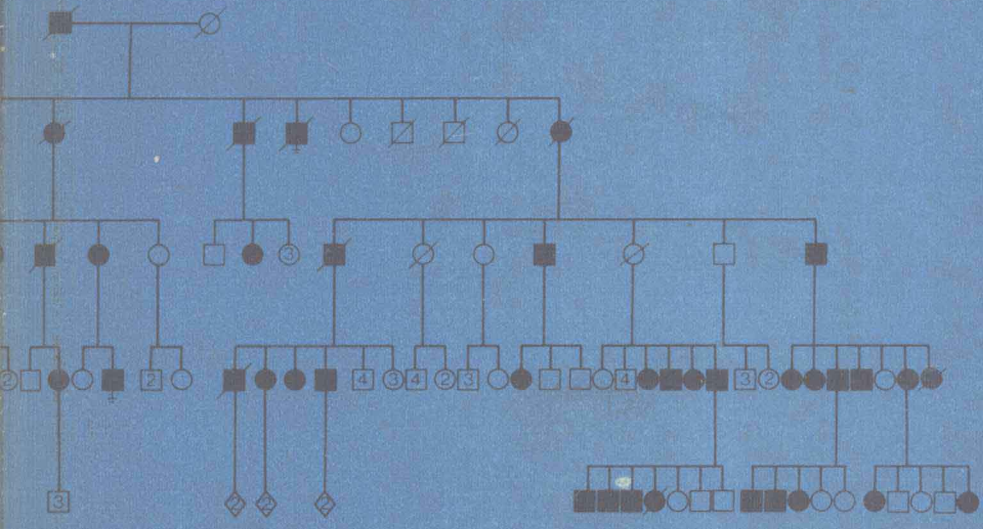
# Practical Genetic Counselling

*Peter S Harper*



SECOND EDITION

WRIGHT

# Practical Genetic Counselling

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*Practical Genetic Counselling*

*To*
Elaine
*and to*
Matthew
Emma Jane
Nicholas
Katy Thi
*and*
Catrin Lucy

# *Preface to Second Edition*

The rapid advances during the past 3 years, together with the encouraging reception given to the first edition of this book by both colleagues and reviewers, has encouraged me to produce this second edition. The detailed material in the second half of the book has been extensively revised and updated, as have the earlier chapters on prenatal diagnosis and chromosomal disorders. I have, however, resisted the temptation to alter greatly the more general parts of the book, since they appear to be as valid today as when they were written; in this way I hope that the book will remain enjoyable to read, as well as useful to consult.

Some readers may question the need at this stage for a new separate chapter on recombinant DNA techniques, but I am in no doubt that this field will rapidly become as integral to genetic counselling and the practice of clinical genetics as are cytogenetic methods today.

Many friends and colleagues kindly responded to the request made in the first edition for corrections and suggestions, and I hope that this valuable 'feedback' will continue. Particular help in revising chapters came from Drs Valerie Cowie, Selwyn Roberts, Mary Vowles, Robin Winter and Ian Young.

Continuing thanks are due to all my Cardiff colleagues for their advice and support, and in particular to Mrs Gill Gulliford for organizing and typing the revision, as well as to John Wright & Sons for their patience and their personal interest in the work.

P.S.H.

# *Preface to First Edition*

During the period of almost 10 years in which I have been running a medical genetics clinic and service, many people have asked me to recommend a simple book to help them in giving genetic counselling. Most of these have been fellow clinicians, chiefly paediatricians and more recently obstetricians, faced in their regular practice with inherited or possibly inherited disorders and wishing to provide patients and their families with accurate information. Increasing public awareness and the possibility in some instances of prenatal diagnosis has increased the importance of such information being readily available.

Until now, I have been unable to recommend fully any book of this type, though numerous detailed works exist on specific groups of inherited disorders, as well as excellent introductory books on human genetics. Indeed, it may be asked whether a single book can any longer cover the amount of detailed information that is relevant to genetic counselling without danger of being superficial and inaccurate. Such dangers are real, but nevertheless, I believe firmly that such a book is needed and, after waiting in vain for my colleagues to provide it, I have attempted to do so myself.

I should emphasize from the outset that this book is written primarily for practising clinicians, whether in family practice or hospital specialties. It does not attempt to provide the extent or depth of information needed for the medical geneticist running a genetic counselling clinic; however I suspect that even my more erudite colleagues would find a simple book useful for those not infrequent occasions when one's memory lapses and there is no immediate access to more detailed literature. I can think of many occasions when I would have appreciated such a book. A further group who may find it useful is the increasing number of paramedical and non-medical staff associated with medical genetics centres and their allied laboratory services.

In writing this book, I owe a considerable debt to many people. Perhaps the greatest is to my former teachers, Professor E. B. Ford, Sir Cyril Clarke and Dr Victor McKusick of Oxford, Liverpool and Baltimore respectively, who not only fired my enthusiasm for the subject, but who influenced my conception of what medical genetics should be, and in particular how it could remain closely linked to clinical practice without losing its scientific basis.

More immediately, I must thank all my colleagues in Cardiff for their suggestions, criticism and support. Special thanks are also due to Professor Cedric Carter, Professor Alan Emery, Dr Rodney Harris and Dr Ian Young for their detailed comments on the entire manuscript, which resulted in a number of errors being corrected and in other sections being extensively rewritten. I should be glad to be notified of

any remaining errors or omissions, or indeed of any suggestions for improvement, since I hope to keep the book updated at regular intervals.

Finally, I should like to thank the Department of Medical Illustration of the Welsh National School of Medicine for redrawing most of the pedigrees, Mrs Edna Long and Mrs Julie Kruydenburg for typing and checking the manuscript, and John Wright & Sons of Bristol for their helpful and efficient role in its publication.

P. S. H.

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CHAPTER ONE

# Genetic Counselling: an Introduction

Although most people working in the field of medicine are familiar with the term 'genetic counselling', and have some idea as to what it means, it is surprisingly rare to see the term actually defined. Closer enquiry among patients and colleagues shows a wide variation in people's concepts of what the process of genetic counselling actually entails. Some envisage an essentially supportive, even psychotherapeutic role, akin to that of counselling processes in the social field; others see genetic counselling as primarily concerned with special diagnostic tests in inherited disease; others again regard it as a complex mathematical process in working out risk estimates.

All these views of genetic counselling contain an element of truth, but all are wide of the mark in identifying what the process of genetic counselling actually involves. Even within the group of professionals for whom genetic counselling is a major activity there are varied opinions as to its proper role and scope, but the following definition includes what the author believes to be the essential features.

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

From this definition it can be seen that all three aspects mentioned in the opening paragraph are indeed involved—a diagnostic aspect, without which all advice has an insecure foundation; the actual estimation of risks, which may be simple in some situations and complex in others; and a supportive role ensuring that those given advice actually benefit from it and from the various preventive measures that may be available. This chapter outlines the main steps in this process, which are then dealt with in more detail in subsequent sections of the book. It is the satisfactory synthesis of these various aspects which makes up genetic counselling as a specific process.

## The Development of Genetic Counselling

The study of human genetics was already well developed by the early decades of the present century; Charles Davenport of the Eugenics Records Office in New York State began to give genetic advice as early as 1910. However, genetic counselling did not emerge as a recognized procedure until much later. During the 1920s and 1930s the development of 'eugenic' policies in both totalitarian Germany and in N. America, accompanied by discriminatory laws prohibiting marriage of those with particular diseases, brought the subject of eugenics into disrepute; it was not until the time of the Second World War that the first genetic counselling clinics were opened in America, in Michigan (1940) and Minnesota (1941).[1] In the UK the Hospital for Sick Children in Great Ormond Street, London, developed the first such clinic in 1946. By 1955 there were over a dozen centres in N. America and a steady development has occurred since that time; the current National Foundation directory[2] lists 450 centres in N. America and 40 in the UK. As with many pioneering developments, the early centres were often the work of far-sighted eccentrics. Sheldon Reed, in his book *Counselling in Medical Genetics*, first published in 1955,[3] gives a delightful description of Edward Dight, responsible for founding the Dight Clinic in Minneapolis, who lived in a house built in a tree and who failed to file income tax returns. Francis Galton, who originated what was to become the Galton Laboratory in London, was another, though more scientific individualist.

Reed's book gives a vivid picture of the main areas covered in the early stages of genetic counselling, and it was Reed himself who first introduced the term. Many of the problems are unchanged today and his examples of individual cases show that the fears and concerns of families have altered little. In other respects there have been profound changes in the 30 years since the book was written. Carrier detection was almost non-existent and prenatal diagnosis entirely so, so the options open to patients at risk were limited; either they took the risk or they did not. An even more important change has been that of the general climate of opinion among the public and the medical profession.

Reed's case histories illustrate the background of ignorance and prejudice which his patients had to cope with and it is no wonder that he found them grateful, even when he could only give them pessimistic advice.

It is of interest that the commonest cause of referral to the Dight Clinic was regarding skin colour and whether a child for adoption would 'pass for white'. Several other problems among the 20 commonest causes for referral listed by Reed are infrequently encountered today, including eye colour, twinning and rhesus haemolytic disease.

The last of these provides a real example of advance in treatment and prevention; the others reflect changes in social attitudes. Many others of Reed's commonest problems remain equally important today, including mental subnormality, schizophrenia, facial clefting, neural tube defects and Huntington's chorea.

## Constructing a Family Tree

Collecting genetic information is the first and most important step in genetic counselling, and is best achieved by drawing up a family tree or pedigree. The use of clear and consistent symbols allows genetic information to be set out much more clearly than does a long list of relatives. Drawing a satisfactory pedigree is not difficult, though it is remarkable how rarely those clinicians without an interest in genetics will attempt the process! A clearly drawn pedigree has a certain aesthetic appeal, but its chief value is to provide an unambiguous and permanent record of the genetic information in a particular family.

*Fig.* 1.1 shows the main symbols used in constructing pedigrees, some of which are briefly explained. The symbols shown for the sexes (□, ○) are preferred to the alternative ♂ and ♀ symbols, which tend to be confused at a distance. Heterozygous carriers can be denoted by half-shaded symbols, or in the case of an X-linked disorder by a central dot. Although the sign for an early abortion can also be used for a stillbirth it is preferable to denote the sex with an appropriate symbol and indicate that it was a stillbirth beneath.

The *proband* or *propositus* (female *proposita*) should be clearly indicated with an arrow. The proband is the individual (or individuals) through whom the family is ascertained. Large families will commonly have several probands. The proband is generally an affected individual, but the person primarily seeking advice may well not be affected. The term '*consultand*' is conveniently used for this individual.

Multiple marriages and complex consanguinity can cause problems in constructing a pedigree, and artistry will have to be sacrificed for accuracy in such cases. It is usually wise to start near the middle of one's pedigree sheet and to leave more room than one thinks will be needed, so that particularly prolific family branches do not become crowded out. *Fig.* 1.2 shows examples of a simple and more complex 'working pedigree'. The following practical points deserve emphasis.

1. Enquire specifically about infant deaths, stillbirths and abortions. These may be highly relevant and the fact that they have not been volunteered may be significant. Thus two children 'lost at birth' by the mother of a woman seen for counselling proved both to have had spina bifida, a fact which considerably altered the risks.

2. Consanguinity should be directly asked about and may be the clue which suggests autosomal recessive inheritance.

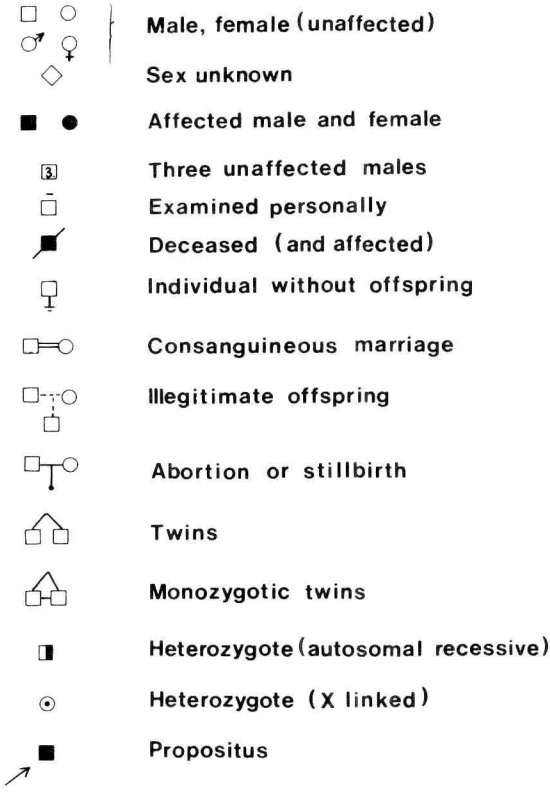


*Fig.* 1.1. Symbols used in drawing a pedigree.

3. Illegitimacy must be borne in mind, especially in a puzzling situation. A family doctor or nurse may well, particularly in a small community, be able to clarify this possibility. Illegitimacy is not of course the problem, but mistaken paternity.

4. Always take at least basic details about both sides of the family, even in a dominantly inherited disorder clearly originating from one side. Unexpected findings may emerge. The family that insists that there is 'nothing on our side' should be regarded with suspicion until this is verified. Taking details about both sides may also help to avoid feelings of guilt or blame resting exclusively on one member of a couple.

5. Record dates of birth where possible rather than ages. Note the date when the pedigree was drawn up.

6. Record maiden names of women; this is especially significant for X-linked disorders, where the surname of affected members is likely to change with each generation.

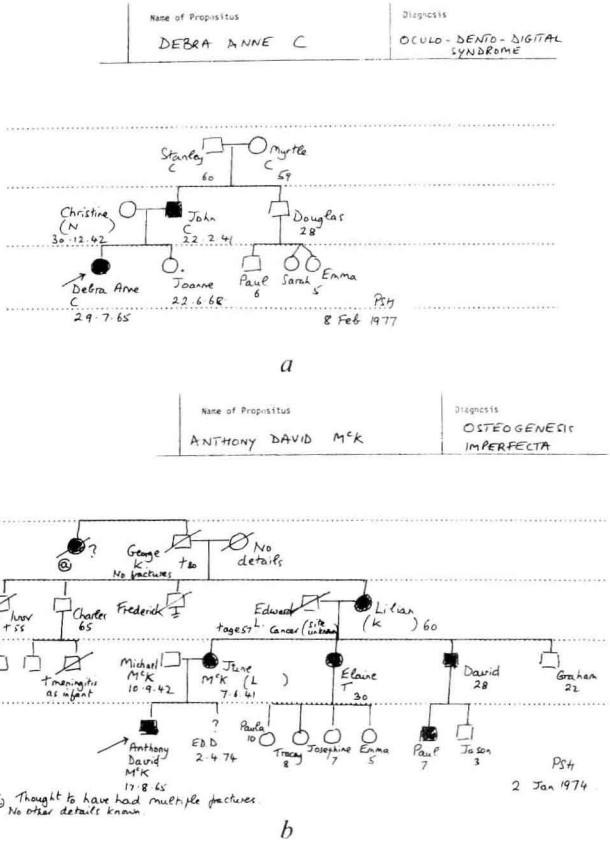


*Fig.* 1.2. Two examples of the 'working pedigree'. These two pedigrees, one simple, the other more extensive, show how family data can be easily but clearly recorded at the time of interview. A simple lined sheet is used; more detailed information on individuals can be recorded at the foot of the pedigree sheet or on the back.

7. Note the addresses of relevant members—this may prove invaluable in obtaining hospital records or in later contact with relatives.

Most of the above points are obvious, yet it is surprising how often vital information is not obtained unless a systematic approach is used.

## Diagnostic Information

It has already been emphasized that a clear diagnosis is the essential basis for accurate genetic counselling. Unfortunately, this basis is all too often a shaky one, and one of the principal tasks of anyone

involved in genetic counselling is to ensure that it is made as firm as possible before risk estimates are given to those seeking advice. Common reasons for lack of a clear diagnosis include the following:

1. *The affected individual may have lived a considerable time ago, when relevant diagnostic investigations were not available.* There is little that can be done about this, but it is surprising how much detailed information may be obtained by questioning close relatives who were involved in caring for the patient. Even if an exact diagnosis cannot be established, it may be possible to *exclude* a disorder. Thus a man with 'muscular dystrophy' who lived to the age of 40 clearly did not have the Duchenne type.

2. *The affected individual may have died without essential investigations having been done, or without autopsy being performed.* This is all too often the case and is inexcusable. Reasons usually offered are reluctance to trouble the parents in distressing circumstances, or the fact that investigations will not alter the patient's management, but usually the real reason is that those involved have not taken the trouble to undertake the studies, nor to make arrangements with those who can undertake them. The tragic consequences of such inertia only become apparent when the question of risk to further family members arises.

3. *A firm diagnosis cannot be reached even with the affected individual living.* This is inevitable in some cases, since our knowledge of many genetic disorders remains very incomplete, but a considerable degree of help can be obtained by enlisting the efforts of colleagues, even at a distance. Photographs, X-rays, urine, blood and cultured skin fibroblast samples can all be sent to distant parts of the world for experts to study, and presentation of puzzling cases at clinical meetings may often result in a diagnosis being provided. Even if it does not, one can feel happier that one is not overlooking a recognizable disorder if one has sought the advice of those most likely to know.

4. *The diagnosis may be wrong.* This is a much more dangerous situation than when the diagnosis is uncertain, for it may lead to false confidence. It is extremely difficult to know how far to rely on other people's diagnoses and how far to insist on confirming them oneself. Clearly neither a medical geneticist, nor any other clinician, can be an expert diagnostician in every speciality, and one will frequently have to rely on colleagues' advice; nevertheless it is essential for anyone involved in genetic counselling to have a wide range of diagnostic ability, to know his limitations—and those of his colleagues—and to develop a healthy scepticism in diagnostic matters and a sensitivity for where error may lie.

Bearing in mind the foregoing problems, how can the clinician involved in genetic counselling ensure that his diagnostic information is as extensive and accurate as may be? There is no simple answer, but the following points may be helpful.