THE EARLY DIAGNOSIS OF CONGENITAL ABNORMALITIES

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CASSELL · LONDON

CASSELL & COMPANY LTD
35 Red Lion Square · London W.C. 1
and at
MELBOURNE · SYDNEY · TORONTO · CAPE TOWN
JOHANNESBURG · AUCKLAND

First Published 1963

Printed in Great Britain by
J. & J. GRAY, EDINBURGH
F.863

Foreword

THE fifty per cent. increase, between 1951 and 1960, in the proportion of infants' deaths attributed to congenital malformations is a major challenge. To meet it, general practitioners, local authority doctors, obstetricians and paediatricians have increasingly felt the need of a book from which they can get useful knowledge on the subject.

Dr. Smithells' book is good for reading and for reference; it is small but up to date, comprehensible and comprehensive. A mine of information in which to work, it is enjoyable as well as productive.

The author starts with chapters on two unusual but valuable topics: *Prenatal Diagnosis* and *Diagnosis During Labour*. The obstetrician who reads these will be forewarned and will have neat opportunities to forewarn his paediatric colleague. Chapter 3, on *Examination of the Symptomless Infant*, will reward reading and re-reading. Chapter 4, *Early Symptoms of Congenital Abnormalities*, approaches the problem of the newborn infant who has a symptom, in a way that is rare but right. A clinician writing for doctors at the cotside or clinic, Dr. Smithells considers in turn the baby who is floppy, the baby who is jaundiced, and so on. After all, the baby does not arrive labelled as 'birth injury' or 'Möbius syndrome', or as having a disorder of the nervous system; he does not arrive as having hepatitis or hypothyroidism; he arrives with a symptom, sometimes one which the doctor will have learnt from Chapter 3 to recognize. The doctor has to start from the symptom and, if the best management is to be planned, he needs to learn how to arrive at the cause.

But even the doctor who knows that bubbly breathing or

cyanosis with dextrocardia on the first day of life implies a probable urgent need for surgery, who knows that persisting rapid breathing in the neonate may be due to heart failure, who knows how to recognize Ehlers-Danlos syndrome may still be neglecting one of the most important opportunities we have of preventing life-long emotional disturbance in parents and children. This major clinical responsibility is discussed in Chapter 5 on *Interviewing Parents of Malformed Babies*; it is an opportunity for initiating preventive mental hygiene which, surprisingly, is omitted or dealt with very inadequately in most textbooks.

This is a book to have in the prenatal clinic, in the delivery room and in the lying-in ward; a copy should be kept in the surgery and in the clinic. It will answer emergency problems as well as less urgent problems of diagnosis and management. It is an excellent present to give to doctors; the recipients will find that it is readable and answers their questions, and the donors will like the low price. Dr. Smithells is known to many as a gifted teacher, clinician and research worker. This book makes his talents available to all.

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TO MY WIFE

Preface

THE infant mortality rate in Great Britain is one of the lowest in the world. Social and economic factors are largely responsible, but the medical services have played a part. During the decade 1951 to 1960, the infant mortality rate fell from 30 to 22 per thousand live births. Having regard to the advances in paediatric surgery which, during this time, saved the lives of many malformed babies, a fall in the number of infant deaths attributed to congenital malformations might have been expected. Far from this being the case, there has been a substantial increase in both absolute and relative numbers, as the following table shows:

	1951	*1960*	*Change 1951–1960*
Live births . . .	677,529	785,005	14% increase
Infant deaths . .	20,223	17,118	15% decrease
Infant deaths attributed to malformations .	2,864	3,549	24% increase
Proportion of infant deaths attributed to malformations . .	14%	21%	50% increase

The *deaths* attributed to malformations are only part of the problem. There are also *stillbirths*, 20 to 25 per cent. of which are associated with malformations. More important, the figures of deaths take no account of the *life-long handicaps* which non-lethal abnormalities may bestow

upon the newborn child—and on his family. In some ways the biggest problems of all are presented by these children —children with paralysed legs and sphincters resulting from myelomeningocele, children with fibrocystic disease of the pancreas, mongol children.

Prevention of these anomalies must clearly be our ultimate aim. At present this is only possible in a negative way. We can attempt to protect pregnant women from viruses, from ionizing radiations, and from potentially teratogenic drugs. We can advise parents of the recurrence risks of genetically determined disorders. But even if we do this conscientiously and efficiently, 2 per cent. of all babies will still be born with serious malformations and a further 3 per cent. with lesser abnormalities. Until by epidemiological and experimental research we have learnt a great deal more about causes, we can do very little to promote normality.

Meanwhile, wherever we can, we must make the abnormal infant normal, and where this is not possible, help him and his family to make the best of his handicap and live as full a life as his capacities allow. Sometimes, as in the case of a simple intestinal obstruction, normality is attainable; at other times, as with a mongol, it is not possible at all. Early diagnosis of each and every abnormality will enable the best use to be made of the resources available. In the example of intestinal obstruction, the earlier the diagnosis is made, the better is the infant's chance of survival. With the mongol, early diagnosis may be less vital, but it gives the physician more time in which to plan how best to help the family. Sometimes it is not only the infant whose life may be endangered by a malformation. The prenatal diagnosis of hydrocephalus and conjoined twins, for instance, may greatly help the obstetrician to avoid dangerous hazards.

It is with early diagnosis that this book is concerned. This is interpreted as meaning early in the infant's life as well as early in the course of the disorder. The emphasis is on diagnosis during the four weeks before and the four

weeks after the birth of the baby. The book is intended for those who have the privilege of caring for mothers and their infants during this critical, exciting, and responsible time.

LIVERPOOL, 1963

R. W. SMITHELLS

Acknowledgements

I OWE an incalculable debt to Dr. Ronald Mac Keith, at whose suggestion this book was written. He has given me invaluable guidance at every stage and is responsible for much of what may be found helpful. The shortcomings are my own.

I should like to thank Professor John Hay and Dr. Elton Goldblatt for their advice on the sections on congenital heart disease; Dr. Norah Walker and Dr. Constance Davies for their assistance with some of the radiographs; and Dr. Bryan Hibbard for helpful discussion of some obstetric problems. Friends who have provided material for the illustrations are acknowledged in the text, and I am grateful to Mr. Charles Fitzsimons for most of the photography.

Finally, I wish to acknowledge the help I have been given by my publishers.

Contents

CHAPTER 1

Prenatal Diagnosis

INDICATIONS FOR INCREASED VIGILANCE

THE prenatal recognition of foetal disorders may be of the greatest importance to obstetrician and paediatrician alike. The obstetrician is concerned with the diagnosis of foetal malformations that may affect the course of pregnancy or labour and influence his management of them. The paediatrician also is concerned with disorders initiated *in utero*, notably asphyxia and haemolytic disease.

In some instances a definite prenatal diagnosis of malformation can be made, but more commonly there are circumstances which merely increase the likelihood that a particular pregnancy will end in the birth of an abnormal baby. These factors should increase the vigilance of those responsible for the care of the mother and baby. The most important of them are:

(1) A family history of heritable disorders.
(2) An excess or deficiency of amniotic fluid.
(3) Persistent foetal malpresentation or abnormal attitude.
(4) Maternal ill-health in the first trimester.
(5) Certain drugs taken in the first trimester.
(6) A history of recurrent foetal wastage.
(7) Increasing maternal age and parity.

Although the majority of congenital abnormalities will be revealed by the routine examination of the newborn baby, others may require more detailed examination or laboratory tests to establish the diagnosis. The selection of infants requiring such special investigations often begins in the prenatal period; they may be impracticable or inadvisable as a routine but are, in some cases, highly important.

Heritable disorders

A family history of heritable disorders will clearly prompt a particularly careful search for evidence of the disease in the new baby. Conditions inherited as Mendelian dominants are far less common than recessive disorders because they tend continually to eliminate themselves. Strictly speaking, it is not the diseases that are dominant or recessive but the genes that control them.* These dominant genes may have been inherited from a parent or may have arisen by mutation. If the gene invariably causes serious disease (for example, achondroplasia), there is little opportunity for it to be handed down to another generation, and the majority of such disorders will arise by mutation. Conversely, if the effect of the gene is relatively trivial (aniridia, for instance) or is delayed until after the reproductive period (Huntingdon's chorea), the disease will usually be found in one or other parent. A third alternative is seen when the gene has variable expressivity, causing only minor symptoms in the parent but severe disease in the infant. An example is fragilitas ossium (osteogenesis imperfecta). The infant may be born with multiple fractures and live only a short time. In about half the cases there is a family history of a less severe tendency to fractures, or otosclerosis, or simply blueness of the sclerotics.

* Geneticists seem to be divided as to whether it is the genes or the characters determined by them that are dominant or recessive. Fortunately, there is authoritative support for either view.

In two of these three groups of dominant disorders, therefore, there may be a positive family history which forewarns the clinician. Each child born to a parent with a dominant gene has a 50–50 chance of inheriting the gene and manifesting the disease. However, the birth of a baby with a gene mutation, for example, an achondroplastic infant born to healthy parents, in no way diminishes the probability that future babies will be normal. Unfortunately, even when there is the closest co-operation between obstetrician and paediatrician, significant family illnesses may come to light only in retrospect. An infant with unexplained jaundice may turn out to have a mother whose spleen was removed for hereditary spherocytosis twenty years previously.

Recessive genes are manifest only in the homozygote, who carries a pair of abnormal genes. One gene has been inherited from each of the parents, who are 'normal' heterozygous carriers. It is now possible to detect some heterozygotes by special tests, but these are rarely done except after the arrival of an abnormal baby. It is, therefore, almost impossible to foresee a recessive condition in the first affected child to be born in a family. Once an affected child has been born, the same condition can be expected, on average, in one-quarter of subsequent siblings. The most common recessive gene in Great Britain is that for fibrocystic disease of the pancreas (mucoviscidosis), but in other countries the gene for sickle haemoglobin is far more widespread. This gene persists because the heterozygotes are at an advantage in terms of resistance to malaria and will presumably become less common if malaria is ever eradicated on a global basis. The heterozygotes for fibrocystic disease must also have some advantage over those without the gene, but nobody yet knows what this advantage is.

The inborn errors of metabolism are almost all inherited as Mendelian recessive characters, albinism, phenylketonuria, and galactosaemia being among the most familiar. Congenital adrenal hyperplasia follows the same pattern,

as do most examples of the lipidoses. The birth of one child with any of these conditions will alert the clinician to the possibility of recurrence in subsequent children.

In sex-linked inheritance the abnormal gene is borne on an X chromosome. In the female, this gene is usually recessive, being suppressed by the allelomorph on the other X chromosome. In the male, the Y chromosome is very small so that most of the single X chromosome is unpaired; the abnormal gene is therefore manifest. The most familiar examples of sex-linked abnormalities are haemophilia, Christmas disease, pseudohypertrophic muscular dystrophy, and congenital hypogammaglobulinaemia. There may be a history of these conditions in previous male siblings, in maternal uncles or in the male siblings of female forebears, but it is possible for these genes to be carried silently through generation after generation down the female line. The genes determining the production of glucose-6-phosphate dehydrogenase, deficiency of which causes haemolytic anaemia, and the blood group Xg^a are also situated on the X chromosome.

In many congenital abnormalities there is undoubtedly a genetic factor even though the classic Mendelian patterns may not be seen. This is certainly true of central nervous system malformations, but usually these can be diagnosed without much difficulty. It is equally true of congenital 'dislocation' of the hip, which is more easily overlooked. A history of this condition in any close relative is an indication for meticulous and, if necessary, repeated examination of the baby's hips (*see* p. 99).

Whenever there is a history of abnormality in a previous baby in a family, this abnormality must be excluded in the new infant, whether it is believed to have a genetic basis or not. Few mothers have any knowledge of genetics, and there is always a fear, often unspoken, that a malformation may recur. Mothers who have previously had abnormal babies need assurance, therefore, not only that the new baby is healthy, but that the brain, the heart, the palate, or whatever was malformed in the previous baby, is normal.

Sometimes, as in the case of the lipidoses, only the passage of time can provide this assurance.

Excess or deficiency of amniotic fluid

An excess or deficiency of amniotic fluid is often a warning sign that foetal development is not proceeding normally. There is still much discussion about the precise mechanisms of production and circulation of amniotic fluid. However, there is no doubt that foetal swallowing plays a part in its removal, and that foetal micturition contributes towards its production. Congenital abnormalities that interfere with swallowing tend, therefore, to be associated with polyhydramnios, while those that prevent micturition are often associated with oligohydramnios.

The incidence varies widely in reported series, but, in round figures, polyhydramnios complicates about 1 per cent. of all pregnancies. The proportion of these cases associated with foetal malformation also varies very considerably, but in most series the figure lies between 25 and 40 per cent. (Stevenson, 1960). The proportion associated with multiple pregnancy is about 5 per cent. Polyhydramnios is therefore far more likely to be accompanied by malformation than by multiple pregnancy.

By far the most common malformation to be associated with polyhydramnios is anencephaly. It has been shown by amniography that some anencephalic foetuses do not swallow, but the reason for this is a matter of conjecture. It may be that hyperextension of the neck causes mechanical obstruction of the pharynx, or that the swallowing reflex is faulty. Some anencephalic babies born alive have normal sucking and swallowing reflexes, but it has not yet been shown whether these particular infants are associated with maternal polyhydramnios. Iniencephaly is a less common related malformation, in which the base of the skull and the cervical spine are grossly abnormal. The cerebral hemispheres lie immediately behind the pharynx, and the