A Handbook of Clinical Genetics

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To our four children and their future

Preface

This text was originally planned for nurses but when completed was also considered to be suitable for medical students and doctors needing an introduction to clinical genetics. There are many more detailed books on the subject available. Most of the clinical material and pedigrees illustrated have been obtained from the counselling service and we are very grateful to all those patients, consultands and families who have attended over the years. We are also grateful to those health visitors and doctors, in particular Dr J. I. McLachlan MB, DCH, DRCOG, who have contributed to the service since its commencement.

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1 Introduction

During the past decade doctors and nurses have become aware of the increasing interest in clinical genetics and the growing demand for genetic counselling. This has been the case in most specialities and has benefited the management of many patient problems. For example, paediatric nurses now accept genetic counselling for the families of handicapped children as a helpful and much needed service. The midwife and obstetric staff involved in the expanding field of prenatal diagnosis are already reducing the number of children born with serious abnormalities. In the community the health visitor and the primary health care team dealing with a wide variety of medical and surgical problems recognise the hereditary aspects of many diseases. Finally nursing staff in psychiatric or general medical wards will have to deal with the serious consequences of disorders such as Huntington's Chorea with its familial implications. In all these areas therefore it is possible to appreciate the increasing importance of genetics in everyday nursing and medical practice. It is necessary now to look at why some of these changes have come about. The following factors appear to be important.

Changes in Morbidity and Mortality

There have been significant changes in the causes of morbidity and mortality in childhood over the past half-century. As a result of immunisation children no longer die, or very rarely so, from diseases such as poliomyelitis or diphtheria. Antibiotics have helped to prevent deaths from other infections, and ante-natal care has improved the chances of babies surviving the process of birth. Today death in early infancy and childhood is more likely to be the result of a serious congenital abnormality and although we have no evidence that the number of such abnormalities is increasing they have been highlighted by the reduction in deaths from other causes. In 1975 congenital abnormalities accounted for almost 25 per cent of all stillbirths, 20 per cent of deaths in the first week of life and one in

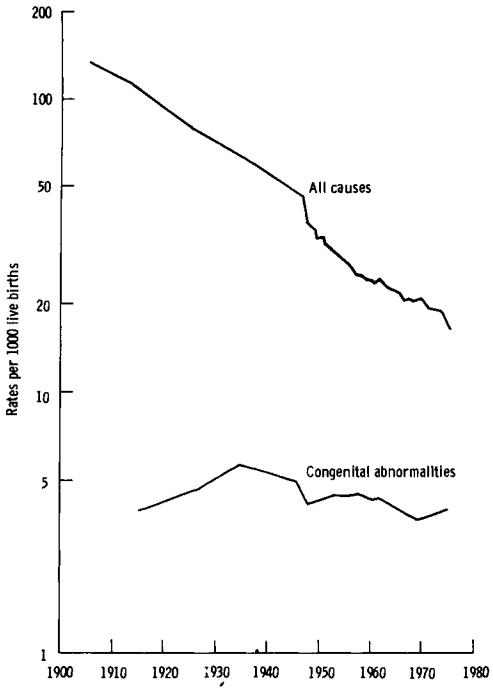

Fig. 1.1 Infant mortality per 1000 live births. Deaths from all causes including congenital abnormalities. England and Wales (After Birth Impairments OHE)

four deaths in the first year of life. Although the infant mortality rate has progressively decreased, the number of deaths from congenital abnormalities has shown little change.

If we now examine the various types of serious congenital abnormalities (Table 1.1), at the top of the list is that group of conditions referred to as neural tube defects and comprising spina bifida, meningomyelocele, anencephaly and some cases of hydrocephalus. The list also includes Down's Syndrome or mongolism and takes account of serious handicapping conditions such as mental retardation, deafness and blindness. By totalling the incidence of these various disorders it can be seen that approximately 25 children per thousand births will suffer from one or more of these serious problems. This is equivalent to 2.5/100 or, more practically, a risk of 1 in 40 of a serious abnormality in any pregnancy. This figure comes as a surprise to many couples and for that reason it is important to put it into perspective. It does also imply a 39 to 1 chance that a child will not have a serious congenital abnormality.

	Approximate Incidence /1,000 births
Neural Tube Defects	3 - 7
Congenital Heart Disease	6
Severe Mental Retardation	4
Downs Syndrome	1.5
Cleft Lip / Palate	1.5
Talipes	1 - 2
Cerebral Palsy	3
Blindness	0.2
Deafness	0.8
Abnormalities of Limbs	1 - 2
Others including Renal Tract Anomalies	2
	25 - 30

Table 1.1 Incidence of serious congenital abnormalities per 1000 births.

Events are now moving so rapidly that as a result of prenatal diagnosis neural tube abnormalities are becoming less commonly the cause of neo-natal or childhood death. It is now congenital heart disease and kidney abnormalities which are the major causes of death in this period.

There have also been demonstrable changes in mortality and morbidity in adults. Improved social circumstances and antibiotics have helped prevent deaths from conditions such as tuberculosis and other infections. Coronary artery disease, various types of cancer and degenerative disease are now the major problems. In some of these conditions, for example some types of coronary artery disease, the genetic component may be clearly recognised. In others, such as diabetes, hypertension and mental illness, it is more difficult to evaluate the contribution of genetic factors. Nevertheless, genetic disease does provide a considerable addition to the total burden of human illness. Although it is difficult to assess this accurately it has been estimated that if we combine adults and children then about 1 in 10 individuals will have serious genetic disease. Another 1 in 50 will have disease of unknown aetiology probably, to some extent, related to genetic factors.

Fall in Birth Rate

In 1977 there were approximately 600 000 infants born in England and Wales and this is the lowest annual delivery rate since records were introduced. For the first time our population was in negative

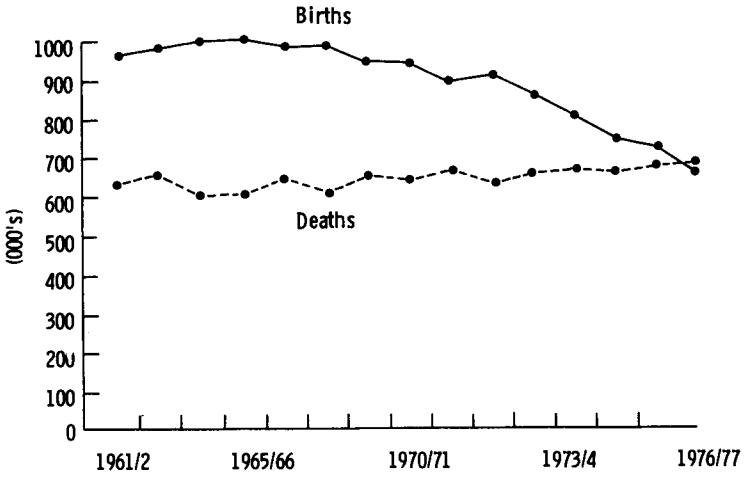

Fig. 1.2 Birth rate and death rate. England and Wales (After Population Trends HMSO)

balance; deaths from all causes outnumbering births. There has been a predicted rise in the birth rate during 1978–1979 due to an increase in the number of women entering the childbearing years. This was the result of the 'baby boom' of the 1960 period but there is no evidence to suggest that it reflects any long term trend.

As a consequence of the fall in the birth rate the average number of children per family has decreased and it is important to note that this trend is not a new one. Records from 1850 show that the decrease has been a steady one and in 1977 the average number of children per family in this country was two or slightly less than two.

Parents rightly wish their children to be born healthy and able to enjoy a normal, active life. Because each child is now more likely to be the result of a planned pregnancy this desire is more often expressed. Fifty years ago with larger families it was not unusual for a child to be born with a serious handicap. Today, such an occurrence is more likely to be seen as preventable and many young couples appear to seek some means of guaranteeing that their children are born healthy and stay that way. Another consequence of fewer pregnancies is that a miscarriage is now a much more significant event and couples may be referred to genetic counselling clinics for advice about some aspects of this problem. As with other conditions it is only possible to give sensible advice if the cause of the miscarriage or stillbirth can be established. It is important therefore to obtain more detailed post-mortem examination of aborted fetuses and stillborn babies.

Advances in Technology and Treatment

Changing patterns of disease in our community have influenced thinking on medical research and practice. There is now more emphasis on the preventative aspects of medicine and health education. However, the prevention of conditions such as Down's Syndrome and spina bifida have had to wait for advances in technology which have become available over this past few years. Increasing experience with amniocentesis and the advent of ultrasound have made prenatal diagnosis possible and safer. In addition there have been significant advances in *cytogenetics*, i.e. the study of chromosomes and their abnormalities. An important landmark in the development of this science was the finding of an extra chromosome in patients with Down's Syndrome. Subsequently changes in the number and structure of chromosomes were demonstrated in other disease states. All of these changes may be identified in a preparation of chromosomes referred to as a *karyotype* and shown in Fig. 1.3.

In the past few years it has been confirmed that there is an increased level of a fetal protein, alpha-fetoprotein, in the amniotic fluid surrounding a fetus with spina bifida or anencephaly. This has made it possible to offer prenatal diagnosis and selective abortion to couples at risk of having a child with this serious abnormality. A

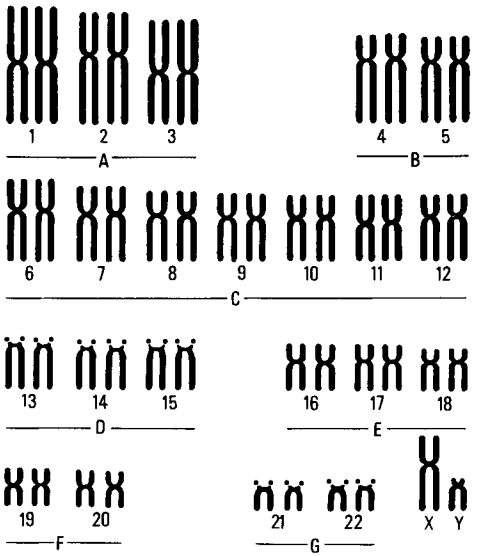

Fig. 1.3 Normal unbanded karyotype. The chromosomes are numbered and grouped according to size. Sex chromosomes bottom right. This is a male.