Part I

Approach to the child with special needs

Children with special health care needs account for a substantial proportion of pediatric hospital and outpatient visits. While the individual disorders causing chronic disease may be rare, the aggregate impact of chronic care occupies a significant fraction of the health professional’s time. It is often cited that the sickest 1% of the population consumes 30% of the health care resources while the sickest 5% consumes 50%. The impact of chronic illness is similarly exaggerated in pediatric practice, with disproportionate demands on practitioners. Preventive management offers an important opportunity to minimize complications in children with special health care needs, and the key to preventive management is a specific diagnosis and approach.

This section previews those on specific disorders by outlining general approaches to the child with genetic disease and developmental disability. The practitioner should realize that the many rare genetic and developmental disorders can be grouped into disease categories, providing general guidelines for specialty referral and preventive management. Rather than being overwhelmed by long lists of eponyms or symptoms, the primary care provider can recognize categories such as multiple defect syndromes or increased muscle tone and use these introductory chapters to refine their approach to the diagnosis and management or congenital disorders.

Chapter 2 examines different causes of developmental disability, with an overview of assessment and therapy. Early recognition of developmental disabilities is emphasized, so that a Chronic Condition Management protocol can be instituted that optimizes pivotal functions like hearing and vision. Chapter 3 reviews the rationale for preventive management and applies these principles to the child with special health care needs. The chapter concludes with an overview of the preventive measures used in this book, and highlights common strategies that can be used for children with disabilities but without a specific diagnosis.
Medical genetics is a harlequin specialty. One side is bright with the power of DNA diagnosis and genotyping; the other is darkened by ignorance of complex phenotypes. Fortunately, the molecular revolution is proceeding so rapidly that even complex syndromes are being drawn into the light of genetic analysis. For a growing number of developmental and/or metabolic disorders, proper recognition and referral can lead to definitive diagnostic testing. It is thus extremely important for practitioners to be familiar with common presentations of genetic and developmental diseases, allowing affected children and their families to receive the benefits of informed management and genetic counseling.

A correct diagnosis is the gateway to anticipatory guidance and case management. Although the primary care physician may not be the first practitioner to establish the correct diagnosis, it is essential that he or she be able to incorporate specialty opinions and laboratory data into a comprehensive care plan. It is not necessary for practitioners to know long lists of eponymic disorders, but it is necessary that they recognize the possibility of genetic or congenital disease so that appropriate referrals and information can be obtained. Computerized databases such as Online Mendelian Inheritance in Man (OMIM – www.ncbi.nlm.nih.gov/entrez) with links to genome and literature databases of the National Institutes of Health, Recognizable Patterns of Human Malformation (Jones, 1997), Syndromes of the Head and Neck (Gorlin et al., 2001), and The Metabolic and Molecular Bases of Inherited Disease (Scriver et al., 2001) are available to provide details on particular diseases. This chapter will review the clinical approach to children with morphologic and/or metabolic alterations, beginning with the important component of family history and presenting for management based on categories of disease. Italicized terms are defined in the glossary at the end of the book.

The family history: A preventive measure for all children

The documentation of a family history is a key first step in the care of all children, especially for those with developmental disabilities. The family history is important...
for two reasons: first, for recognizing general risk factors that can apply to any child and second for revealing specific genetic disease that explains or affects a particular child. This latter use of family history is less common, but recognition of a Mendelian or chromosomal inheritance pattern is essential for early referral and diagnosis of at-risk families.

The general use of family history in defining risk factors is receiving increased attention as advances in genetic technology accumulates DNA markers for risk modification. DNA testing is increasingly available to identify individuals with higher risks for disorders such as coronary artery disease, breast cancer, autoimmune disease, learning disabilities, or mental illness. The American surgeon general has recently emphasized the need for all individuals to know their family history as a guide to disease susceptibility and prevention.

A more traditional use of the family history is to determine if a particular medical disease or disability is inherited. This step is particularly crucial for congenital anomalies and syndromes, since every parent has anxiety and guilt that they have contributed to their child’s illness by their habits or genes. Education of the parents that the majority of disabilities are inborn allows the practitioner to allay fears about prior habits or pregnancy exposures. When a disorder is clearly genetic, as in chromosomal disorders like Down syndrome, the cause is often a spontaneous mutation that was not inherited and thus is not the fault of either parent. A key finding of the human genome project is that every individual carries numerous genetic changes that are not inherited (spontaneous mutations), and conveying this information to parents when appropriate is simple and powerful information.

Documenting a family history

Figure 1.1a provides an easily understandable template that can be used by parents or prospective parents to record their family history. An excellent time to present this form is during the prenatal conference with pediatricians and family practitioners, and it can supplement the information already collected during obstetric visits. The history is taken from the perspective of an affected child or patient that has attracted medical attention, but the form could also be used as a general screening measure in pediatrics. The family should be told that the form gives them a template for tracking down necessary information, and that confusion or incomplete information will be clarified by later interview with their health care provider. The family will at least have knowledge of the types of information needed, allowing them to contact informed relatives and gather records preparatory to a more formal pedigree at a later visit.

Figure 1.1b provides a template for health care professionals to convert the family history into a more formal pedigree. Pedigree symbols are listed as a reminder, and the scheme for numbering generations and individuals allows documentation
### FAMILY HISTORY FORM (For couples to fill out prior to their or their child's medical evaluation; questions will be resolved during the medical visit)

1. List your relatives from the perspective of your union or marriage (wife and husband); list relatives by first name, last name initial, and age in years (e.g., John R, 45) in the appropriate spaces.

2. List siblings (brothers or sisters) and half-siblings of the patient, parents, and grandparents. Indicate miscarriages or stillbirths by putting a Q in the box (see key below).

3. Indicate the number of offspring for each sibling in the spaces indicated. For example: John R 6 boys 5 girls for John R having 6 boys and 5 girls can be added for each miscarriage/stillbirth.

4. Show relatives affected with medical problems by putting the appropriate number(s) below next to their name and circle them for clarity. For example: “John R 45” to indicate he has mental illness.

5. Modify the key below for the illnesses in your family – specify the type of problem if necessary, and use numbers 25–28 for problems that are not listed.

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#### 1. Miscarriage/stillbirth
1. Miscarriage/stillbirth ( )
2. Early/sudden death ( )
3. Obesity, other ( )
4. Cancer < age 45 (type )

#### 2. Mental retardation/disability
1. Mental retardation/disability ( )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

#### 3. Mental illness (type)
1. Mental illness (type: )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

#### 4. Behavior problem
1. Behavior problem ( )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

#### 5. Learning problem ( )
1. Learning problem ( )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

#### 6. Speech disorder ( )
1. Speech disorder ( )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

#### 7. Autism/PDD ( )
1. Autism/PDD ( )
2. Multiple birth defects ( )
3. Birth defect ( )
4. Other ( )

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**Pregnancies/losses**

- **Wife’s mom’s siblings**
  - Boys: ___
  - Girls: ___

- **Wife’s dad’s siblings**
  - Boys: ___
  - Girls: ___

- **Wife’s siblings and offspring**
  - Boys: ___
  - Girls: ___

- **Wife’s mom**
  - Boys: ___
  - Girls: ___

- **Wife’s dad**
  - Boys: ___
  - Girls: ___

- **Wife**
  - Boys: ___
  - Girls: ___

- **Husband**
  - Boys: ___
  - Girls: ___

- **Husband’s mom**
  - Boys: ___
  - Girls: ___

- **Husband’s dad**
  - Boys: ___
  - Girls: ___

- **Husband’s siblings and offspring**
  - Boys: ___
  - Girls: ___

- **Half-sibs through wife and offspring**
  - Boys: ___
  - Girls: ___

- **Half-sibs through husband and offspring**
  - Boys: ___
  - Girls: ___

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**Notes:**

1. List your relatives from the perspective of your union or marriage (wife and husband); list relatives by first name, last name initial, and age in years (e.g., John R, 45) in the appropriate spaces.

2. List siblings (brothers or sisters) and half-siblings of the patient, parents, and grandparents. Indicate miscarriages or stillbirths by putting a Q in the box (see key below).

3. Indicate the number of offspring for each sibling in the spaces indicated. For example: John R 6 boys 5 girls for John R having 6 boys and 5 girls can be added for each miscarriage/stillbirth.

4. Show relatives affected with medical problems by putting the appropriate number(s) below next to their name and circle them for clarity. For example: “John R 45” to indicate he has mental illness.

5. Modify the key below for the illnesses in your family – specify the type of problem if necessary, and use numbers 25–28 for problems that are not listed.

---

**Fig. 1.1** (a) Family history form for patients to fill out.
PEDIGREE FORM (Generations I–V)

1. Record family history from perspective of union (wife and husband for short) or wife and husband’s child being evaluated. Use symbols as listed at the bottom of the pedigree form.
2. Score individuals with disease or trait by placing number from key below next to their symbol. For example, male affected with autism and mental illness (specify type on key).
3. If several individuals have the same genetic disease, you can mark their symbols with , , , or and list the symbol on the key.
4. At bottom, list here all risk factors for the couple/children ascertained from the pedigree and record them on the preventive medical checklist (i.e., juvenile diabetes, hypertension).

<table>
<thead>
<tr>
<th>Risk factors:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage/stillbirth</td>
</tr>
<tr>
<td>Mental disability</td>
</tr>
<tr>
<td>Mental illness (type: )</td>
</tr>
<tr>
<td>Learning problem</td>
</tr>
<tr>
<td>Behavior problem</td>
</tr>
<tr>
<td>Speech disorder</td>
</tr>
<tr>
<td>Autism/PDD</td>
</tr>
<tr>
<td>(b) Autism/PDD</td>
</tr>
<tr>
<td>Cancer &lt; age 45 (type: )</td>
</tr>
<tr>
<td>Obesity, other</td>
</tr>
<tr>
<td>Heart disease (type: )</td>
</tr>
<tr>
<td>Heart disease</td>
</tr>
<tr>
<td>Birth defect (type: )</td>
</tr>
<tr>
<td>Birth defect</td>
</tr>
<tr>
<td>Multiple birth defects</td>
</tr>
<tr>
<td>Infertility</td>
</tr>
<tr>
<td>Divorce</td>
</tr>
<tr>
<td>Related</td>
</tr>
<tr>
<td>Adopted</td>
</tr>
<tr>
<td>Either sex</td>
</tr>
</tbody>
</table>

Fig. 1.1 (b) Pedigree form for health professionals.
7 Approach to the child with genetic disease

of diseases above the diagram without cluttering the body of the pedigree. Health care providers should not focus unduly on the “correctness” of pedigree symbols, and individuals can be numbered as they are discussed during interview rather than worrying about the formal numbering by pedigree position that is listed in textbooks. The template facilitates conversion of family information into a readable and permanent document that is available for all care providers.

Once the pedigree is documented, multiple instances of common diseases like diabetes or heart disease can be recognized and entered on the bottom line as risk factors for the particular child. These risk factors can then be entered on the appropriate preventive checklist for the child, allowing consideration of glucose or blood cholesterol testing in children with positive family histories. These general risk factors are particularly important for children with special health care needs, because co-morbidities can be so devastating for fragile patients. Note that Fig. 1.1b emphasizes cancers with onset before age 45, an arbitrary limit that encourages focus on premature illness rather than common afflictions of the aged. As a general rule, earlier onset and increased severity reflects greater contribution of genes (e.g., juvenile versus adult diabetes mellitus or multifactorial coronary artery disease versus that due to familial hypercholesterolemia).

If a specific genetic disorder like Marfan syndrome is encountered in a pedigree, symbols for the affected individuals can be scored to help with recognition of a particular inheritance pattern. The correlation of pedigree patterns and inheritance mechanisms is discussed below, but this special aspect of family history taking is too-often emphasized and very little used (less than 5% of family histories are positive for a specific genetic disorder even in a genetic specialty practice). Practitioners certainly need to recognize pedigrees with specific medical disorders, but their main and most important role will be to highlight risk factors due to common, multifactorial diseases (see below).

Categories of genetic disease

Hereditary factors are involved in more than 5000 diseases. The hereditary contribution may be partial, as with multifactorial inheritance of cleft palate, or major, as with Mendelian inheritance of sickle cell anemia. Because they are congenital disorders, malformation syndromes are included within the specialty of pediatric genetics even though many, including fetal alcohol syndrome, are caused by environmental factors. Table 1.1 summarizes the number, frequency, morbidity, and mortality of genetic diseases and syndromes classified according to their mode of inheritance (Wilson, 1990, 1992, 2000). Several studies have suggested that genetic disorders are estimated to account for 15–25% of admissions in a general pediatric hospital. Yoon et al. (1996) reported that 12% of hospital admissions in the states...
of California and South Carolina were related to birth defects and genetic diseases, generating about twice the charges per patient compared to other diseases.

Table 1.2 indicates that patients with genetic diseases come to attention in three ways: those requiring genetic counseling, those with congenital anomalies, and those with metabolic disorders. Each patient category is associated with particular inheritance mechanisms and laboratory evaluations (Table 1.2). Individuals requiring genetic counseling represent the largest category, since genetic diseases can affect any organ system. The patient with cystic fibrosis or the patient with sickle cell anemia is usually not managed by geneticists, but these patients share a need for genetic counseling. Because genetic counseling is frequently a complex process, it will often involve individuals with specialized training. Nevertheless, the key role of practitioners in bringing families to attention mandates that they be aware of risk factors such as the multiple miscarriages, consanguinity, or advanced parental age listed in Table 1.2.

A second category of patients referred for genetic evaluation is the child with congenital anomalies (dysmorphology). This category includes children with single anomalies, multiple anomaly syndromes, or chromosomal disorders and accounts for 3–5% of all births. The third category of referral consists of inborn errors of metabolism, which affect an estimated 1 in 600 births. Metabolic disorders may present in the neonatal period, but often become evident in later infancy or childhood when symptoms of episodic illness, visceromegaly, and/or neurodegeneration become evident.

The categories of morphologic and metabolic disease present with different signs and symptoms, and their diagnosis requires different laboratory measurements (Table 1.2). Intrauterine growth retardation and breech presentation frequently accompany congenital malformations and syndromes, as do altered head size, delayed or accelerated growth, and skeletal disproportion. Subtle (minor) anomalies such as epicanthal folds or single palmar creases raise questions of a syndrome pattern, particularly when several are detected. Observation of a surgically or cosmetically

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Table 1.1. Numerology of genetic disease

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
<th>Frequency (%)</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mendelian</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autosomal dominant</td>
<td>2557</td>
<td>0.7</td>
<td>34</td>
<td>61</td>
</tr>
<tr>
<td>Autosomal recessive</td>
<td>1477</td>
<td>0.25</td>
<td>74</td>
<td>87</td>
</tr>
<tr>
<td>X-linked</td>
<td>310</td>
<td>0.5</td>
<td>62</td>
<td>85</td>
</tr>
<tr>
<td>Multifactorial</td>
<td>&gt;100</td>
<td>3–5</td>
<td>&gt;50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Chromosomal</td>
<td>&gt;100</td>
<td>0.5</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>Syndromal</td>
<td>&gt;1000</td>
<td>0.8</td>
<td>&gt;90</td>
<td>98</td>
</tr>
</tbody>
</table>

significant (major) anomaly should always initiate a search for other anomalies, so the different prognoses for children with isolated versus multiple anomalies are correctly assigned. Since the nervous system is affected in at least 55% of hereditary syndromes (Wilson, 1992), developmental delay is also an indication for syndrome evaluation. Chromosomal and skeletal radiographic studies are important laboratory considerations in a child with growth and/or developmental delay.

Inborn errors of metabolism may occasionally present with congenital malformations, but maternal metabolic compensation will usually protect fetal morphogenesis. A common scenario is the normal newborn who becomes irritable, lethargic,
and comatose after feeding, often with accelerated physiologic jaundice or unusual odors. Hypoglycemia and acidosis are also frequent accompaniments of metabolic disease, particularly when the hypoglycemia is not combined with the appropriate ketotic response. Other presentations for metabolic disease include visceromegaly, bone marrow suppression, developmental delay or regression, and episodic vomiting or hypoglycemia.

**Approach to genetic counseling**

Genetic counseling is an educational process that provides individuals with information about a genetic disease and their recurrence risks. To paraphrase its definition by the American Society of Human Genetics, genetic counseling is a communication process which deals with the occurrence, or the risk of occurrence, of a genetic disorder in a family. During this communication process, appropriately trained individuals assist the family to understand:

1. the diagnosis and management options for the disorder;
2. the contribution of heredity to the disorder and how this translates to recurrence risks among family members;
3. the alternatives (i.e., prenatal diagnosis) for dealing with these recurrence risks.

The counseling process should also assist the family choose a course of action based on their particular family goals or ethical/religious background and to make the best possible adjustment to the presence and future implications of a genetic disorder.

The need for genetic counseling often arises from a family history, which should be part of every medical evaluation. A pedigree is simply a codified family history, with generations, individuals, and the presenting patient (proband or propositus) diagrammed in a standard format as discussed above regarding the template in Fig. 1.1. Numbering of the generations (Roman numerals) and individuals (Arabic numerals) facilitates documentation of a clear pedigree diagram.

Once a pedigree is constructed, inheritance mechanisms are often evident from the pattern of affected individuals (Fig. 1.2). Autosomal dominant or X-linked inheritance often exhibits a vertical inheritance pattern, with male-to-male transmission ruling out the possibility of X-linked inheritance. Horizontal patterns of affected individuals (i.e., siblings) suggest the operation of autosomal recessive inheritance, and this mechanism is sometimes made more plausible by parental consanguinity (inbreeding).

In order to begin the process of genetic counseling, the physician must document the family history, inspect the pedigree for evidence of inherited diseases, and understand the genetic risks implied by particular inheritance mechanisms. The Online Mendelian Inheritance in Man database (www.ncbi.nlm.nih.gov/entrez) provides a useful resource for deciding which, if any, inheritance mechanism has
been established for a pediatric disease. Since diseases may exhibit genetic heterogeneity with several possible inheritance mechanisms (e.g., Charcot–Marie–Tooth disease, retinitis pigmentosa, cleft palate), referral to a genetic specialist is often necessary for accurate genetic counseling. Practitioners can then review this specialty counseling with the family, utilizing their rapport and knowledge of the family to place the genetic information in context.

It is important to avoid a judgmental attitude towards reproductive options or disabilities, since overly negative portrayals of disorders such as Down syndrome can rupture the parent–physician relationship. In the case of prenatal diagnosis, anticipation, adoption or foster care should be mentioned as alternatives to abortion. Parent support groups are very useful in arranging contact with affected individuals so at-risk families can become familiar with disease manifestations.

For a growing number of diseases, genetic counseling can include the provision of DNA diagnosis for at-risk family members. Some understanding of the methods and requirements for DNA diagnosis are useful for practitioners, and these are summarized below. It is important that pediatricians be attuned to genetic risks in parents (or other relatives) that result from a child’s diagnosis.

![Pedigrees](https://example.com/pedigrees.png)

Fig. 1.2 Pedigrees typical of (a) autosomal dominant; (b) autosomal recessive; (c) X-linked recessive; and (d) chromosomal inheritance displaying symbols for males (squares), females (circles), affected individuals (filled symbols), consanguinity or inbreeding (double line), abortions (small symbols), death (diagonal line), and individuals coming to medical attention (arrows).