Pediatric Surgery

Prem Puri • Michael Höllwarth
Editors

Pediatric Surgery

Diagnosis and Management

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To Veena and Susan for their love and patience.

Preface

During the last two decades there has been a dramatic improvements and expansion in the field of paediatric surgery. Major advances in perinatal diagnosis, imaging, resuscitation, intensive care, minimally invasive surgery, transplantation and improved operative techniques have radically altered the management of infants and children with surgical conditions. Surgical procedures are now routinely performed in neonates and children with serious and complex disorders. Monitoring techniques for the sick child pre and post operatively have become more sophisticated and there is now greater emphasis on physiological aspects of the child undergoing surgery.

This book, which is primarily aimed at paediatric surgical trainees and young paediatric surgeons, provides a comprehensive description of various surgical conditions in infants and children with major emphasis on diagnosis and management. The book contains contributions from outstanding and well known paediatric surgeons and paediatric urologists. Each contributor was selected to provide an authoritative, comprehensive and complete account of their respective topic. Most chapters are well illustrated with the use of tables, radiographic images, clinical photographs and operative techniques.

This book comprises of 97 chapters from 119 contributors from all five continents of the world. We wish to thank all the contributors most sincerely for their outstanding work in producing this innovative text book. We wish to express our gratitude to Vanessa Woods and Silvia Harding (Dublin) and Gudrun Raber (Graz) for their skilful secretarial help. Finally, we wish to thank the editorial staff of Springer, particularly Ms Gabriele Schroeder and Ms Stephanie Benko, who have been behind each step of this book from its original concept to its delivery.

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Part I

General

The Epidemiology of Birth Defects

1

Edwin C. Jesudason

Contents

1.1 Introduction

The surgical correction of birth defects helped create the speciality of paediatric surgery during the middle of the last century. Around this time, pioneering neonatal operations were successfully performed to allow survival of babies with conditions like oesophageal atresia or congenital diaphragmatic hernia (CDH). Indeed, along with innovations such as parenteral nutrition, the concentration of surgical, anaesthetic, nursing and critical care expertise now allows high survival rates to be achieved for many previously fatal anomalies. For certain conditions that have high mortality and morbidity, fetal surgery aims to further reduce the harm of birth defects.

1.2 Birth Defects Are Leading Causes of Global Infant Mortality

Given the huge progress made in the treatment of infectious diseases in particular, birth defects are now emerging as the leading cause of infant mortality. Moreover, this state of affairs pertains not only to places with expensive healthcare systems but in fact anywhere that infant mortality rates have significantly fallen. Hence, as progress against other infant killer diseases continues it is likely that birth defects will gradually become one of the most significant global causes of infant mortality. In addition, birth defects are a leading contributor to both premature birth (itself a major cause of infant mortality) and chronic disability (with its substantial personal and societal costs). Tragically, many such problems are already preventable; for example, the birth defects associated with congenital rubella syn-

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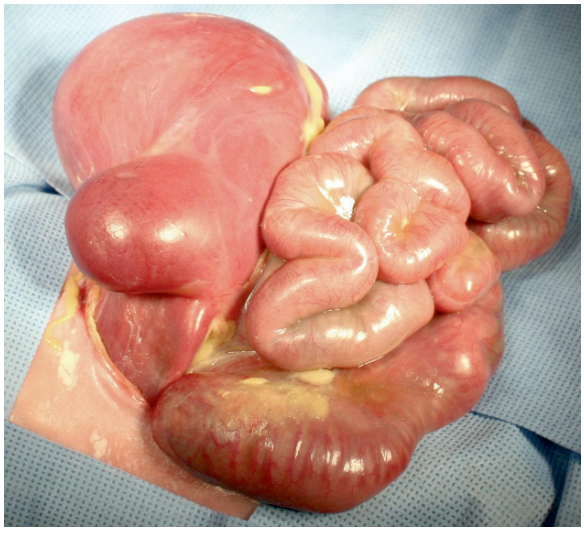

Fig. 1.1 Gastroschisis – a birth defect on the move? Data from birth defect registries indicate a real and unexplained increase in gastroschisis prevalence. It remains to be seen if the severity of gastroschisis is also increasing: in this example, in addition to the gut, most of the liver lies outside the neonatal abdomen (image used with permission, courtesy of the author)

drome may be virtually eradicated by an effective programme of maternal immunisation. Furthermore, a subset of neural tube defects continues to occur due to inadequate implementation of pre-conceptual folate prophylaxis. However, the epidemiological challenges for clinicians extend beyond the known, preventable defects to unsolved conditions and their changing circumstances (for instance, the increasing prevalence of gastroschisis Fig. 1.1).

1.3 Birth Defects Epidemiology and Teratology

Although birth defects have been described with horror and fascination since antiquity, teratology and scientific birth defects epidemiology date, like paediatric surgery, from the mid-twentieth century. Key historical developments include the recognition of congenital rubella syndrome (noted by clinical ophthalmological examination) and the thalidomide disaster (phocomelia and other defects associated with maternal thalidomide administration for morning sickness). These episodes vividly illustrated the devastating consequences of prenatal infection and drug exposure. In addition, these chastening experiences highlighted the urgent need to formalise birth defects surveillance. Such monitoring of birth defects can now be said to serve a range of important purposes including early warning of an outbreak, identification of possible environmental or genetic causes, rational planning for neonatal surgical provision, facilitation of prenatal counselling based on accurate data, establishment of associations between birth defects and comparison of outcomes.

1.4 Causation of Birth Defects Remains Often Complex and Uncertain

Before considering the methods of birth defects surveillance, it is worth sketching the developmental biology that underpins birth defects from a surgeon's perspective. Causes of birth defects can be classified as parental, fetal and environmental. Examples of the former include the impact of maternal and paternal age on the prevalence of Downs and Aperts Syndromes, respectively. Alternatively, maternal diseases such as diabetes are well-described risk factors for the formation of birth defects. Fetal causes include genetically determined inborn errors of metabolism such as those causing intersex anomalies in congenital adrenal hyperplasia, chromosomal lesions such as Downs Syndrome, Edwards Syndrome etc. and twinning with its increased risk of birth anomalies. Environmental causes include those related to prenatal addiction and drug exposure, such as alcohol, smoking, thalidomide, valproate, phenytoin, warfarin etc., as well as the impact of intrauterine infections, such as toxoplasmosis, rubella and cytomegalovirus. The impact of assisted reproductive technologies such as in vitro fertilisation and intracytoplasmic sperm injection on the prevalence of birth defects are actually quite difficult to assess. The suggestion that anomaly rates are higher in such assisted pregnancies needs to contend with the confounding increased rates of multiple pregnancy. Also, given the parents' need to use assisted reproductive technology, it may be that they are importantly different to parents conceiving naturally; increased anomaly risk could therefore be due to parental abnormality and predisposition rather than a result of the techniques themselves.

Other environmental contributors to birth defects include "endocrine disrupters"; these oestrogenic compounds are conjectured to contribute to anomalies of sexual development in fetal males (e.g. hypospadias)

as well as putative impairment of adult male sperm quality. In light of such difficulties in attributing causes, it is important to recognise that only a minority of birth defects are known to arise from a simple genetic or environmental cause. At present, the majority of birth defects appear to have multi-factorial origins. Therefore, it is helpful to consider birth defect causation as the result of complex interactions between genes and environment. Hence some cases of spina bifida may result from micronutrient deficiency in the context of predisposing enzyme polymorphisms. Similarly, teratogenic drugs may interact with pharmacogenomic predispositions to help explain why certain pregnancies are affected. Beyond considerations of even complex causation, it remains likely that simple chance has a major role to play (similar to stochastic effects seen in radiation biology).

1.5 Birth Defects Appear to Arise Typically (But Not Exclusively) in the First Trimester

Developmental biologists refer to "competence windows" to describe periods in development when particular cells and tissues are capable of responding appropriately to certain growth and transcription factors. In a similar manner, developing organs are contended to have particular temporal windows when an otherwise non-specific teratogenic stimulus will impact disproportionately on the formation of that organ system.

During the first trimester, organ morphogenesis predominates while later trimesters are devoted to organ growth and maturation. Unsurprisingly, therefore, sensitivity to teratogens is held to peak during the first trimester. Hence, pregnant women are advised to avoid medications during this part of gestation in particular. Teleologically, "morning sickness" that peaks during the first trimester is postulated to help reduce ingestion of potential teratogens during this period of maximum vulnerability. While the model of first trimester teratogenesis appears appropriate for many birth defects, it is now clear that certain anomalies may arise during later development as a result of fetal events, such as amniotic band formation or vascular accident. Gastroschisis and intestinal atresia may be considered in this latter category. Indeed, the contrast between exomphalos and gastroschisis in terms of associated anomalies (and hence prognosis) can be considered due to the different times they are held to originate during development. Exomphalos is considered an embryonic lesion that is accompanied by contemporaneous lesions of organogenesis in other systems such as the heart. In contrast, intestinal atresia in gastroschisis is thought to result from a discrete fetal vascular accident and hence lacks extra-intestinal manifestations. A similar contrast between duodenal atresia and small bowel atresia may be likewise understood as the result of their differing onsets and aetiologies. Duodenal atresia is commonly explained as an embryonic failure of luminal recanalisation; as expected, therefore it is strongly associated with other dysorganogenesis, such as cardiac, Downs and oesophageal atresia. In contrast, small bowel atresiae are thought to follow mesenteric vascular occlusion usually in fetal life. Hence, aside from gastroschisis, associated structural lesions are unlikely. Between these two "extremes" are birth defects where an embryonic lesion has deleterious "knock-on" effects later in fetal development; based on experimental models, the neurological sequelae of spina bifida are postulated to result from not only the primary failure of neural tube closure but also from consequent exposure of the neural placode to amniotic fluid. Similarly, lung hypoplasia in CDH may emerge as an embryonic lesion prior to CDH only for compression by the visceral hernia to exacerbate the pulmonary lesion. In circumstances such as these, where the pathology is thought to progress during fetal life, prenatal surgical correction has been a logical proposal to meet the challenge of refractory mortality and morbidity.

1.6 Classification of Birth Defects for Epidemiological Purposes

Birth defect epidemiology involves the registration of anomalies by type. At present, birth defects registries such as EUROCAT (European Surveillance of Congenital Anomalies) use a classification scheme based around organ systems (see Table 1.1), specific diagnoses and ICD codes (see Table 1.2; both tables are derived from data published by EUROCAT—http://www.eurocat.ulster.ac.uk/pubdata/tables.html).

Cooperation between registries helps by pooling data and also by building consensus on issues such as the exclusion of minor anomalies without major and long-term sequelae (e.g. cryptorchidism or congenital hydrocoele) or on how abnormalities of gut fixation in CDH might be recorded. Although anomalies are

Table 1.1 Birth prevalence of malformations 1980–2004 grouped by EUROCAT category. Note, rates for each category are inclusive of cases with chromosomal lesions and derived from registries with full EUROCAT membership

Organ system	Live birth + fetal death + termination/10,000 births
All	210
Cardiac	62
Limb	40
Chromosomal	31
Urinary	27
Nervous system	23
Digestive system	19
Genital	15
Musculo-skeletal	11
Other malformations	10
Abdominal wall defects	4.7
Eye	4.7
Genetic syndromes + microdeletions	4.6
Ear, face, neck	4.4
Teratogenic syndromes (inc. infection)	0.9

Table 1.2 Birth prevalence of malformations of relevance to paediatric surgery (1980–2004) grouped by diagnosis from registries with full EUROCAT membership

Anomaly	Live birth + fetal death + termination/10,000 births
Down's	18
Hypospadias	11
Congenital hydronephrosis	8.5
Spina bifida	5.4
Cystic kidney disease	5.3
Edward's	3.7
Anorectal malformations	3.0
Diaphragmatic hernia	2.8
Exomphalos	2.8
OA/TOF	2.3
Gastroschisis	1.8
Bilateral renal agenesis	1.7
Duodenal atresia/stenosis	1.2
Hirschsprung disease	0.87
Posterior urethral valves/ prune belly	0.8
Indeterminate sex	0.8
Intestinal atresia/stenosis	0.74
Bladder extrophy/epispadias	0.58
Situs inversus	0.54
Amniotic band	0.35
CCAM	0.33
Biliary atresia	0.28
Conjoined twins	0.18

Note (a) rates for each category are inclusive of cases with chromosomal lesions; (b) the time frame examined (1980–2004) may obscure recent rising incidence of gastroschisis and, for example, the impact of modern prenatal diagnosis of CCAM; (c) these are birth prevalences (including fetal death/terminations) and not necessarily the prevalences at paediatric surgical units.

currently classified by structural anomaly (e.g. CDH, oesophageal atresia) or defined diagnosis (e.g. Downs), it is likely that, in the future, anomalies may be classified or at least subgrouped by genotypic differences rather than anatomic details alone. Such distinctions may be prognostically and therapeutically important, e.g. in contrast to isolated omphalocoeles, exomphalos in Beckwith-Wiedemann syndrome is associated with hypoglycaemia, macrosomia and increased tumour risk due to disordered gene imprinting. Hence, the anatomic defect (exomphalos) becomes less important than the genetics and its multi-system sequelae. Similarly, it is postulated that subgroups of spina bifida may be folate resistant due to underlying genetic or enzymatic variation. Designing pre-conceptual prophylaxis for birth defects may need to acknowledge pharmacogenomically distinct subgroups to avoid benefits within one subgroup being overlooked due to a larger surrounding non-responder cohort.

Having a system of classification is however only part of the task. Notification and classification in practice are subject to local variations. When resources exist for expert-mediated classification of birth defects by diagnosis, this approach to birth defects epidemiology appears the best currently available. However, even some North American registries lack clinician input in the classification and assignment of observed birth defects. The consequence(s) of this omission for data quality remain to be determined. In the contrasting circumstances of rural China, expert-led assignment of cases has been substituted by simple photographic recording of malformations; this system not only allows the registry to function but also allows difficult cases to be assigned later after remote assessment of images by experts. In addition, the photographs potentially allow the classifiers to calibrate their judgments against those from other registries.

1.7 Counting of Birth Defects Is Affected by the Definition of Stillbirth

The epidemiology of birth defects becomes difficult whenever the classification of defects is not uniform or straightforward. This task is complicated by practical barriers to case ascertainment (e.g. inadequate resources),

the definition of stillbirth and the effects of prenatal diagnosis and terminations.

Recording of anomaly prevalence lies at the core of birth defects epidemiology. To account for the unknown incidence of a defect among vast numbers of naturally miscarried pregnancies, epidemiologists measure the prevalences of defects within a defined birth cohort, i.e. the number of live and stillborn cases of the defect, as a proportion of all births (live and stillborn). This definition depends on the artificial distinction between miscarriage and stillbirth; EUROCAT's recommendation is that spontaneous pregnancy losses prior to 20 weeks of gestation are counted as miscarriages (and do not contribute to anomaly prevalence), while similar losses at 20 weeks of gestation and beyond are counted as stillbirths (and included in prevalence statistics).

Despite these guidelines, several countries have established different demarcations (e.g. 24 or 28 weeks or even 500 g weight). Clearly, some estimate of prenatal birth defects is required to avoid seriously underestimating overall prevalences. However, the demarcation of stillbirths begins to complicate matters. Countries where later gestational cut-off points are used may underestimate the prevalence of birth defects compared to registries where 20 weeks is used. Hence, minor changes in convention can lead to large but artificial differences in anomaly prevalence. While a definition of stillbirths is needed for data collection, the sharp demarcation (whether 20 weeks or later) also appears arbitrary from a biological perspective. Consider a hypothetical prenatal medical therapy that reduces the prevalence of a specific birth defect. When the anomaly is rare (as most are), it may be difficult to determine whether an observed reduction in prevalence is truly due to fewer malformations or instead due to the promotion of earlier loss of affected pregnancies (i.e. prior to the 20 weeks or other agreed margin). This latter phenomenon, termed "terathanasia", has even been invoked to explain how folate supplementation reduces neural tube defect prevalence.

1.8 Prenatal Diagnosis: The Greatest Challenge to Birth Defect Epidemiology?

While classification of birth defects and the definition of stillbirth make anomaly surveillance complex, the impact of prenatal diagnosis is arguably still more important. Prenatal diagnosis (in particular non-specific ultrasound screening) confounds birth defects surveillance in a number of ways: (i) it increases identification of birth defects within the cohort of assessment (still and liveborn) by diagnosing those who may otherwise have perished prenatally (and uncounted), or those who may have presented beyond the neonatal period (if at all). For example, in prenatal identification of cystic lung lesions, some would never have been diagnosed (either regressing spontaneously or persisting asymptomatically), while even symptomatic lesions would often have presented later (beyond the scope of the birth defects registry); (ii) prenatal diagnosis alters antenatal management and results in terminations (or fetal intervention) that affect the numbers of birth defects being counted; most registries therefore attempt to keep separate data on terminations for birth defects. However, where prohibitions on termination exist, such data becomes still harder to find; (iii) prenatal diagnosis may be inaccurate but unchecked; pathological verification after termination may be incomplete or absent, yet the diagnosis is included in the birth defect tally; (iv) resources and expertise to perform prenatal sonography vary with location thereby hampering national and international comparison of the prevalence of birth defects. In summary, the apparently simple task of counting live and stillborn cases for birth defects surveillance is fraught with difficulty once (a) the arbitrary definition of stillbirth is imposed and (b) ubiquitous prenatal imaging prompts both terminations and identification of previously occult "cases".

Given these challenges in data collection, epidemiologists are aided by being able to compare a variety of surveillance databases. Many European registries are incorporated into the EUROCAT initiative. Similarly, several other registries feed into birth defects' surveillance data furnished by the World Health Organisation (WHO). Their Birth Defects Atlas is an interesting publication available in the public domain (http://www.who.int/genomics/publications/en/). Most importantly it is instructive to read and consider the caveats that EUROCAT and WHO place on their data. The interpretational issues raised highlight not only the problems discussed in the previous sections but also allude to the ongoing challenge of inadequate resources and expertise for reporting birth defects. This in turn impairs the data accuracy and may help explain insufficient action upon findings.

1.9 Paediatric Surgeons Often Report Institutional Series of Birth Defects

Given the difficulties in collecting and interpreting data from population-based registries, it should come as no surprise that similar issues afflict institutional series that are the staple of paediatric surgeons' reporting. Again, ascertainment is the most significant problem; prenatal diagnosis, terminations, or deaths prior to transfer, of high-risk cases can give the misleading impression that changed institutional practice is impacting on outcome (when in fact it is pre-institutional interventions that are changing the results). Moreover, paediatric surgeons like to estimate disease severity in their cohort to show that their (good) results are not simply the product of low-risk caseload. However, in such circumstances it can be highly misleading to use the frequency of interventions (e.g. decision to patch and use ECMO or nitric oxide in CDH) to estimate severity in a birth defect cohort; use of these techniques may in fact owe more to institutional protocols rather than any pathophysiological differences between cases. Ultimately, institutional series are subject to often substantial biases (with apparently poorer results perhaps not even being submitted for publication).

1.10 The Challenge for Modern Paediatric Surgery

Despite its confounding influence on modern birth defects surveillance, the impact of prenatal diagnosis will not disappear. On the contrary, advances in prenatal imaging may only serve to identify more "defects" of unknown significance. Moreover, functional fetal imaging and genotyping may evolve to allow better prenatal prognostication and hence case selection for future fetal therapies. In the midst of all these potentially exciting developments, paediatric surgeons retain a key role; using the best available birth defects epidemiology, we may gradually learn to match the defects with the required type and time of intervention appropriately. To achieve this, paediatric surgeons need to keep abreast of birth defects epidemiology and work collaboratively with other surgeons, perinatologists, obstetricians and public health physicians. As a model for such cooperative endeavours, the organisation, previously termed the UK Children's Cancer Study Group (UKCCSG), was led by collaborating paediatric oncologists and surgeons; they achieved remarkably high recruitment rates of paediatric cancer cases into multicentre trials that helped transform clinical management. A similar consortium approach to birth defects and their surgical correction may allow paediatric surgeons to retain a central role in this evolving field. Conversely, overlong adherence to single institution reporting may see the speciality sidelined as governments are advised by public health specialists and others on the pre- and post-natal management of birth defects. Given the opportunities generated by "Web 2.0", the tools for such networked initiatives are within our grasp. As a beginning, the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS) has undertaken a year's census of gastroschisis in the UK (that is, in part, a response to the UK Chief Medical Officer's concerns about rising gastroschisis prevalence). Hence, as birth defects emerge as the leading cause of infant mortality, this project will help us establish how paediatric surgeons can work together to understand these human healthcare problems.

Further Reading

Carmona RH (2005) The global challenges of birth defects and disabilities. Lancet 366(9492):1142–1144

Cragan JD, Khoury MJ (2000) Effect of prenatal diagnosis on epidemiologic studies of birth defects. Epidemiology 11(6):695–699

Davidson N, Halliday J, Riley M, King J (2005) Influence of prenatal diagnosis and pregnancy termination of fetuses with birth defects on the perinatal mortality rate in Victoria, Australia. Paediatr Perinat Epidemiol 19(1):50–55

Howse JL, Howson CP, Katz M (2005) Reducing the global toll of birth defects. Lancet 365(9474):1846–1847

Khoury MJ (1989) Epidemiology of birth defects. Epidemiol Rev 11:244–248

Khoury MJ, Millikan R, Little J, Gwinn M (2004) The emergence of epidemiology in the genomics age. Int J Epidemiol 33(5):936–944

Li S, Moore CA, Li Z et al (2003) A population-based birth defects surveillance system in the People's Republic of China. Paediatr Perinat Epidemiol 17(3):287–293

Lin AE, Forrester MB, Cunniff C, Higgins CA, Anderka M (2006) Clinician reviewers in birth defects surveillance programs: Survey of the National Birth Defects Prevention Network. Birth Defects Res A Clin Mol Teratol 76(11): 781–786

Puri P, Höllwarth ME (eds) (2006) Pediatric Surgery. Springer, Berlin, Heidelberg

Shiota K, Yamada S (2005) Assisted reproductive technologies and birth defects. Congenit Anom (Kyoto) 45(2): 39–43

Fetal Counselling for Surgical Congenital Malformations

2

Kokila Lakhoo

Contents

2.1 Introduction

Paediatric surgeons are often called to counsel parents once a surgical abnormality is diagnosed on a prenatal scan. The referral base for a paediatric surgeon now includes the perinatal period. Expertise in surgical correction of congenital malformations may favourably influence the perinatal management of prenatally diagnosed anomalies by changing the site of delivery for immediate postnatal treatment; altering the mode of delivery to prevent obstructed labour or haemorrhage; early delivery to prevent ongoing fetal organ damage; or treatment in utero to prevent, minimise or reverse fetal organ injury as a result of a structural defect. Favourable impact of prenatal counselling has been confirmed to influence the site of delivery in 37% of cases, change the mode of delivery in 6.8%, reverse the decision to terminate a pregnancy in 3.6% and influence the early delivery of babies in 4.5%.

Counselling parents about prenatally suspected surgically correctable anomalies should not be solely performed by obstetricians or paediatricians. Similarly the paediatric surgeon performing these prenatal consultations must be aware of differences between the prenatal and postnatal natural history of the anomaly. There is often a lack of understanding of the natural history and prognosis of a condition presenting in the newborn and the same condition diagnosed prenatally.

The diagnosis and management of complex fetal anomalies require a team effort by obstetricians, neonatologists, genetecists, paediatricians and paediatric surgeons to deal with all the maternal and fetal complexities of a diagnosis of a structural defect. This team should be able to provide information to prospective parents on fetal outcomes, possible interventions, appropriate setting, time and route of delivery and

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expected postnatal outcomes. The role of the surgical consultant in this team is to present information regarding the prenatal and postnatal natural history of an anomaly, its surgical management and the long-term outcome.

2.2 Congenital Malformation

Congenital malformations account for one of the major causes of perinatal mortality and morbidity. Single major birth defects affect 3% of newborns and multiple defects affect 0.7% of babies. The prenatal hidden mortality is higher since the majority abort spontaneously. Despite improvements in perinatal care, serious birth defects still account for 20% of all deaths in the newborn period and an even greater percentage of serious morbidity later in infancy and childhood. The major causes of congenital malformation are chromosomal abnormalities, mutant genes, multifactorial disorders and teratogenic agents.

2.3 Prenatal Diagnosis

Prenatal diagnosis has remarkably improved our understanding of surgically correctable congenital malformations. It has allowed us to influence the delivery of the baby, offer prenatal surgical management and discuss the options of termination of pregnancy for seriously handicapping or lethal conditions. Antenatal diagnosis has also defined an in utero mortality for some lesions such as diaphragmatic hernia and sacrococcygeal teratoma so that true outcomes can be measured. Prenatal ultrasound scanning has improved since its first use 30 years ago, thus providing better screening programmes and more accurate assessment of fetal anomaly. Screening for Down's syndrome may now be offered in the first trimester (e.g. nuchal scan combined test) or second trimester (e.g. Triple blood test). Better resolution and increased experience with ultrasound scans has led to the recognition of ultrasound soft markers that have increased the detection rate of fetal anomalies but at the expense of higher false positive rates.

Routine ultrasound screening identifies anomalies and places these pregnancies in the high-risk categories with maternal diabetes, hypertension, genetic disorders, raised alpha fetoprotein, etc. High-risk pregnancies may be offered further invasive diagnostic investigations such as amniocentesis or chorionic villous sampling. Structural abnormalities difficult to define on ultrasound such as hindbrain lesions or in the presence of oligohydramnios are better imaged on ultra fast magnetic resonance imaging. With the increasing range of options and sophistication of diagnostic methods, parents today are faced with more information, choice and decisions than ever before, which can create as well as help to solve dilemmas. The different tests and screening procedures commonly in use are outlined below.

2.3.1 Ultrasound Examination

Ultrasound scan is routinely performed at 18–20 weeks gestation as part of the prenatal screening for all pregnancies in England and Wales. Older mothers are routinely screened and in addition are offered invasive testing. Pregnancies with maternal risk factors such as raised alpha fetoprotein levels, genetic disorders and family history of chromosomal abnormalities or monochorionic twins that carry a high risk for chromosomal anomalies are offered scans in the first trimester. Abnormalities such as diaphragmatic hernia may be detected as early as 11 weeks of gestation. First trimester scans are also useful for accurately dating pregnancies and defining chorionicity in multiple pregnancies.

More recently, nuchal translucency (NT) measurements have emerged as an independent marker of chromosomal abnormalities with a sensitivity of 60%, structural anomalies (particularly cardiac defects) and for some rare genetic syndromes. It involves measuring the area at the back of the fetal neck at 11–14 weeks of gestation (Fig. 2.1). The mechanisms by which some abnormalities give rise to this transient anatomical change of nuchal translucency are poorly understood. Although some abnormalities can be seen at the time of the nuchal scan (11–14 weeks), most are detected at the 18–20 week anomaly scan. Some abnormalities such as gastroschisis have a higher detection rate on a scan than others, for example, cardiac abnormalities.

If the nuchal translucency measurement is increased and the karyotype is normal, there is a higher risk for a cardiac anomaly and these high-risk fetuses may be

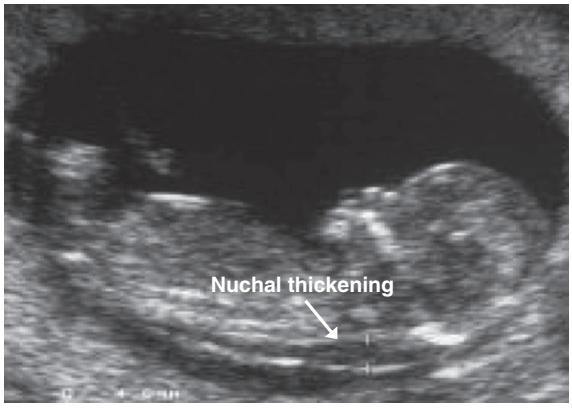

Fig. 2.1 Nuchal translucency scan

referred for fetal echocardiography, which provides better prenatal cardiac assessment than the routine screening scan. Ultrasound surveillance is essential during the performance of invasive techniques such as amniocentesis, CVS and shunting procedures. It is also useful for assessing fetal viability before and after such procedures. Some abnormalities such as tracheo-oesophageal fistula, bowel atresia, diaphragmatic hernia and hydrocephaly may present later in pregnancy and thereby may not be detected during the routine 18-weeks scan.

Overall, around 60% of structural birth defects are detected prenatally but the detection rate varies from 0% (isolated cleft palate) to close to 100% (gastroschisis) depending on the defect. True wrong diagnoses are rare but false positive diagnoses do occur; some are due to natural prenatal regression, but most are due to ultrasound "soft markers".

Ultrasound "soft markers" are changes noted on prenatal scan that are difficult to define. Examples are echogenic bowel, hydronephrosis and nuchal thickening. Their presence creates anxiety among sonographers because the finding may be transient with no pathological relevance or may be an indicator of significant anomalies such as chromosomal abnormalities, cystic fibrosis (echogenic bowel), Down's syndrome (nuchal thickening) or renal abnormalities (hydronephrosis). Once soft markers are detected, the dilemma faced by obstetricians is whether they should be reported or further invasive tests offered. Reporting these markers has increased detection rates at the expense of high false positive rates.

Ultrasound is routinely performed as a prenatal screening test. The reliability of the information obtained is dependent on the expertise and experience of the person performing the scan. In a recent study, congenital anomalies noted at birth were diagnosed on prenatal scan in 64% of cases with 0.5% opting for termination.

2.4 Invasive Diagnostic Tests

Amniocentesis and chorionic villous sampling (CVS) are the two most commonly performed invasive diagnostic tests.

2.4.1 Amniocentesis

Amniocentesis is commonly used for detecting chromosomal abnormalities and less often for molecular studies, metabolic studies and fetal infection. It is performed after 15 weeks of gestation and carries a low risk of fetal injury or loss (0.5–1%). Full karyotype analysis takes approximately 2 weeks but newer RAPID techniques using FISH (fluorescent *in situ* hybridisation) or PCR (polymerase chain reaction) can give limited (usually for trisomies 21,18,13) results within 2–3 days.

2.4.2 Chorionic Villous Sampling (CVS)

CVS is the most reliable method for first trimester diagnosis and may be performed at 10–14 weeks of gestation. The test involves ultrasound-guided biopsy of the chorionic villi. The added risk for fetal loss is approximately 1–2%. The samples obtained may be subjected to a variety of tests including full karyotype, rapid karyotyping (FISH—PCR), enzyme analysis or molecular studies. Approximate timing of chromosomal results is 1–2 weeks for karyotyping and 2–3 days for FISH and PCR.

2.4.3 Prenatal Maternal Serum Screening

Interest in detecting circulating fetal cells in maternal blood for diagnostic purposes has grown since the