophilia population: subdivided by number of grandchildren and sex.

	Female	Male	Total	%	% APKD
None	48	38	86	95.6	85.6
One or more	3	1	4	4.4	14.4
Total	51	39	90	100.0	100.0

17.3.2 Testing of children for haemophilia

Respondents were asked whether they thought that their daughters (or granddaughters) should be tested for haemophilia carrier status. Over 85% of them (77 out of 90 or 86%) said that they thought that their daughters should be tested. The proportion is not very different from that in the APKD population (79%) (see Table 17.3.6), and the proportions giving other answers were also similar.

Table 17.3.6

Haemophilia population: responses to 'should your daughters be tested for haemophilia carrier status', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	44	33	77	85.5	79.4
No	2	3	5	5.6	7.2
Already tested	4	1	5	5.6	4.6
Not applicable	1	-	1	1.1	3.1
Don't know	-	2	2	2.2	5.7
Total	51	38	90	100.0	100.0

Respondents were asked at what age (of the child) they would like to know whether their daughter had inherited haemophilia carrier status. The responses, subdivided by sex, are shown in Table 17.3.7a. The distribution of responses is similar to that for the APKD population, a majority favouring early testing, and a second group favouring higher ages, but starting in the 10-14 group rather than in the 15-19 group.

Table 17.3.7a

Haemophilia population: responses to 'at what age would you like to know whether your daughter had haemophilia carrier status', subdivided by sex.

	Female	Male	Total	%	% APKD
Prenatally	18	14	32	35.6	34.0
0-4 years	12	13	25	27.8	24.7
5-9 years	2	2	4	4.4	5.2
10-14 years	8	4	12	13.3	4.6
15-19 years	6	4	10	11.1	8.8
20 years & over	2	-	2	2.2	7.2
Don't know	3	2	5	5.6	15.5
Total	51	39	90	100.0	100.0

Respondents were asked at what age they would like to know whether their son had haemophilia. The answers are given in Table 17.3.7b. The choice is really between prenatal and postnatal knowledge; a haemophiliac male is usually identified at quite an early age. Rather more than half (57%) favoured prenatal knowledge.

Table 17.3.7b

Haemophilia population: responses to 'at what age would you like to know whether your son had haemophilia', subdivided by sex.

	Female	Male	Total	%
Prenatally	31	20	51	56.7
0-4 years	20	18	38	42.2
5-9 years	-	1	1	1.1
Total	51	39	90	100.0

17.3.3 Screening of relatives for haemophilia

In answer to the question whether other members of the family (e.g. aunts, sisters, cousins) who may be at risk for haemophilia carrier status should be told of their risk, a large majority (80 or 89%) were in favour, just as for APKD. See Table 17.3.8.

Table 17.3.8

Haemophilia population: responses to 'should your relatives be told of their risk of haemophilia carrier status', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	46	34	80	88.9	92.3
No	2	3	5	5.6	2.6
Don't know	3	2	5	5.6	5.2
Total	51	39	90	100.0	100.0

When asked whether these same relatives should be tested for haemophilia a few changed their answers to 'no', again just as for APKD. Fewer than among the APKD population replied that their relatives had already been tested. See Table 17.3.9.

Table 17.3.9

Haemophilia population: responses to 'should your relatives be tested for haemophilia carrier status?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	40	27	67	74.4	68.6
Already tested	3	6	9	10.0	21.6
No	1	3	4	4.4	3.6
Not applicable	2	-	2	2.2	1.5
Don't know	5	3	8	8.9	4.6
Total	51	39	90	100.0	100.0

17.3.4 Prenatal screening and termination of pregnancy

Respondents were asked whether they thought couples should take a test, if such a test were to become available, to test a male fetus for haemophilia prenatally. As for the APKD population a majority (72%) thought that couples should take such a test. See Table 17.3.10.

Table 17.3.10

Haemophilia population: responses to 'should couples take a test for haemophilia during pregnancy?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	39	26	65	72.2	69.1
No	7	7	14	15.6	18.6
Don't know	5	6	11	12.2	12.4
Total	51	39	90	100.0	100.0

One more respondent thought that they personally would take such a test to see whether the baby had haemophilia. See Table 17.3.11.

Table 17.3.11

Haemophilia population: responses to 'would you consider taking a test for haemophilia during pregnancy?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	39	27	66	73.3	69.6
No	11	12	23	25.6	21.6
Don't know	1	-	1	1.1	8.8
Total	51	39	90	100.0	100.0

When respondents were asked whether they would take such a test if it were to followed by termination of pregnancy if it were shown that the baby had haemophilia, a considerable majority (70%) replied that they would not, just as for the APKD population. See Table 17.3.12.

Table 17.3.12

Haemophilia population: responses to 'would you consider taking a test followed by termination if the baby had haemophilia?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	11	4	15	16.7	14.9
No	35	28	63	70.0	61.9
Don't know	5	7	12	13.3	23.2
Total	51	39	90	100.0	100.0

The responses to the questions about prenatal diagnosis followed by termination of pregnancy in the first or the second trimester of pregnancy were very similar to those for the previous question, and similar to those for APKD. All but 15 (16.7%) gave the same answers to all three questions (8 'yes' to all three; 61 'no' to all three; 6 'don't know' to all three), very similar to the APKD responses. It made little difference to the

responses whether termination of an affected fetus could be carried out in the second or the first trimester of pregnancy. See Tables 17.3.13 and 17.3.14.

Table 17.3.13

Haemophilia population: responses to 'would you consider testing followed by termination in the second trimester?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	6	2	8	8.9	12.9
No	39	28	67	74.4	63.9
Don't know	6	9	15	16.7	23.2
Total	51	39	90	100.0	100.0

Table 17.3.14

Haemophilia population: responses to 'would you consider testing followed by termination in the first trimester?', subdivided by sex.

	Female	Male	Total	%	% APKD
Yes	12	5	17	18.9	18.6
No	35	27	62	68.9	57.7
Don't know	4	7	11	12.2	23.7
Total	51	39	90	100.0	100.0

17.3.5 Termination of pregnancy

The views of respondents when asked which of three statements best reflected their views on termination of pregnancy are shown in Table 17.3.15. The proportions are quite similar to those for the APKD population, with a majority considering that it should be available sometimes.

Table 17.3.15

Haemophilia population: responses to 'which best represents your views on termination of pregnancy?', subdivided by sex.

	Female	Male	Total	%	% APKD
Available on request	4	10	14	15.6	18.6
Available sometimes	40	23	63	70.0	66.5
Totally against	7	6	13	14.4	14.4
Total	51	39	90	100.0	100.0

The responses to the question about which of the seven circumstances, relating to the situation of the mother, could justify termination of pregnancy are shown in Table 17.3.16. The proportions saying 'yes' are similar to those in the APKD population, and the sequence of proportions is identical.

Table 17.3.16

Haemophilia population: numbers replying 'yes' to 'would you consider termination of pregnancy in the circumstances described?', subdivided by sex.

	Female	Male	Total	%	% APKD
One parent has AIDS	30	28	58	64.4	64.9
Mother's physical health	32	26	58	64.4	64.4
Mother's mental health	28	18	46	51.1	47.4
Mother a young teenager	9	8	17	18.9	12.9
Mother over 40	6	4	11	11.1	9.8
Family too large	7	-	7	7.8	4.6
Mother unmarried	5	2	7	7.8	3.1
Maximum	51	39	90	100.0	100.0

The same is true for the question relating to the views of respondents on termination early in pregnancy for ten specific conditions from which the baby might suffer, as shown in

Table 17.3.17. The proportions are similar to those for APKD and the sequence is identical.

Table 17.3.17

Haemophilia population: numbers replying 'yes' to 'would you favour termination of pregnancy if it could be determined early in the pregnancy that the baby would definitely have the condition described?', subdivided by sex.

	Female	Male	Total	%	% APKD
AIDS	34	29	63	70.0	68.6
Severe mental handicap	32	27	59	65.6	66.0
Severe physical handicap	29	27	56	62.2	60.3
Disease likely to cause death before age 5	16	22	38	42.2	39.2
Disease likely to cause death aged 6-10	13	18	31	34.4	30.9
Disease likely to cause death aged 11-15	12	16	28	31.1	25.3
Haemophilia	9	5	14	15.6	23.2
Mild mental handicap	8	6	14	15.6	12.9
Slight physical handicap	5	3	8	8.9	7.7
Maximum	51	39	90	100.0	100.0

17.3.6 Analysis by sub-groups

As for the APKD population, the responses to the 27 questions asked so far about testing, screening and termination were analysed by each of the six possible explanatory variables, to see whether there were any significant differences in the responses according to sex, age, marital status, relationship to the disease, number of children or number of grandchildren. The same Pearson statistic was calculated and compared with χ^2 for the appropriate number of degrees of freedom.

Only two of the 162 tests showed probabilities of χ^2 that were less than 0.01. The apparently significant results noted below might therefore be the result of chance. Both relate to attitudes to termination for specific reasons.

Marital status: those who were single and also those who were divorced, separated or 'other' were more likely to favour termination if the baby was likely to die before the age of 5. While overall only 42.2% were in favour, 57.1% of the single (16 out of 28) and 77.8% of the divorced (7 out of 9) were in favour (probability 0.0070).

Number of children: those with only one child were less likely to favour termination for a baby that might have AIDS. While overall 64.4% were in favour, among those with one child only 30.8% (4 out of 13) were in favour (probability 0.0046).

17.3.7 Perception of severity of illness

The final two questions, as for the APKD population, asked respondents to rate on a five point scale firstly how they perceived the degree of impairment that might be caused to individuals by ten different conditions including haemophilia and secondly how others, for example the manager of a life insurance company, might view these conditions.

The responses are shown in Tables 17.3.18 and 17.3.19, in the approximate order of severity as assessed by the respondents. Further discussion of these results, in conjunction with those for the APKD population, follows in Section 17.4.

Table 17.3.18

Haemophilia population: numbers assessing each degree of impairment for each condition shown.

	Not given	Very mild	Mild	Mode-rate	Severe	Very severe
AIDS	5	1	-	3	9	72
Cancer	8	2	4	10	25	41
Previous heart attack	7	5	8	47	19	4
Haemophilia	8	6	10	33	26	7
Chronic bronchitis	6	2	7	27	39	9
Epilepsy	6	6	16	43	17	2
Diabetes	6	7	27	32	18	-
High blood pressure	5	7	26	40	10	2
Stomach ulcer	5	9	29	41	6	-
Overweight	5	25	31	24	2	3
Total	61	70	158	300	171	140
% of 839	-	8.3	18.8	35.8	20.4	16.7

Table 17.3.19

Haemophilia population: numbers assessing how others might assess each degree of impairment for each condition shown.

	Not given	Normal	Slight	Mode-rate	High	Unacc-eptable
AIDS	7	1	-	1	7	74
Cancer	8	2	1	6	29	44
Previous heart attack	8	3	10	27	38	4
Haemophilia	8	5	15	25	21	16
Chronic bronchitis	7	6	11	33	27	6
Epilepsy	8	6	18	36	17	5
Diabetes	7	11	31	33	7	1
High blood pressure	7	13	35	27	6	2
Stomach ulcer	7	28	32	17	5	1
Overweight	7	24	38	15	4	2
Total	74	99	191	220	161	155
% of 826	-	12.0	23.1	26.6	19.5	18.8

17.4 ANALYSIS OF THE PERCEPTIONS OF THE SEVERITY OF ILLNESS

Tables 17.2.18, 17.2.19, 17.3.18 and 17.3.19 show the numbers of respondents in the APKD and the haemophilia populations who rated eleven conditions (ten each, including APKD for the APKD population and haemophilia for the haemophilia population, but not *vice versa*), first in order of severity as perceived by themselves, and secondly in order of severity as the condition might be perceived by others. In this section the two sets of results are compared.

For these comparisons the ridits for all questions were used. All four sets of answers for all eleven questions were combined, and aggregate ridits were calculated. Table 17.4.1 shows the calculation.

Table 17.4.1

Combined populations: calculation of ridits for degree of impairment for ten conditions.

Self-assessment:	Very mild	Mild	Mode-rate	Severe	Very severe	
Others:	Normal	Slight	Mode-rate	High	Unacc-eptable	Total
APKD self	152	316	762	370	340	1,940
APKD others	326	425	494	360	335	1,940
Haemophilia self	70	158	300	171	140	839
Haemophilia others	99	191	220	161	155	826
Total	647	1,090	1,776	1,062	970	5,545
Ridits	0.0583	0.2150	0.4734	0.7293	0.9125	

The ridit for the first column is calculated as the average cumulative proportion in that cell or ½×647/5,545 = 0.0583; that for the second as (647 + ½×1,090)/5,545 = 0.2150; and so on. The average ridit for all cases is necessarily 0.5.

The average ridit for each condition, for each population, and the average ridit for all conditions were then calculated, and the results are shown in Table 17.4.2, with the conditions being ranked in order of overall average ridit. Although there were some differences in the average ridits, the ranking of the impairments was similar for each of the populations, and for both self-assessment and assessment by others. Thus AIDS came first in every list, followed by cancer. The next four, previous heart attack, haemophilia, chronic bronchitis and APKD, changed sequence among themselves but always came after cancer and before epilepsy, which always came next. High blood pressure and diabetes filled the next two positions, in either order, and stomach ulcer and overweight always filled the last two places, in either order.

There is no doubt that the respondents had a clear order of severity among the different conditions, which are not ranked all equal in any of the four sets of results. A Kruskal-Wallis test (Agresti 1984 p182) on the average ridits shows that the average levels of the four sets are not the same, although they are fairly close. The APKD self-assessment has a significantly higher overall average ridit (0.5245), and the APKD assessment by others has a significantly lower overall average ridit (0.4703) than either of the haemophilia sets, which do not themselves differ significantly from one another.

Table 17.4.2

Both populations: average ridits for each of eleven conditions for APKD and haemophilia populations, for self-assessment and for assessment by others.

		APKD self	APKD others	Haemo-philia self	Haemo-philia others	Total
1	AIDS	0.8627	0.8693	0.8676	0.8815	0.8686
2	Cancer	0.7944	0.7977	0.7482	0.7862	0.7875
3	Previous heart attack	0.5614	0.5784	0.5032	0.5667	0.5594
4	Haemophilia	-	-	0.5301	0.5520	0.5410
5	Chronic bronchitis	0.5684	0.4856	0.6078	0.5241	0.5388
6	APKD	0.5463	0.5101	-	-	0.5282
7	Epilepsy	0.4505	0.3980	0.4568	0.4661	0.4354
8	Diabetes	0.4098	0.3094	0.4106	0.3487	0.3657
9	High blood pressure	0.4032	0.3208	0.4006	0.3285	0.3629
10	Stomach ulcer	0.3627	0.2228	0.3594	0.2544	0.2972
11	Overweight	0.2860	0.2113	0.2786	0.2580	0.2546
	Total	0.5245	0.4703	0.5155	0.4962	0.5000

The Kruskal-Wallis test can be used to show whether any of the differences between mean ridits for the four sets for any of the individual conditions are significant. In the two populations there were 24 such overall comparisons, of which two in each population showed probabilities less than 0.02.

For the APKD population, in the assessment of others, those who were 15-19 or in the 35-39, 40-44 or 45-49 age groups ranked the conditions more seriously overall than those in the intermediate (20 to 34) and higher (over 50) age groups. The average ridit for the 45-49 age group (0.584) was the highest (probability 0.0011).

For the APKD population, in the assessment of others, those who had no grandchildren ranked the conditions more seriously overall than those with some grandchildren, particularly those with four or more (average ridit 0.422) (probability 0.0016). This may be associated with the previous result, because naturally those with grandchildren are older and all of those with four or more grandchildren were over 50.

For the haemophilia population, in the self-assessment, males (average ridit 0.467) ranked the condition less severely than females

(average ridit 0.527) (probability 0.020). This is particularly influenced by the low ranking given by males to haemophilia, as noted below.

For the haemophilia population, in the self-assessment, those who are affected (and therefore all males) ranked the condition less seriously than the others, all but one of whom were females (probability 0.0188). This is the same point as the preceding one.

The Kruskal-Wallis test can also be used to compare the rankings for sub-sets of the population for any one condition or for all conditions combined. There are six possible explanatory variables: sex, age, marital status, relationship to disease, number of children and number of grandchildren, and tests of each variable with each of the ten conditions, for both self-assessment and assessment by others, within each population were carried out. This gives 120 tests within each population. It is only reasonable to look at those which gave a probability level of less than 1 in 100 or 0.01, and even then one should expect one or two tests to show significance in such a number.

Four of the tests in the APKD population showed probability levels of less than 0.01, and two in the haemophilia population. While some of these appear to have little logic, others are, however, of interest.

In the APKD population the following tests showed probabilities less than 0.01:

Sex and other's assessment of chronic bronchitis: males assess this condition more seriously than females (average ridit 0.575 against 0.453, probability 0.0024). Although the average ridit for males for the haemophilia population is also greater than that for females, the difference is far from significant (probability 0.4454), and the average ridits for self-assessment for both populations are quite close.

Age and overweight for self-assessment: those in the 15-19 and 20-24 age groups assess this condition as less serious than older people (probability 0.0057); there seems little reason for this, and little supporting evidence in the other population.

Age and APKD for self-assessment: those in the 15-19, 20-24 and 25-29 age groups assess this as more serious than those who are older (probability 0.0075); however, this is best explained by consideration of the next significant test.

Relationship to disease and APKD for self-assessment: those who are affected and the spouses of those who may be affected or at risk assess this condition much less severely (average ridits 0.452 and 0.420 respectively) than those have been screened and been found unaffected

(average ridit 0.594) and those who are at risk but unscreened (average ridit 0.625) (probability 0.0010). The connections with age (see the previous test) are that spouses are substantially older than average and those at risk but unscreened are substantially younger than average. The same tendency can be seen in the assessment of others, but not to a significant extent.

This last significant result is of importance, and is corroborated by the two results from the haemophilia population that show probabilities less than 0.01:

Sex and haemophilia for self-assessment: males (who are almost all affected) assess this condition as much less serious than do females (average ridit 0.414 against 0.574, probability 0.0089).

Sex and haemophilia for assessment by others: the same is true as in the previous test; males expect others to assess this condition as less serious than do females (average ridit 0.407 versus 0.576, probability 0.0068).

17.5 Discussion

The first observation to make about these results is the high degree of agreement between the results of the APKD and the haemophilia populations. The majority of respondents in both populations would like to know at a young age whether or not their child had APKD or their daughter was a carrier of haemophilia or their son had haemophilia, with a slightly greater number in both populations favouring knowing about the situation prenatally than at age 0-4. An even greater proportion (98%) would wish to know at an early age that their son had haemophilia; this may be explained by the fact that the sooner there is an accurate diagnosis of haemophilia the sooner appropriate treatment can be given.

The great majority of respondents in both populations (APKD 92%, haemophilia 89%) thought that relatives should be told of their risk with a slightly smaller but still considerable majority believing that relatives should be tested for APKD or haemophilia carrier status. This finding could be interpreted in a variety of ways. If both APKD and

haemophilia respondents perceived the respective illnesses as very serious then they themselves may cope by denying the genetic nature of the illness as some people with Huntington's chorea have been reported to do (Phillips 1982). However the evidence from the findings of this study suggests that respondents may simply think that such genetic information is important for relatives to have and that there are unlikely to be any problems for the relatives in receiving such information or in getting such information to the relative. These respondents do not deny the presence of the illness.

The majority of both populations (70% APKD and 73% haemophilia) would consider having prenatal diagnosis for APKD and haemophilia. This is consistent with their desire to know at an early age whether or not their child is affected.

Although the majority of both sets of respondents would consider prenatal diagnosis, the majority (62% APKD and 70% haemophilia) would not consider prenatal diagnosis to be followed by termination of pregnancy. The availability of termination in the first trimester of pregnancy marginally increased the percentage of those who would favour termination of fetus affected by APKD or haemophilia to 18% in both populations.

These findings are in contrast with those of Hodgkinson et al (1990) where only a minority of the APKD population studied said that they would be interested in prenatal diagnosis for APKD. It is not known from the Hodgkinson study whether respondents assumed that termination of a fetus with APKD would normally follow prenatal diagnosis. Prenatal diagnosis is usually offered with the intention that if a serious abnormality is detected then the woman may have her pregnancy terminated (Henderson 1987) and indeed some obstetricians restrict prenatal diagnosis only to patients who will make a prior decision to terminate the pregnancy in the event of a positive diagnosis (Richards 1987).

In the current study, respondents were asked their views of prenatal diagnosis, not associated with termination. Respondents had also made it clear that they favoured early

knowledge of APKD or haemophilia in their child, either prenatally or from birth to 4 years. A possible explanation is that the interests of those considering having prenatal diagnosis on one hand and the obstetricians on the other may be different. Farrant (1985) points to a significant difference in the perspective of the professionals, the obstetricians, and the laity, the parents, considering prenatal diagnosis and suggests that for the majority of women the prime goal of fetal diagnosis is to obtain reassurance about the good health of their fetus while obstetricians place priority on the diagnosis and termination of an affected fetus.

Neither the APKD nor the haemophilia population is against, in principle, termination of pregnancy, with considerable agreement demonstrated between the populations. The majority of both populations believe that termination of pregnancy should be available sometimes and both populations display consistent and identical discriminatory views as to the circumstances in which they consider it appropriate for termination of pregnancy to be carried out. If one parent has AIDS and for reasons of the mother's physical health are seen as the two most important reasons with respondents expressing less certainty about reasons of the mother's mental health. There is little support for termination of pregnancy for reasons of the mother's age, for the size of the family or for the marital status of the mother.

Over 60% of respondents in both populations were in favour of termination early in pregnancy if it could definitely be shown that the fetus would have AIDS, severe mental handicap or severe physical handicap. Respondents were also quite consistent in their views on termination of pregnancy for illnesses where the child would die before 5 years old, between 6-10 and between 11-15 with more support for termination when the child might die younger. Only 15% of the APKD population would consider termination of pregnancy for a fetus with APKD and 15.6% of the haemophilia population would

consider termination of pregnancy for haemophilia. This part of the study was carried out in 1986/7 when media coverage of HIV and AIDS was high and this may help explain the emphasis on the severity of AIDS by both populations.

It is clear that while both populations are in favour of termination of pregnancy for specific 'serious conditions' neither population views their respective disorders as sufficiently serious to merit termination.

When the results of patients' perceptions of serious illness are examined, an interesting finding is that respondents affected by APKD perceive APKD much less severely than the screened unaffected and the at risk but unscreened. A similar finding was found in the haemophilia population where male respondents, who were almost all affected by haemophilia, perceived haemophilia to be much less serious than did female respondents. In a parallel study in which the researcher was involved, HIV positive and HIV negative haemophiliacs were asked the same rating questions to assess the perception of HIV. An examination of the self ratings of HIV antibody positive patients on the seriousness of HIV showed that this sub-group of patients did not consider HIV to be such a serious condition as did other sub-groups in the study, all of whom were HIV antibody negative (Markova et al 1990). These authors offered explanations for their findings (p78):

> "One possibility is that their coping strategy was to deny the seriousness of HIV ... Another possible reason for diminishing the seriousness of HIV infection is that the severely affected patients who were HIV antibody positive had overcome many of the life threatening problems of haemophilia and for these patients HIV infection was yet another problem to cope with and therefore relatively of a smaller importance than for those with mild/moderate haemophilia".

In the above example the HIV antibody positive haemophiliacs may be 'distracted' from HIV by the problems created by their severe haemophilia. However that argument does not apply to the APKD population. Another possible explanation is that the HIV antibody haemophiliacs have spent their life overcoming the problems of haemophilia and

HIV is merely a continuation of that. This explanation would apply to the APKD population where many of the affected respondents have experienced some of the symptoms and treatments for APKD.

The medical definition of ill-health is largely based on objectively demonstrable physical changes in the structure of the body or function of the body. These changes can be quantified by reference to 'normal' physiological measurements and according to Fabrega and Silver (1973) it is often assumed that these changes are the same regardless of the society or culture in which they appear. This medical model of ill health does not include factors which clarify the meaning of the illness for the patient. It is likely that many doctors would define APKD as a serious illness. It is also likely that insurance underwriters would also view APKD as serious. As Brackenridge (1977 p383) states:

> "It is obvious that applicants who are known to suffer from familial polycystic disease of the kidneys cannot be offered terms for ordinary life assurance."

If our society is able to continue to offer the same or improved standard of treatment and care for people with APKD then it is unlikely that the perceptions of patients to APKD will change. However if more stringent rationing of health resources is introduced and dialysis and transplant facilities are reduced, then the perceptions of people with APKD to this illness may change.

CHAPTER 18: DISCUSSION OF FINDINGS AND CONCLUSIONS

This thesis was concerned with knowledge, perceptions and understanding of genetic counselling amongst patients with APKD.

18.1 Experience of genetic counselling

The information for this study was collected retrospectively from patients attending the Renal Unit of Glasgow Royal Infirmary. There had been no particular policy in the Renal Unit to give genetic counselling to patients with APKD. Yet at the time of the first interview 75% of patients remembered receiving some genetic counselling and this had in the great majority of cases been given by doctors in the Renal Unit. So some genetic counselling was being included in the management of the patients.

18.2 Knowledge of symptoms and treatment

The majority of respondents at the time of the first interview knew about anti-hypertensive therapy, transplant and haemodialysis as treatments. In addition two-thirds of respondents recollect being told about cysts.

Patients were not asked in the study what they understood by 'cysts', and it is not known what patients think a cyst is. Is a cyst a growth which may be cancerous, or do cysts simply go away? Furthermore, it is doubtful whether the meaning attached to renal cysts by renal physicians would be the same as the meaning for the patients. The cysts of APKD resemble blisters. But blisters burst and go away, with the skin usually healing afterwards. So there is a potential knowledge gap between the professional and the lay, in that patients may not be told of the implications of the presence of renal cysts in APKD for normal renal function.

By the third interview patients were generally knowledgeable about the symptoms and treatment of APKD. However, information about the symptoms of and treatments for APKD were perceived by patients in both the first and third interviews as the two most important elements to be included in genetic counselling. This finding supports the suggestion by Gerhardt (1990) that, as new and more effective treatments become available for chronic illnesses, the expectation of what medicine has to offer can lead patients into searching for more information that makes more sense to them. It is also possible that this search by patients for information gives them a sense of security, as suggested by Moscovici and Hewstone (1983). A sense of security could be particularly important for patients suffering from a chronic illness such as APKD which by the very variability of the illness may create considerable uncertainty for the patient. Knowledge may also give the patient a feeling of control over an illness over which there is actually no control.

Lay organisations can be a very helpful source of information for patients. Such organisations often produce useful literature about the disease as well as providing opportunities for members to meet. Very few patients in this study were members of the local Kidney Patients Association (see Appendix B.10). At the time of the study there was no specific APKD organisation.

In view of the finding of the importance of knowledge of the symptoms and treatment of APKD for patients and, considering how complicated renal medicine is as well as how many and varied are the functions of the kidneys, I would recommend that in genetic counselling patients with APKD be given some written information about renal function, and the symptoms of and treatments for APKD. In addition some patients may find references such as Gabriel's *A Patient's Guide to Dialysis and Transplantation* (1981)

or Mills's *The Gift of a Kidney* (1992) helpful. Patients should also be told about the Kidney Patients Association and be given a contact address.

18.3 PREVENTION IN GENETIC COUNSELLING

The topics most frequently remembered by respondents as having been included in genetic counselling were the risk to children, having no more children, sterilisation and prevention of APKD, and so this model of genetic counselling falls firmly into the second paradigm of genetic counselling described in Chapter 2.

It is not surprising that renal physicians in giving genetic counselling should be concerned with prevention. Renal physicians are likely to be aware of the extent of the medical and social problems associated with APKD. Some may be concerned about the costs of treating renal patients including those with APKD. In 1983, Gabriel and also Pincherle and Mancini, in a symposium on renal medicine, discussed the problems of scarce resources and escalating costs of the treatment for patients in ESRF. And in 1992 Sibbald et al and Wilkie et al, in their study on prescribing at the hospital-general practitioner interface, demonstrated that hospitals in England and Wales were cutting back on the prescribing of drugs such as erythropoietin used in the treatment of anaemia in patients with ESRF. APKD can be an expensive illness. It is therefore not surprising that doctors concentrate on the prevention of future cases of APKD.

18.4 WHO SHOULD GIVE GENETIC COUNSELLING?

A majority of respondents were in favour of genetic counselling being given by doctors in the renal unit, although a rather larger number of patients preferred a specialist genetic counsellor. The possibility of research bias in this last result has already been referred to in Section 14.7. Nevertheless this finding would suggest the usefulness of

having a specialist non-medical counsellor as part of the team, who could give genetic counselling and could evaluate the results. In the United Kingdom, genetic counselling has traditionally been given by doctors. However, gradually other professionals including specialist nurse counsellors, psychologists and other social scientists are becoming involved.

Patients were not asked whether they would be prepared to go to another hospital or place for genetic counselling, but it was evident from comments made by patients that they did not wish to have to make a journey to another hospital for genetic counselling. In some hospitals it is possible that the genetic department and the renal unit are in the same building, and genetic counselling could then be offered by the genetic department. However, in the foreseeable future it is likely that genetic counselling will be given to patients with APKD by renal unit staff.

18.5 THE ORGANISATION OF GENETIC COUNSELLING

Most patients remembered having received genetic counselling on one occasion only, during a routine medical consultation, and on their own. A genetic illness has implications not only for the person with the illness but also for other family members. In this study there was seldom a record kept of the information that had been given to patients. The information in genetic counselling is complex and the patient may find it difficult to remember, particularly if he or she becomes distressed. I would, therefore, recommend that when genetic counselling for APKD is given by doctors in a renal unit:

(a) a separate appointment be made especially for genetic counselling;

(b) the patient be invited and encouraged to bring their partner, other family member or friend; and

(c) a record of the discussion, which may be in the form of a letter to the patient detailing the discussion, be kept in the patient's notes.

18.6 KNOWLEDGE OF INHERITANCE AND TRANSMISSION

The concept of genetic information must include information both about the inheritance of the illness and about the pattern of transmission. It is a misconception to assume that if a person understands that they have inherited APKD then they also understand that they have the ability to pass the illness on to the next generation. The objective assessment of risk may be described as the probability of some unwanted outcome multiplied by the severity of that outcome. But Pearn (1973) suggests that the subjective interpretation of risks by patients in genetic counselling is much more complex than this.

There is another possible explanation why patients may have difficulty in understanding genetic inheritance and transmission. In Chapter 5 different ways used by lay persons to explain their illness were described. Blaxter (1983), in her study of the attitudes of Scottish women to health and disease, found that the most commonly cited cause of illness was family susceptibility and heredity. However, these family susceptibilities were often seen as inherited weaknesses. This attitude was also found amongst some of the respondents in Herzlich's (1973) study, who restricted the meaning of heredity to abnormality and social weakness. It is not surprising that such views of heredity associated with abnormality and social weakness should be held by some lay people, since these were the views of the 'professionals' in paradigm 1 described in Section 2.3.

Furthermore, the gene is 'inside the body' and therefore difficult to fight, thus discouraging patients from accepting heredity as the cause of their illness. It is also

arguable that, apart from the speciality of clinical genetics, the medical profession appears to have been relatively slow to accept heredity as the cause of illness, although this may change in the future with the mapping of the human genome. Doctors may then be more ready to attribute the cause of illness as genetic and this may then influence lay ideas about the cause of illness.

18.7 Language of genetics

In this study patients showed some confusion in their understanding of the genetics of APKD. In the first interview while 72% of respondents knew that APKD was 'inherited' only 59% reported that APKD was 'genetic'. Furthermore 67% knew that APKD 'ran in the family'.

While 80% of respondents said that APKD could be passed on, only a small minority understood how APKD is passed on. This finding was confirmed in the third interview with respondents showing considerable uncertainty about whether on average half the children of an affected person are at risk of developing APKD or all the children are at risk. These findings suggest that some of this group of patients found it difficult to understand that all the children of an affected person are at risk of inheriting APKD but on average only half of these children will become affected. This is a difficult concept to understand. It is also a difficult concept to explain, and it is possible that some of the doctors themselves were unsure about this principle. However, if patients are to make informed choices based on the information they receive in genetic counselling then it is important that this information be clearly explained to them. I would, therefore, recommend that patients be given some written information about the genetic inheritance and transmission of APKD in their family. This information can then be kept by the patient for reference.

18.8 PERCEPTION OF THE SIZE OF RISK OF APKD

Within the field of clinical genetics, if the risk of transmission of a disease is greater than 1 in 10, then the risk is generally considered to be a high risk and amongst professionals it would be described as such. In this study the majority of respondents thought that the risk of inheriting APKD and the risk of transmitting APKD were both medium risks. Furthermore 65% of respondents knew that the risk of inheriting APKD was 50-50. This is an interesting finding and possibly worthy of further study. It is not illogical for patients to consider a 50-50 risk as a medium risk; the chances each way are equal. However, there may be a problem for those offering genetic counselling, since they may perceive a risk of 50-50 as a high risk and may assume that the patient also thinks this way.

18.9 PERCEPTION OF PROBLEMS ASSOCIATED WITH APKD

In this study patients perceived certain physical problems associated with APKD as more problematic than social problems that may be associated with the illness. In particular Lethargy was seen as the most important problem in both the first and the third interviews. Lethargy is not a symptom normally referred to in articles about APKD, and it is not known whether there is any physiological explanation for this finding. Lethargy is certainly perceived by patients as a very problematic symptom of APKD. This finding may be of interest to renal physicians, and may also be useful when explaining the nature of the illness to patients.

There are two other findings of interest concerning the problems associated with APKD. The first is that female patients found abdominal pain, nausea and sickness much more problematic than did male patients. No reference to this difference in symptoms according to sex has been found in the literature.

The second finding is that male patients found the possible loss of job and reduction in standard of living particularly problematic. Patients with APKD, regardless of the nature of their employment, may find that, as the illness progresses, they have to give up work. However, this is much more likely if they are involved in manual work. Bury (1991) argues that the meaning of chronic illness for the individual is to be found not only in the symptoms of the illness but also in the effect of these symptoms on everyday life at home and at work and that these effects could influence how that patient regards himself.

In order to minimise feelings of worthlessness because the patient no longer has a job, I would recommend that patients with APKD, and particularly male patients, be advised and encouraged to seek employment appropriate to their illness.

18.10 ATTITUDES TO SCREENING AND TESTING OF AT-RISK RELATIVES AND CHILDREN

In this study the very great majority of patients thought that those relatives at risk for APKD should be told of their risk and that they should be tested. It is however important that the interests of individual relatives are considered (Harding 1990). Some relatives may neither wish to know of their risk nor be tested. The confidentiality of all relatives, who are not necessarily patients, must be protected.

Almost all the respondents also thought that their children should be tested, with the majority suggesting that the most appropriate age for children to be tested was between 16 and 20. This finding was also supported by the results from the secondary study on prenatal diagnosis, with the very great majority of both the APKD and the haemophilia populations reporting that their relatives should be told of their risk and should be tested.

The availability of ultrasound had made presymptomatic diagnosis of APKD easy, and the non-invasive nature of ultrasound made it an acceptable procedure for patients. However DNA linkage analysis has possibly made early presymptomatic diagnosis of

APKD even more accurate than ultrasound. The availability of the technology and the desire of patients for genetic information raise questions that have not necessarily been considered previously.

One particular question concerns the possibility of discrimination as a consequence of the diagnosis of a genetic disease and in particular of presymptomatic diagnosis. Authors such as Nelkin and Tancredi (1989) describe the early diagnosis of a presymptomatic illness as 'diagnostic labelling' and, once diagnosed, the way is open to discrimination; similar comments are made by Natowicz et al (1992).

Another form of discrimination concerns life insurance. In this study relatively few patients had experienced difficulties with life insurance (see Appendix B.14). However, it is likely that, if an individual has been presymptomatically diagnosed as having APKD, should that individual apply for insurance, the application would be rejected. A principle of insurance is 'uberrima fides', good faith on both sides. When an applicant knows that there may be a problem that could affect the risk on the policy they must disclose this information otherwise the insurance company may declare the policy void (Wilkie 1987).

Billings et al (1992) found that, because of the fear of discrimination, several respondents in their study either withheld or 'forgot to mention' potentially important medical or family history information to insurers, and some respondents reported that their insurance agents had suggested that they give incomplete or dishonest information on insurance application forms. In the case of APKD it may be many years before symptoms appear by which time the policy may have matured, so there is less risk of any dishonesty being discovered.

Respondents in the study of Billings et al (1992) also experienced discrimination in employment, a problem also faced by some of those who are HIV asymptomatic antibody positive (Anderson and Wilkie 1992). Indeed those working in HIV have been very sensitive to the problems of discrimination in employment that may be faced by those

who are HIV antibody positive and asymptomatic, and such potential difficulties may be included in HIV pretest counselling (Anderson and Wilkie 1992).

The past history of eugenics and the current evidence of genetic discrimination are reminders also of the use of scapegoats, which can be acute in times of economic hardship (Holtzman and Rothstein 1992). Avoiding the birth of a fetus prenatally diagnosed as having a genetic disease is likely to be less expensive to the health services in society than clinical management of the disease.

The findings described above clearly have implications for renal physicians. Should they consider establishing a screening and counselling service to ensure that relatives at risk for APKD can be informed of their risk and offered testing? I would recommend that the concerns about genetic discrimination referred to above and described more fully in Chapter 5 are taken into consideration and included in the information given to any patient considering presymptomatic diagnosis of APKD.

18.11 PERCEPTION OF PRENATAL DIAGNOSIS

The majority of respondents in the secondary study favoured knowing prenatally whether or not their child had APKD and in the parallel haemophilia group the majority of respondents also wanted to know whether or not their daughter was a carrier or their son had haemophilia. Whilst the majority of both these populations would consider prenatal diagnosis, they would not consider prenatal diagnosis followed by termination of pregnancy of a fetus affected by APKD or Haemophilia. It was clear from this secondary investigation into prenatal diagnosis that respondents would like to know the genetic status of their child prenatally. However, the risks of miscarriage from the diagnostic procedures were not discussed with the respondents in this study, since they were given self-administered questionnaires. Nor were the prenatal diagnostic procedures described to the patients.

One possible explanation for this finding, that patients would like to know the genetic status of their child prenatally but would not consider termination of pregnancy either for APKD or for haemophilia, is that all parents have a strong desire to have a 'normal' baby. Parents may also assume that parental love is unconditional. It is also possible that more people stated that they would consider prenatal diagnosis than would actually be prepared to use it.

18.12 Attitudes to termination of pregnancy

Neither the APKD nor the haemophilia population were in principle against termination of pregnancy, with both populations agreeing that termination should be available sometimes. Over 60% of respondents in both populations were in favour of termination early in pregnancy if it could certainly be shown that the fetus would have AIDS, severe mental handicap or severe physical handicap. In comparison only 15% of the APKD population and 16% of the haemophilia population would consider termination of pregnancy for their respective illnesses.

These findings suggest that neither APKD nor haemophilia is viewed as sufficiently serious by respondents for them to consider termination of pregnancy if it could certainly be shown that the fetus had APKD or haemophilia. I believe that this area deserves further research, and I would recommend that there be very careful discussion about what the patients want with those for whom these procedures would be appropriate.

18.13 Perception of seriousness of APKD

Respondents had a very clear idea of the order of severity of several well known illnesses, with AIDS and cancer consistently being perceived as the most serious. APKD, like haemophilia, was ranked as an illness of medium severity. If patients' perception of the burden of the illness is important in their decision about whether to have termination

of pregnancy of a fetus with APKD then it is not surprising that patients with APKD or with haemophilia, who viewed the severity of their respective illnesses as medium, would not consider termination of a fetus affected by these illnesses.

An additional finding was that respondents affected by APKD perceived APKD much less severely than those who had been tested and were unaffected, and less severely than those who were at risk but had not yet been tested. It is not known what proportion of the population at risk for APKD would decline to be tested if testing were offered to them on a systematic basis. It would be relevant to establish whether there were particular characteristics of those who declined testing and in particular whether those who declined to be tested viewed APKD as a serious illness.

18.14 Ethical issues

In the final fourth paradigm of genetic counselling, which was discussed in Section 2.6, I suggested that new technologies in clinical genetics created **ethical** issues that had previously not been addressed. There are three ethical issues that need to be considered: presymptomatic testing; prenatal testing not followed by termination; and the confidentiality of data.

In this study there are two almost contradictory findings. Patients in the main study thought that children should be tested between the ages of 16 and 20; but this was before the gene marker technology was available. Then, when the possibility of prenatal diagnosis of APKD was introduced, respondents in the secondary study were in favour of learning prenatally whether or not their child had APKD. There may be difficulties for any parent about telling their child of that child's risk of having APKD. But if respondents do not discuss this with their child until he or she is older, as the majority of respondents in the main study suggested, then the child can be brought up 'ignorant' of their risk.

To confirm prenatally that the fetus has the gene for an illness where the symptoms do not normally appear until adulthood may raise other difficulties. The parents have still to decide when to tell the child. In addition it is not known whether the fact that the child has the gene for APKD and is very likely to develop symptoms in the future will affect the way that the parents bring up the child. Will this child face discrimination within the family, at school, in employment and with life insurance, because he or she is the carrier of a gene? Will any medical problem that the child develops be attributed to the fact that he or she carries this gene even though the problem is not obviously associated with APKD?

It is not known what are the long term implications of presymptomatic diagnosis of APKD both for the patient and for their parents. These are new problems created by the new technologies and they are worthy of further investigation.

Respondents in the secondary study wished prenatal diagnosis but did not wish this to be followed by termination of an affected fetus. There is an ethical question in whether patients should be offered prenatal diagnosis when they state that they will not consider termination. Prenatal diagnosis itself is not without a small risk and it is a labour-intensive procedure. It is often assumed that prenatal diagnosis would usually be followed by termination of an affected fetus. However, it is interesting to note that more than half the medical geneticists in the study by Wertz (1990) stated that "performance of prenatal diagnosis should not depend on the use that patients intend to make of the information" (p 1210). If the technologies are available and the patients want these tests, who will decide what they can have?

The third ethical issue concerns the confidentiality of data. This topic has already been referred to in Chapter 2. The findings of this study suggest that genetic counselling should be part of the management or care given to patients with APKD attending a renal unit. It is essential that genetic data be confidential. This becomes critical when details of

at risk relatives who are not patients are included in the records. It is not appropriate to hold information about the at risk relatives in the notes of an index patient, since many people have access to patients' notes. Renal physicians considering offering presymptomatic diagnosis of those at risk for APKD will need to consider (a) who has access to the genetic information and (b) how and where this information will be stored.

Those offering genetic counselling also need to consider on one hand their duty to protect the confidentiality of their patient and on the other hand a perceived obligation to offer the genetic information to at risk relatives. When blood samples are required for genetic linkage analysis, it is important that there is an awareness that family pressures on relatives to participate can result in harm to those relatives and to family relationships (Nolan and Swenson 1988).

18.15 FURTHER STUDIES

The study described in this thesis was of an exploratory nature, but I believe that it raises some very critical issues for genetic counselling, issues that are worthy of further investigation, which have been indicated above.

In this thesis a statistical approach to the analysis of the data has been used. Inevitably qualitative data is lost thereby. The study of genetic counselling requires sensitive treatment of the respondent by the interviewer. An alternative and possibly more sympathetic approach to the research would have been to emphasise and use direct quotations from the respondents to highlight particular points. This would have added a richness to the study that is missing in the tabulated numbers. Yet another approach would have been to use video recordings of the interviews, and to analyse body language, hesitations and expressions of the patients. But such methodology would have added length to a thesis that is already long. I would recommend, however, that these alternative approaches should be considered in future by those working in this field.

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