CAUSES of INTELLECTUAL and DEVELOPMENTAL DISABILITIES:

BIOLOGICAL CONSIDERATIONS and PREVENTION

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Overview

This document is intended for educators and/or students with interest in intellectual and developmental disabilities. It discusses disabilities under four main categories- genetic transmission, chromosomal abnormalities, cranial malformations, and other congenital factors. In each section, several examples of disabilities are explained with emphasis on causation, diagnosis, and treatment. The table below summarizes the disabilities discussed in this document.

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Within this paper, pre-to-post natal concerns are discussed. Included is an explanation of strategies that can be used to prevent intellectual and developmental disabilities. These strategies range from those that can be implemented within the preconception stage to early childhood. There is an explicit description of ethical considerations that may arise in the effort to prevent intellectual disabilities. The paper concludes with final thoughts and a summary of key points.

The information provided in this document can be used for general knowledge, as part of course content in special education classes and/or reference material. However, please note that all information is the property of the authors and so full credit must be given to authors whenever any material is used. Please address all inquiries to the senior author.
Objectives

After reading this chapter, the student should be able to:

- provide an overview of causation
- discuss the basic principles of genetics
- identify and discuss the major biological causes of intellectual and developmental disabilities
- identify areas in which treatment implications are indicated
- discuss various ways that intellectual disability can be prevented
- identify and discuss selected ethical issues facing the field

The task of sorting out the many causes of intellectual disability is formidable. From the beginnings of the study of intellectual disability in the earliest part of recorded history to the more advanced efforts in the 21st century, the search for causation has been challenging. The goal of this chapter is to provide a foundation for understanding the complexities in the causes of intellectual and developmental disabilities.

Causes of intellectual and developmental disabilities have traditionally been divided into two categories: biological (or physiological) and environmental (or psychological and sociological). Such a taxonomic grouping of causes might be thought to create clear dichotomy of specific causes. However, factors from both of these domains are often relevant in individual cases of these disabilities.

Although hundreds of specific factors have been identified as causative agents of intellectual disability, the number of cases of with unknown causes are still as large as those that are known and specifiable; that is, in 50% or more of cases can a specific cause (i.e., biological
factor) be identified (Dykens, Hodapp & Finucone, 2000; van Karnebeek et al., 2005). A key problem is that causes may be undetermined for the many persons identified as having a “mild” disability (which constitute perhaps 60% of persons with intellectual disabilities; PCPID, 2007).

A traditional perspective of causation is the two-group model that includes a group with organic (i.e., specific biological) causes and a second group presumed to be socio-cultural or, historically cultural familial (Spinath, Harlaar, Ronald, & Plomin, 2004). The first group consists of known and specifiable biological causes that often classified as pathological and/or clinical. Although such causes may result in intellectual disabilities at all levels, most attention in the past was drawn to their etiology of more significant disabilities. Biological pathology can be identified in from 60% to 75% of cases IQs falling below 50 (McLaren & Bryson, 1987) or higher (Heikura et al., 2005). But the traditional association of a single, organic cause just with significant disabilities is too simplistic; many individuals with high incidence disabilities (i.e., mild intellectual disabilities) may also be affected because of physiological factors.

The other traditional assumption—that mild disabilities are the result of multiple, unspecifiable environmental events—has also given way to the fact that this is only a “broad brush” distinction (Moser, 2000) and thus estimates over the past two decades have concluded: up to 40% of all cases of mild disabilities may have a specific identifiable cause (Harris, 2006; McLaren & Bryson, 1987); 10-50% of cases of mild intellectual disabilities are related to genetic etiologies (Dykens et al., 2000); and only 33% are unknown (Heikura et al. 2005). Further the assumption that sociocultural factors are all environmentally-based has been challenged by studies of possible genetic influence (e.g., Spinath et al., 2004).

Clearly these data are influenced significantly by state prevalence rates (see USDOE, 2007), in that states with high rates of identified intellectual disabilities (for ages 6-17) (e.g.,
West Virginia, 2.47%; Wyoming, 2.25%) are likely to have a larger number of students with mild disabilities and an associated lower percentage of identified biological causes than would a state with a lower prevalence (e.g., New Jersey, 0.34 %; California, 0.34 %) (see Polloway, Lubin, Smith, & Patton, 2008). Despite these data, it is nevertheless important to recognize that many individuals with mild disabilities are also affected by genetic and other biological causes and that psychological and social influences are equally important in cases of severe disability. Finally, there is increasing confidence that the cause of virtually all cases of intellectual disabilities may become identifiable (Moser, 2000).

Given this confounding complexity, why should educators, psychologists, and other behavioral scientists spend time studying causation of intellectual disabilities? Kolstoe (1972), in his classic work, noted that familiarity with these causative factors facilitates multidisciplinary communication, is an essential element of professionalism, and is important in enabling professionals to make accurate information available to parents. Clearly, parents have the right to know information that may be related to inherited forms of intellectual disabilities and also should be well-informed about preventable environmental hazards that might otherwise be associated with disabilities (Percy, 2007). Furthermore, in most situations, etiological information from educators and childcare professionals can contribute to a more accurate diagnosis. The role of teachers, for example, may include monitoring the effects of ongoing or progressive disorders that may hinder daily performance, preventing future occurrences through parent counseling, or facilitating immediate change (e.g., intervention in a case of child abuse).

Finally, research is beginning to identify certain educational and psychological intervention strategies that may be etiology-specific. Therefore, an understanding of causation may ultimately lead to alternative approaches to curriculum and instruction (e.g., Powell,
Haughton, & Douglas, 1997; Hodapp, 1997). Hodapp (1997) suggested that the field has generated conflicting views of the relationship between etiology and behavior; on the one hand, the position is that, for example, specific genetic disorders have no specific effects on behavior while an alternative is that genetic disorders are regularly and consistently associated with a distinctive behavioral pattern. He recommended a compromise between these two positions:

a few different genetic disorders show an identical behavior among those affected, and this behavior differs from the behavior of individuals with other types of mental retardation. Thus, it is not as if all genetic disorders have identical effects on behavior or that each genetic disorder has unique effects. Instead a few disorders show similar effects, which are, in turn, not shared by mixed etiological groups (p. 70).

Dykenes (2001) noted that the value of etiological information continued to grow in part because:

Behavioral researchers are playing a pivotal role in this ground swell of syndromic research. One long-term goal of this line of work is to examine links between genes, brain, and behavior …. Simply put, behavioral experts are needed to solve the behavioral half of these gene-behavior puzzles. In the short-term, behavioral … data can be put to immediate good use as guideposts for treatment and intervention, and such syndrome-specific recommendations have already been made for fragile X, Down, Prader-Willi, Williams, and other syndromes (p.1).

With specific regard to the question of whether genetic disorders matter, it is interesting to note the points summarized by Dykens, Hodapp, and Finucane (2000) who spoke to three specific
myths. The first myth that syndromes occur rarely was questioned because approximately 1/3 or all persons with intellectual disabilities may result from genetic causes. Second, the question of whether syndromes only provide labels that are unnecessary was refuted in part by the fact that the effects of genetic disorders can sometimes be modified such as through intervention efforts (see the succeeding discussion on PKU and dietary controls). Third, biological syndromes have been questioned as not mattering for practical concerns but, as in the example of Prader-Willi syndrome, syndrome identification can matter significantly in this case in terms of eating habits and intervention. Cutting and Denckla (2004) noted that “with advances in behavioral, neuroimaging, and genetic methodologies, the next decade should yield a deeper understanding of the complexities of cognition and different types of disabilities, with the end goal of producing effective, school–based treatments for students with an array of cognitive weaknesses” (p.174).

Such research reflects the study of behavioral phenotypes which focuses on determining relationships between specific genetic, chromosomal, or neurodevelopmental disorders and the mental, intellectual, and behavioral features that are causally related to the specific condition. Harris (2006) noted that “behavioral phenotypes are stereotypical patterns of behavior that are reliably identified in groups of individuals with known neurodevelopmental disorders and are ‘not learned’, . . . this does not mean that the behavior is present in all instances but the probability of its incurrence is increased” (p.195).

While a general awareness of causative factors is necessary for all professionals, the mechanisms of specific causes require multidisciplinary involvement. Input from various disciplines (e.g., biology, medicine, epidemiology, social work, psychology, psychiatry) and special education often is essential to determine whether a cause can be specified or is even
relevant to treatment and/or education. That many causes of intellectual disabilities cannot be currently identified also serves as a stimulus for continuing research.

Finally, while considering information on causation, it is important that the reader not lose sight of the fact that behind these terms are people responding to special challenges in their lives. As Blatt (1987) cautioned, “Treatises that deal with etiological conditions rarely recognize the human being [in] the superficially unattractive trappings of the condition” (p. 128). Readers must not overlook the fact that we are talking about real people who happen to have a given disability.

Our discussion of causes begins with attention to terminology and then focuses on genetics, other biological causes, and environmental influences. It concludes with attention to prevention and related ethical issues.

**TERMINOLOGY**

As noted earlier, the task of understanding the causes of intellectual and developmental disabilities is challenging, and translating specific terms for known causes into useful information can be particularly difficult. This section offers ways to understand some of the labels ascribed to selected causative factors.

First, it is helpful to consider the causes of intellectual disabilities through a developmental lens. This can be conceptualized as a series of concentric circles representing (from inner to outer) that relate to: inherited traits: factors related to inheritance; conditions that refer to all influences through the time of conception; congenital conditions also inclusive of factors taking place during pregnancy; and constitutional considerations that encompass all biological influences (Polloway & Rucker, 1997).
Much of the focus of attention related to the causation of intellectual disabilities has to do with specific syndromes. As Percy et al. (2007) noted, “syndrome” derives from the Greek words *syn*, meaning “together with” and *drome*, referring to “to run”. As a result, syndromes focus on considerations that “run together”, and thus that represent “a complex of concurrent things” (p. 229). The terminology used to identify various syndromes comes from three sources: (a) conventional wisdom or practices related to a specific historical era, (b) names of persons who initially identified or described the condition, and (c) biomedical terms describing the cause or the resultant disabilities.

Several examples illustrate how historical names have been associated with intellectual disabilities for syndromes. Perhaps best known is the certainly archaic (and offensive) term *mongolism*, which was coined by J. Langdon Down in 1866, two decades after Seguin’s initial identification of the condition (Menolascino & Egger, 1978). For 100 years, this term, which was assigned simply because of Down’s inaccurate observation that one frequent characteristic of the syndrome was facial similarity to Asians, prevailed in medical and psychological circles. Jordan (2000, p. 325) summarized the context within which Down made his observations:

‘the inescapable observation that the expanding centers of manufacturing contained a population of overcrowded, chronically ill, malnourished Britons led to an alarming conclusion, namely, that the population was increasingly unhealthy and their retrogression in health and habits would be increased with each succeeding generation.’  Down noted that ‘the largest proportion of idiocy is to be found among the lower orders, how can it be expected but that the mother . . . should propagate an enfeebled race?’  In short, the British race appeared to be deteriorating at a rapid rate. In them, the appearance of features
from other ethnic groups, in particular ‘the great Mongolian family,’ as Down phrased it, led him to see the degeneracy problem writ large on Britain’s population.

Realization that Down syndrome is found in all racial groups (including persons from Mongolia) eventually aided in the much-needed elimination of this racist term from the vocabulary of most professionals. Its use, however, unfortunately persists, particularly in some popular media.

A second, more direct way to identify a clinical syndrome is to attach to it the name of the researcher who contributed in a major way to its understanding. For instance, professionals now identify as Down syndrome the chromosomal condition disorder that J. Langdon Down originally described as mongolism. Other relatively well-known syndromes so named include Tay-Sachs, after the British and American physicians who described the characteristics of the condition in the late 1880s, and Lesch-Nyhan syndrome, named for two of the three researchers who first identified this disorder in 1964.

The third source of syndrome labels is biomedical terminology. Although some of these terms are frequently used by laypersons, their meanings are often obscure, in spite of their grounding in common forms. Thus, many of the labels convey primary features of the disorder, either causal or characteristic.

Although labels are only an attempt to refer to complex phenomena, simply being familiar with the derivatives can be of assistance in understanding the nature of these disorders and the terms related to them. Several specific terms illustrate the system. For example, *toxoplasmosis* indicates a condition (*-osis*) of poisonous (*toxo*) blood (*-plasm*). Although the clinical definition of toxoplasmosis is much more specific, the word, when analyzed, gives a fair suggestion of what the condition is about. Another example is *hydrocephalus*. The term refers to
a disorder resulting from a blockage of cerebrospinal fluid, but breaking the word down into
“water” (hydro-) and “head” or “brain” (cephalo-) provides a descriptive, if admittedly
simplistic, picture of the condition. A third example is the disorder called myelomeningocele. As
the term suggests, this condition is characterized by a saclike mass (-cele) on the spinal cord
(myelo-) containing membrane tissue of the central nervous system (-meningo-).

**GENETIC CONSIDERATIONS**

Genetics is the study of heredity and its variations. As such, its scope is enormous and its
complexities great. Advances in genetics over the past 70 years rival those in any area of science.
The contributions of geneticists to understanding the causes of developmental disabilities are
particularly noteworthy. In the last three decades, this knowledge base has mushroomed due to
research on gene mapping and DNA sequencing; most of it done under the auspices of the
Human Genome Project (see Box 1).

### BOX 1  The Human Genome Project

In 1990, a huge international research endeavor . . . was officially launched. This project is involving many
scientists and is equivalent in scope and cause to putting man on the moon. Its objective is to determine the
sequence of all the DNA in the human genome . . . This work will enable all of the genes in the human body .
. . to be identified. It also will aid in the identification of defects causing virtually every known genetic
disorder. As genes causing genetic disorders are identified, it will become possible to test individuals for
increasing numbers of inherited disorders, including intellectual disabilities associated with brain
malfunction. The identification of genetic causes of specific intellectual disabilities will become the search
for specific treatments, preventions, and cures. . . The human genome project is also examining the ethical,
legal, and social implications of human genetic research and is developing guidelines to help society deal
with such issues.

MD: Paul H Brookes.
An understanding of heredity begins with the study of genes. As Bryson (2004) eloquently stated, “genes are nothing more (nor less) than instructions to make proteins. . . . In this sense, they are rather like the keys of a piano, each playing a single note and nothing else, which is obviously a trifle monotonous. But combine the genes, as you would combine piano keys, and you can create cords and melodies of incident varieties. Put all these genes together and you have the great symphony known as the human genome” (p. 404). Genes are the basic biological units carrying inherited physical, mental, or personality traits.

Genes occupy specific positions on chromosomes, the thread like or rod like bodies that contain genetic information and material. As the Human Genome Project has progressed, the careful mapping and sequencing has reached a point where the full human genome will soon be completed.

Chromosomes vary widely in size and shape, but for human cells, the normal pattern is consistent. Each cell contains 23 pairs of chromosomes. The embryo initially receives one member of each pair from each parent. There are two types of chromosomes: autosomes and sex chromosomes. Autosomes are matching pairs and constitute 44 of the 46 chromosomes within the usual human complement (i.e., 22 of the 23 pairs). Sex chromosomes make up the other pair. The letter X is used to represent the female sex chromosome and Y to represent the male sex chromosome. While the X chromosome contains a substantial amount of genetic information, the Y functions primarily as a determinant of male gender. At conception, an X chromosome is contributed by the mother, while either an X or a Y is contributed by the father. The XX combination creates a female, and the XY a male.

Ridley (1999) described the genetic process in a unique way that facilitates further understanding. He noted:
The human body contains approximately 100 trillion cells. Inside each cell there is a black blob called a nucleus. Inside the nucleus are two complete sets of the human genome (except in egg cells and sperm cells, which have one copy each, and red blood cells, which have none). One set of the genome came from the mother and one from the father. In principle, each set includes the same 30,000 genes on the same twenty-three chromosomes. In practice, there are often small and subtle differences between the paternal and maternal versions of each gene, differences that account for blue eyes or brown, for example. When we breed, we pass on one complete set, but only after swapping bits of the paternal and maternal chromosomes in a procedure known as recombination. Imagine that the genome is a book. There are twenty-three chapters, called chromosomes. Each chapter contains several thousand stories, called genes.... There are one billion words in the book, which makes it longer than 5,000 volumes the size of this one, or as long as 800 Bibles.... This is a gigantic document, an immense book, a recipe of extravagant length, and it all fits inside the microscopic nucleus of a tiny cell that fits easily upon the head of a pin (p. 7).

The precise and rather fragile roles of genes and chromosomes as building blocks of development are dramatically represented in intellectual disabilities research. There are estimated 750-1000 genetic disorders associated with intellectual disabilities (Harris, 2006; Tartaglia, Hansen, & Hagerman, 2007). In Table 1, an illustrative list of some relatively common genetic causes is provided. The most prevalent general groups of biological causes of intellectual disabilities are genetic transmission of traits (i.e., genetic disorders) and
chromosomal abnormalities. A range of 17.47% to 47.1% for genetic causes has been reported in research on intellectual disabilities (van Karnebeek et al., 2005); Heikura et al. (2005) found it to be 36.1%, with 19.3% chromosomal and 7.6% single gene conditions. But even in seemingly clear-cut cases of genetic transmission, it is important to keep in mind that development is still shaped significantly by environmental influences. Ridley (2003) pointed out that because research has revealed that there are only 30,000 genes in the human genome rather than the 100,000 anticipated by genetics researchers and thus environmental influences have taken on an even greater potency in human development.

**TABLE 1**

Most Prevalent Genetic Conditions

- Down syndrome (1.3/1000)
- Klinefelter syndrome (0.8/1000)
- Fragile X (0.6/1000)
- Neurofibromatosis (0.33/1000)
- Hypothyroidism congenital (0.25/1000)
- Williams syndrome (0.1/1000)
- Phenylketonuria (0.067/1000)
- Prader-Willi syndrome (0.67/1000)

GENETIC TRANSMISSION

Many traits are transmitted from one generation to the next according to the makeup of a specific gene pair. Transmission can occur through autosomal dominant or autosomal recessive inheritance and through sex-linked dominant or recessive inheritance. In dominant inheritance, an individual gene can assume “control” over, or mask, its partner and will operate whether the two elements of an individual gene pair are similar or dissimilar to each other. Recessive inheritance refers to genes that cannot control their partners. In a sense they “recede” when paired with a dissimilar mate and become influential only when matched with another recessive gene. Pairs of genes carrying the same trait are called homozygous; pairs carrying different traits are heterozygous. Homozygous pairs are necessary for the case of recessive inheritance, whereas either homozygous or heterozygous pairs can lead to instances of dominant inheritance.

The dynamics of dominant and recessive inheritance are illustrated in Figure 1. Capital letters typically are used to indicate dominant traits; lowercase letters commonly denote recessive traits. In the typical case of dominant inheritance (Example A), only one parent would have the specific dominant trait in question, which is transmitted, theoretically, to two of their four children. In the common case of recessive inheritance (Example B), probability suggests that at each conception, chances are one in four that the child will be homozygous and will manifest the recessive trait (hh), two in four that he or she will be a heterozygous carrier for the succeeding generation (Hh, hH), and one in four that he or she will be homozygous, for the dominant gene, therefore lacking the recessive gene altogether (HH). Autosomal recessive transmission is responsible for approximately one-third of all single-gene disorders, autosomal dominant transmission for over one-half, and X-linked dominant and X-linked recessive transmission for the balance (Harris, 2006). While the genetic disorders associated with
recessive, dominant, and sex-linked transmission are individually and collectively very rare, nevertheless they warrant careful attention. Percy, Lewkis, and Brown, (2007) noted that, in spite of their relative rarity, each individual in the general population carries an average of 4 to 8 genes for different hereditary conditions.

![Diagram of Dominant and Recessive Inheritance]

**FIGURE 1**
Dominant and Recessive Inheritance

**Dominant Transmission**

Dominant inheritance determines a variety of common traits, including brown eyes and prematurely white hair. Several rare physical disorders are carried as dominant traits. Frequently these disorders are structural; that is, they occur with visible, physical signs. General examples include Marfan syndrome (which manifests itself through tall stature, loose joints of the limbs, and heart disorders) and achondroplasia (dwarfism). Relevant to our focus in this chapter, neurofibromatosis and tuberous sclerosis are examples of dominant gene disorders that may involve intellectual disabilities.

**Neurofibromatosis:** Neurofibromatosis (NF) is also known as von Recklinghausen’s disease (for the man who first described the disorder in 1882). According to Cutting and colleagues (2004), NF is the most common single gene disorder affecting the central nervous system; it
occurs approximately one in 2500 births. Most commonly the syndrome is associated with NF1, a mutation on chromosome #17. The second most common version (NF2) results from a mutation on chromosome #22. The majority of the research that has taken place relates to NF1, which is approximately ten times more common than NF2. About 50% of all cases of NF are inherited and the remainder caused by genetic mutations occurring spontaneously and thus sporadically.

NF1 is identifiable by light brown patches (called café-au-lait) on the skin and/or by multiple, soft, fibrous swellings or tumors (neurofibromas) that grow on nerves or appear elsewhere on the body and can result in severe physical deformities (Clayman, 1989). It had been speculated that neurofibromatosis was the disorder that affected John Merrick (the “Elephant Man”), but this was later disproved (he was identified as having Proteus syndrome). Surgical procedures for tumors may be recommended (i.e., when the growths cause complications or have a major effect on comfort or appearance), although the tumors may recur.

Neurofibromatosis varies greatly in how it is expressed (i.e., variable expressivity) from case to case. The café-au-lait patches are primarily a cosmetic concern, but the locations of the tumors will have an effect on mental development, which may be severe if they occur on the brain. Otherwise, the individual may function in the normal range of intelligence. The majority of children with NF, however, are likely to have academic problems, with an estimated 30%–60% having learning disabilities (Rasmussen & Friedman, 1999). Key characteristics include problems in decoding and phonological aspects of reading, receptive and expressive language, complex motor tasks, the occurrence of attention deficit hyperactive disorder, and executive function (such as self-management and strategic learning) deficits (Cutting, Clements, Lightman, Yerby-Hammack, & Denckla, 2004). A continuing concern is for the psychological
consequences for individuals who see themselves as deformed and question whether they should have children.

**Tuberous sclerosis:** The condition of *tuberous sclerosis* is also an autosomal dominant disorder. The word “tuberous” is derived from the potato-like growths that occur. The key focus is on growths on the central nervous system and brain. The birth incidence is about 1 in 6000 (Curatolo, 2004). The causation of tuberous sclerosis is autosomal dominant inheritance or cell mutation. The sites noted are on chromosomes #9 (TCS1) and 16 (TSC2) with TSC2 more often associated with severe manifestations. The key characteristics of tuberous sclerosis may include (Curatolo, 2004):

- 96% have skin lesions
- 90% exhibit cerebral pathology
- 84% have seizures
- The functioning range is from average intelligence to severely impaired
- Approximately 50% of the affected persons are in the average range but may have LD-type traits
- Higher occurrence of BD, ADHD, and autism has been reported.

**Huntington’s disorder:** A third autosomal dominant disorder is *Huntington’s disorder*. Although the age of onset, typically in the 30s, precludes this condition being associated by definition with intellectual and developmental disabilities, nevertheless it has received significant attention because of multi-generational tracking since the 1600s. The disorder received particular attention through the life of Woody Guthrie. His description of what was then called *Huntington’s chorea* illustrates this point (see Box 2).
BOX 2  Chorea and me

I got my first good early look at my chorea on back several years ago as I watched how it worked on my mother, Nora Belle Guthrie, back in my old homey town of Okemah, Oklahoma.

I got myself such a good clear look at it (chorea) that I want to try to show you what things it caused her to do and how I fell heir to it through her. I’m still glad I did fall heir to my chorea because it makes me stay dizzy and drunk all the time without guzzling down or without paying my bartender one little blue cent.


Recessive Transmission

Recessive inheritance is commonly associated with blue eyes and a variety of other physical traits, but it also involves disorders capable of producing severe disabilities and serious health impairments. General health-related examples include sickle-cell anemia and cystic fibrosis, while examples of recessively transmitted intellectual disabilities include phenylketonuria, Tay-Sachs, and galactosemia. Because transmission of recessive traits is a function of the union of two carriers (see Figure 3), controlling these disorders entails using genetic screening measures to identify unknowing carriers.

Recessive transmission is often related to those disorders that can be traced to dysfunction in the body’s mechanisms for the processing of food—so-called inborn errors of metabolism. As Garrod (1909, cited by Ripley, 2000) observed, perhaps that was what genes were: devices for making proteins. Garrod’s classic observation was that: “inborn errors of metabolism are due to a failure of a step in the metabolic sequence due to loss or malfunction of an enzyme” (p. 40). In particular, imbalances related to fats, carbohydrates, and amino acids have been well established as causative agents of retardation and related disabilities. However, their rarity is such that they result in a limited number of cases of intellectual disabilities. Collectively they occur in approximately 1 in 4,000 births (Hall, 2000).
Metabolic disorders resulting from an increase in lipids, or fats, in the body’s tissues are frequently progressive, degenerative diseases. The developmental profile is typically that of a normal progression until onset of the disorder, from which point the condition rapidly worsens. *Tay-Sachs disease*, for example, is inherited as an autosomal recessive trait. It is disproportionately prevalent among persons of Ashkenazi (from northern, central, or eastern Europe) Jewish background (about 90% of Americans of Jewish descent are Ashkenazi and about 1 in 25-30 are carriers; Graziano, 2002), although recent findings have shown that it occurs more frequently among the general population than originally thought. Infants with Tay-Sachs disease appear normal at birth. The disease is typically manifested late in the child’s 1st year as *ganglioside*, a lipid or fatty substance, accumulates in the brain’s nerve cells (Percy, 2007), followed by a course of severe retardation, convulsions, blindness, paralysis, and death by the age of 4. There is no cure for Tay-Sachs disease, and it remains one of the most devastating causes of disabilities.

**Phenylketonuria:** *Phenylketonuria* (PKU) is the most common of the genetic disorders and the most publicized success story in the preventive literature. PKU is caused by an autosomal recessive gene and, if left untreated, may be associated with aggressiveness, hyperactivity, and intellectual disability. Erickson (2012) explained that PKU is an autosomal recessive disorder where the enzyme that breaks down the amino acid phenylalanine into tyrosine is not working properly. The mechanism that results in these impacts relates to the toxic effect of increased amino acid level in the brain, leading to severe disorder (Trunk, 2005). However, since it was first described by Ivar Asbjörn Folling in 1934, PKU has been virtually eliminated as a causative factor leading to significant disabilities, despite its incidence of 1 in every 12,000 to 15,000 births. PKU has played a significant role in the field because it was the
first inborn metabolic anomaly proven to cause retardation. Its discovery led to both increased research into etiology and a pronounced change in the aura of hopelessness that once surrounded intellectual disabilities.

Figure 2 illustrates the historical discovery process for PKU, while “Robert Guthrie and the PKU Story” Box 3 provides an overview of his key work in this field. Much of the research on PKU reflects the indomitable will of individuals seeking out the causation of, and treatments for, the condition. For example, Virgie Adams Eggleston, the chief medical technologist at Central Virginia Training Center for 1952-1978, worked with a population of persons who were significantly disabled and directly supported initiatives to ensure the implementation of mandatory screening of infants for PKU (Rodriguez, 2005). The screening test for PKU in newborns is universally mandated in the US (Harris, 2006).

As noted in Figure 2, the treatment regimen for PKU is related to restrictions in intake of phenylalanine, common in high-protein foods. Thus, the diet is predicated on the need for the substitution of other foods and synthetic proteins. With the elimination of phenylalanine from the diet, the deleterious effect is significantly reduced. Guest et al. (2013) stated that a low phenylalanine diet within the first 21 days of birth can prevent intellectual disability.
FIGURE 2
History of Phenylketonuria (PKU)

Advances in the field of intellectual and developmental disabilities have come in a variety of ways. Certainly key societal commitments have included support for research as well as for enabling legislation for educational programs and litigation to confirm basic human rights. However, behind most of these achievements often are individuals who have made a significant difference. As discussed in Koch’s (1997) biography of Robert Guthrie, it is clear that he was one. Schroeder (1999) writes in his review of this book that it:

captures the science, the drama, the serendipity, and the chance events that resulted in the development over the last 50 years of screening tests for phenylketonuria (PKU) and of mass screening methods for metabolic errors in general as a major tool for the prevention of intellectual disabilities. How did it happen that hundreds of millions of newborn infants around the world have been screened for a variety of metabolic disorders largely due to the efforts of one man? That is a story worth tracing. One needs to observe Bob Guthrie’s contributions as a scientist and as a human being....

Three major contributions to newborn screening programs earn Bob Guthrie a place in the history of research in intellectual disabilities: (a) he showed the blood specimens of three tiny spots on filter paper were safe and useful screening methods; (b) he developed the bacterial inhibition assay for phenylalanine in the blood spot, the first method of diagnosing PKU using blood; and (c) he advocated for mass screenings of newborns and children all over the world. This was a revolutionary concept, which required proselytizing in wide sectors of the medical and public health communities. His devising of inexpensive analytic methods was the key to their acceptance. That was the breakthrough from a public health standpoint.

Levitas (1998) summarized the nature of the treatment:

Persons on this diet may not partake of the most common and widely enjoyed fast foods and barbecued staples in the American diet, making participation in
family and community events difficult.... The diet can be heavy in carbohydrate snack substitutes, making it almost the opposite of what most people think of as a “diet”; new caregivers, and even casual contacts in the person’s life, must be educated about the basis for the components of the diet, which must be strictly adhered to. The caregivers must be reminded to avoid all “diet foods” sweetened with Aspartame, which is a potent source of phenylalanine. The caregivers must learn to tolerate the liquid tyrosine supplement, which smells and tastes extremely “fishy.” Fortunately, the liquid can be flavored with fruit juices, vanilla, [and] honey and can be frozen into a “slushy” with flavorings. (p. 113)

The supplement recommended for individuals placed on a restricted diet provides tyrosine. The lack of phenylalanine as a result of the restricted diet leads to deficits in the tyrosine level in the body. The lack of tyrosine is known for being affiliated with depression (a common characteristic of persons with PKU). Tyrosine also “aids in the production of melanin (pigment responsible for hair and skin color) and in the function of organs in the body responsible for making and regulating hormones, including the adrenal, thyroid, and pituitary glands.” (University of Maryland Medical Center, 2002, p.1)

Kuvan (sapropterin dihydrochloride) is the first prescription drug approved by the FDA, which lowers the high phenylalanine levels found in the blood especially when used together with a restricted diet. The FDA explained that Kuvan increases an enzyme activity in PKU patients which leads to an increase in the metabolism of phenylalanine, which then results in lower levels in the blood (Jurecki, 2008; University
of Maryland Medical Center, 2008; US FDA, 2007). While these drugs are promising, other researchers have questioned the use of the drug and argued instead for a focus on continued dietary restriction (Kronmal & Sasich, 2008).

The early results of diet treatment for PKU were most encouraging. Johnson, Koch, Peterson, and Friedman (1978) reported that a group of 148 treated PKU children did not significantly differ from the general population in the prevalence of congenital anomalies or major neurological defects. Intellectual development near or within the normal range thus was found to be achievable. Children treated very early—before they were a month old—had significantly higher IQs than those whose treatment began in the 2nd month (Koch et al., 1988); continued adherence to the diet had positive results as well, while diet cessation in individuals continued to show a decrement in IQ (Levitas, 1998).

Two major problems remained, however. First, the diet prescribed for children with PKU can be unappealing and hard to follow, and it may be difficult to balance protein restrictions against the protein needs of developing children. For years, the special diet was generally discontinued by approximately school age, but this practice caused concern. For example, Matthews, Barabas, Cusack, and Ferrari (1986) reported decreases in social quotients for individuals for whom the diet was discontinued at age 5½ years. In children who maintained their diets to the age of 10, Fishler, Azen, Henderson, Friedman, and Koch (1987) found higher school achievement, intellectual level, language, and perceptual skills. Guest et al. (2013) highlighted that the probability of a child with PKU having an average level of intellectual functioning increased if sufficient phenylalanine levels were maintained throughout childhood.

Research continues on the issue of treatment discontinuation in adolescents and adults with PKU. Levitas (1998) reviewed research in the area and gave a compelling case for a
life-long phenylalanine-free diet treatment for persons with PKU, which is increasingly supported by contemporary research. As Percy et al. (2007) noted, reports of untreated adults indicate the occurrence of behavioral and psychological problems, including intellectual disability. Mazur et al. (2011) investigated the effects of untreated and undiagnosed adults with PKU in Poland, and several neurological abnormalities were observed. They included “severe speech impediments, balance and gait disturbances, impaired coordination, hypertonicity, and seizure activity” (p. 486). In fact, they reported that neurological symptoms were almost double in people with PKU who stopped the low phenylalanine diet as opposed to those who stayed on it. The study showed that the effects of high levels of phenylalanine were almost irreversible if left untreated until adulthood. As a result, the continuation of the restrictive diet throughout the lifespan has been recommended.

The acceptance of a lifelong diet has faced some setbacks, as people with PKU suffer some nutritional deficiencies even when sticking to the restrictive diet (Belanger-Quintana, Burlina, Harding & Muntau, 2011). Guest et al. (2013) highlighted that “89% of patients who remained on a restricted diet for the first 36 years of life appeared to receive less than the recommended optimum amount of prescribed amino acids supplements” (p. 577). Acceptance of this recommendation has also had an effect on a second issue (discussed next) that emerged from the study of PKU.

This second issue concerns women who were treated in childhood for PKU. As adults, their metabolic imbalances can harm their unborn children. In this instance, the problem is not a genetic one but rather an increased risk to the fetus during pregnancy due to the mother’s elevated level of inadequately processed phenylalanine. These elevated levels also can increase the risk of miscarriages (Williams, Mamotte, & Burnett, 2008). Other consequences can include
congenital abnormalities and cognitive disability (Percy et al., 2007). Therefore, women should reinstate their restricted diet during pregnancy. Evidence of this concern can be noted by consumers in common product warnings—for example on diet sodas or some low-fat foods (e.g., yogurt)—that these items contain phenylalanine. Unless pregnancy is avoided or dietary restrictions honored, Koch et al. (1988) indicated that the effects of maternal PKU could offset the preventive benefits of screening programs and dietary treatment interventions in infants.

**Galactosemia**

Galactosemia is an autosomal recessive inherited disorder (Shriberg, Potter & Strand, 2011). It is a metabolic disorder that affects how the body processes the sugar, galactose. There are three types of galactosemia, which are caused by mutations in a particular gene and enzymes that break down galactose. Classic galactosemia, also known as type I, is the most common and most severe form of the condition. It occurs in 1 in 48,000 in the United States (National Newborn Screening and Genetics Resource Center, 2012). Galactosemia type II, also called galactokinase deficiency, affects less than 1 in 100,000 newborns (National Newborn Screening and Genetics Resource Center, 2012). Type III, which is also called galactose epimerase deficiency, is very rare.

Infants who go untreated for galactosemia may die during the first few weeks of life as a result of accumulation of toxins and weakness from starvation. The signs and symptoms of galactosemia result from an inability to use galactose to produce energy. Gershen (1975) explained:

If the infant survives, accumulation of galactose in the liver, kidney, eyes and/or brain may result. The resulting symptoms include jaundice, hepatomegaly, edema, hypoprothrombinemia, acidosis proteinuria, aminoaciduria, cataracts, and mental
retardation; failure to thrive, susceptibility to infection, vomiting and diarrhea may occur.

(p. 20)

Despite early diagnosis, many patients have intellectual and developmental deficits and many adult females are infertile due to ovarian failure (Pitt, 2010).

Lee (1972) conducted a study to examine and assess the intellectual and emotional status of sixty children in the United Kingdom with galactosemia. The findings indicated that children with galactosemia were physically underdeveloped and had lower IQs compared to typically developing peers. These differences seemed to worsen with age. Additionally, children showed poor social relationships, increase sensitivity to criticism, and poor perceptual and coordination abilities.

Several methods exist for neonatal screening for galactosemia. Brosco, Seider and Dunn (2006) explained that methods for mass screening for galactosemia have been available since 1964. Some of the methods include Guthrie’s E. coli test (1964), Beutler and Baluda specific GALT enzyme assay (1966), and Paigen’s test (1971). Paigen’s test is the most commonly used for neonatal screening (Jensen et al, 2001). The treatment of galactosemia includes dietary controls such as excluding the intake of foods with galactose. A small amount of galactose is present in many foods. It is primarily part of the larger sugar, lactose, which is found in all dairy products and many baby formulas. Gershen (1975) noted that a restricted diet can reverse most of the symptoms of galactosemia.

Sex-Linked Inheritance

A third type of genetic transmission is through sex-linked (or X-linked) inheritance. This name derives from a variety of recessive traits carried on the X chromosome. Females have two X chromosomes, and a specific gene carrying a disorder can be dominated by its mate. But males
(XY) will be affected by a single recessive gene carried on the X chromosome, because there is no second X chromosome whose genes could potentially dominate the pathology-producing recessive trait. Males have a Y chromosome, which does not carry genes that will counterbalance the X-linked gene. It has been estimated that there are 1098 gene sites on the X chromosome but only 54 counterpart sites on the Y chromosome (Ross et al., 2005; Spencer & Dieffenbach, 2005). Males are at significantly greater risk for sex-linked disorders. This susceptibility may account for the fact that there are approximately 25% more males with intellectual disabilities than females (Tartaglia et al., 2007). A female can be affected only if her father is affected and her mother is a carrier. Thus, the problem of sex-linked inheritance is particularly significant for males. Dykens et al. (2000) noted that more than 70 causes of disabilities can be traced to X-linked inheritance patterns. While the X chromosome contains only 4% of all human genes, X accounts for 10% of all intended diseases and disorders (Spencer & Diffenbach, 2005).

In the general population, X-linked recessive traits of concern include color blindness, hemophilia, and Duchenne-type muscular dystrophy, and a variety of other conditions that may be as much as ten times more common in males than in females. The unique nature of sex-linked recessive inheritance is perhaps best illustrated by the presence of the disorder of hemophilia within the royal families of Europe. In a story often told, many of the ancestors of Queen Victoria of England, a carrier for hemophilia, either carried the disease or, in the case of some males, experienced the impact of this disorder. Most notably, the son of the last czar of Russia, Nicholas II, had hemophilia, which ultimately became a contributor to the downfall of the Romanov dynasty (see Massie, 1967, for an ancestral outline reflecting the recurrence of hemophilia).
According to Dykens et al. (2000), there are more than 70 different X-linked disorders that are associated with intellectual and developmental disabilities. Further, they indicated that as much as 25% of the cases in males may be related to X-linked genes. While the more common pattern is X-linked recessive disorders, as discussed below relative to Lesch-Nyhan Syndrome, there are also some conditions that are carried as dominant genes. The most common syndrome related to X-linkage, which follows a unique pattern, is fragile X syndrome (discussed in full below).

Lesch-Nyhan Syndrome: One example of sex-linked recessive inheritance is Lesch-Nyhan syndrome. The disorder, first identified in 1964 (Lesch & Nyhan, 1964), is inherited as an X-linked recessive and thus is much more common among males. According to Nyhan (1976), it is the second most common metabolic disorder (after PKU). The most striking manifestation of Lesch-Nyhan syndrome is an apparently uncontrollable urge to cause injury to oneself and, to a lesser extent, to others.

Typically, children with Lesch-Nyhan syndrome will begin displaying extreme self-injurious behavior (SIB) when acquiring teeth. They may bite ferociously and, in their frenzy, rip and tear tissue (Libby, Polloway, & Smith, 1983; Nyhan, Johnson, Kauffman, & Jones, 1980). Aside from SIB, they may hit, pinch, and bite others; use obscene language; spit; and engage in a variety of disruptive actions because of their inability to control their impulses (Hoefnagel, Andrew, Mireault, & Berndt, 1965). When unrestrained, they may scream as if terrified of the pain they might inflict on themselves, while when restrained they seem more calm.

Harris (2006) provides an apt summative description of the key characteristics of this condition:
Self-mutilation in Lesch-Nyhan disease is conceptualized as a compulsive behavior that the child tries to control but generally is unable to resist. With increasing age, the affected child becomes more adept at finding ways to control his self-injury. He may enlist the help of others to protect him against these impulses or may learn to self-restrain . . . Moreover; (he) may be compulsively aggressive and inflict injury to others through pinching, grabbing, or verbal forms of aggression. Frequently, he will apologize for this behavior immediately afterward and say that the behavior was out of his control (p.221).

Both biomedical and educational interventions have been used with children who have Lesch-Nyhan syndrome. Drug treatment to alter metabolism has proven efficacious on a short-term basis. Behavior management strategies can have a positive impact in reducing unacceptable behaviors. Pharmacological interventions have been used to decrease self-injurious behavior and aggression and enhance mood.

**Fragile X syndrome:** A disorder that was first noted in 1943 but began to receive significant attention after its formal discovery in 1979 is *fragile X syndrome*. After Down syndrome, this syndrome is the most common clinical type of intellectual disability. It is also the most common hereditary cause of retardation (Roberts et al., 2007). In fact, Symons, Byiers, Raspa, Bishop and Bailey (2010) concurred that “fragile X is the leading inheritable cause of intellectual disability” (p. 473).

The actual mechanism for genetic transmission is complex and varies from the recessive pattern discussed above. The causation mechanism for Fragile X relates to a mutation on a gene (FMR1) on the X chromosome that essentially switches off a protein, which ultimately then results in a variety of behavioral impacts. There is no male-to-male transmission in Fragile X and the most common transmission is from mother to son. The actual process of inheritance may
involve transmission through: a carrier mother (1 in 260 women are carriers) to an affected son; an affected mother to an affected daughter or son; a carrier mother to a carrier daughter; and a carrier father to a carrier daughter.

A full discussion of the transmission patterns of Fragile X is beyond the scope of this chapter. However, it is important to note while that everyone possesses the FMR1 gene on each X chromosome, mutations in the gene are the cause of the condition itself. Geneticists use the term *premutation* to commonly refer to carriers for the disorder who typically who are unaffected but also might experience some of the characteristics associated with the condition. *Full mutation* refers to those instances in which “the full mutation essentially silences the genes so that they do not produce its protein or produce insufficient amounts of protein”, which results in the clinical features associated with the fragile X syndrome (Mazzocco & Holden, 2007, p. 175). Of the individuals with the full mutation, it has been estimated that approximately 85% of males and approximately 25% of females will have intellectual disabilities, with the balance likely experiencing learning disabilities (Tartaglia et al., 2007).

Typical estimates for fragile X have been in about 1 in 1,500 males and about 1 in 1,000 females in the general population (Clayman, 1989), Mazzocco and Holden (2007), basing their data on a report from the Centers for Disease Control, note a much lower prevalence rates of 1 in 9,000 for females and 1 in 4,000 for males; the rationale for the difference in rates is likely to be in part because these figures were based on instances of full mutations. Of particular note is the fact that fragile X may be causative in 2-6% of the cases of males who have intellectual disabilities that are otherwise not explained and also 2%-4% of such females (Harris, 2006).

Given that the problem is the absence or severe deficiency of a specific protein (FMRP) essential for the functioning of the brain (Bailey, Hatton, Tassore, Skinner, & Taylor, 2001), it is
as expected that the protein level found in individuals was a key contribution to developmental outcomes (Bailey et al., 2001) and thus that children with higher levels of FMRP have higher levels of adaptive behavior (Hatton et al., 2003).

The diagnosis of fragile X can be made prenatally, although most often it is made clinically during early childhood after observation of developmental delays and/or the appearance of large ears (Buyse, 1990). Maes, Fryns, Ghesquiere, & Borghgraef (2000) provide a screening checklist for use with persons suspected of having the syndrome (see Table 2).

According to Barker (1990), common physical characteristics of fragile X include prominent jaws, macro-orchidism (large testes), long and thin faces, long and soft ears and hands, prominent foreheads, and enlarged heads. The syndrome has been associated in males with significant disabilities, although reports of its occurrence in individuals with various levels of intellectual disabilities (and also with normal intelligence) suggest the need for careful consideration of the contributions of environmental experience (Rogers & Simensen, 1987). Maes et al. (2000) reported on a sample of persons with fragile X. For children, the statistics were 6.59%, profound; 29.9%, severe; 48.1%, moderate; and 15.6%, mild. The nature of the sample, however, limits its generalizability to the overall population.

Behavioral manifestations of fragile X may include attention difficulties, repetitive speech, repetitive behaviors, and gaze avoidance, while speech and language patterns may include echolalia, preservative use of given utterances, and palilalia (i.e., repeating statements at increasing rates of speed and loudness) (Belser & Sudhafter, 2001). Roberts, Hennon, Price, Deer, Anderson, and Vondererify (2007) published a comprehensive analysis of the characteristics of individuals with Fragile X syndrome. The key findings related to language include that boys with Fragile X (without autism) did not differ from younger typically
developing boys in receptive and expressive vocabulary and speech production when compared at similar levels of nonverbal cognitive skills and that boys with Fragile X (without autism) and typically developing boys had higher receptive vocabulary and speech production than boys with Down syndrome.
Further, according to Roberts et al. (2007), individuals with Fragile X when compared to persons who were non-disabled matched on mental age used less complex phrases and sentence structure, fewer different words, and shorter and less complex utterances. These researchers suggest that this indicates an overall delay rather than a specific vocabulary or syntactic delay. In another study, Shaw and Porter (2012) investigated the emotion recognition abilities and visual scanning of emotional faces of individuals with Fragile X, compared to individuals with matching chronological and mental ages. They discovered that individuals with Fragile X displayed deficits in recognizing angry and neutral expression; made less eye contact, and engaged in unusual facial scanning. They concluded that these differences in behaviors indicate that individuals may be developmentally delayed as opposed to having a deficit in scanning emotional facial expression.

Symons, Clark, Roberts, and Bailey (2001) researched the behavior of individuals with fragile X syndrome in the classroom. They reported:

relatively low overall levels of severe behavior problems associated with gross motor stereotypies (e.g., hand flapping) or self-injury (e.g., hand biting) were observed. The finding that a broad measure of classroom quality, based on environmental and instructional variables, was significantly related to levels of classroom engagement suggests that how the teacher arranges and structures the classroom environment is critical for school success for students with FXS…. it appears that for this sample of students with FXS, classroom ecology was more important than biology for predicting levels of engagement (p. 201).
This initial finding bears further attention as more naturalistic observations are considered in the future. Table 3 provides a summary of other characteristics.

**TABLE 3**

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
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<tr>
<td>Verbal skills</td>
<td>Auditory-verbal short-term memory</td>
</tr>
<tr>
<td>Repertoire of acquired knowledge</td>
<td>Visual-perceptual short-term memory</td>
</tr>
<tr>
<td>Long-term memory for learned information</td>
<td>Sustaining attention, effort</td>
</tr>
<tr>
<td>Expressive and receptive vocabularies</td>
<td>Sequential processing</td>
</tr>
<tr>
<td>Adaptive daily living skills, especially domestic and personal grooming tasks (males)</td>
<td>Certain visual-spatial and perceptual organization tasks</td>
</tr>
<tr>
<td></td>
<td>Shifting problem-solving strategies</td>
</tr>
<tr>
<td></td>
<td>Integrating information (more readily measured in females)</td>
</tr>
<tr>
<td></td>
<td>Adaptive socialization skills (females and males with autism)</td>
</tr>
</tbody>
</table>

Fragile X has been reported to co-occur with several other conditions (Symons et al., 2010). There have been a similar pattern for both boys and girls with Fragile X. Symons et al. (2010) discovered that males with Fragile X who engaged in self-injurious behaviors had a significantly greater number of co-existing conditions than those who did not self-injure. They had been diagnosed with autism, had sleep, sensory and attention difficulties, and were hyperactive. Girls with Fragile X who engaged in self-injurious behaviors had similar problems; but the prevalence of autism was higher, and they showed greater signs of anxiety and sensory problems than girls with Fragile X who did not self-injure.

A consistent relationship between fragile X and autism has been reported in the literature, with males with fragile X having a 5%–46% prevalence of autism or autistic-like behaviors. Demark, Feldman, and Holden (2003) summarized the research findings as follows:
• A definite sub-group of persons with Fragile X appears to have behaviors commonly associated with autism (with some individuals meeting the diagnostic criteria for autism).
• Fragile X mutations may increase the risk of a child developing autistic-like tendencies.
• It is unclear what the precise relationship is between autism and fragile X.
• Fragile X mutations may increase the susceptibility for autism in conjunction with other genes associated with autism susceptibility.

Viewed from the reverse perspective, children with autism are found to have the fragile X pattern in about 15% of cases. However, Klusek, Martin and Losh (2012) noted that there was an under-diagnosis of ASD in children with Fragile X. They explained that a “significant proportion of children with FXS who meet diagnostic criteria of ASD are not identified clinically” (p. 949). This fact may explain the low prevalence of the comorbidity of Fragile X and autism. While males with fragile X often exhibit autistic-type behaviors, they are usually less significant than the behaviors seen in persons who are clinically diagnosed as autistic. However, the similarity in behavior patterns does lead to difficulty in making a diagnosis of typical autistic-like behaviors versus clinical autism (Cantu, Stone, Wing, Langee, & Williams, 1990). Finally it is important to note that individuals with fragile X who are also autistic tend to have lower adaptive skill levels and also more significant developmental and functional delays (Hatton et al., 2003), including in the areas of expressive and receptive language (Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004).

Hall, Lightbody, and Reiss (2008) reported behavioral data on individuals with Fragile X (5- 20). Self-injurious behavior was found in 58% of boys and 17% of girls; compulsive behavior in 72% of boys and 51% of girls; and the diagnostic criteria for autism were met in 50% of boys and 20% of girls. Some of the specific traits that have resulted in an association between Fragile
X and autism include repetitive speech, echolalia, attention deficit, hand flapping, poor eye contact, and gaze aversion. Despite these findings about the connection between Fragile X and autism, professionals in the field of autism lack knowledge about Fragile X (Finucane, Haas-Givler & Simon, 2013). They rarely inquire about etiology when working with students with ASD. However, they agree that knowing the cause of the disorder is important in implementing effective interventions (Finucane et al., 2013).

Mazzocco and Holden (2007, p. 181) provided an apt statement about the importance of attention to Fragile X. They note:

> Despite the significant consequences and high prevalence, public awareness about fragile X is low in many areas. Even healthcare professionals, educators, and other service providers often have little information about this syndrome, creating additional difficulties for families of individuals with fragile X . . . It is important for a wide range of professionals to be familiar with fragile X, because the effects of this condition on a family extend beyond the individual.

Martin et al. (2013) explained that individuals with full mutation Fragile X have a great probability of needing at least one type of therapy (speech and language therapy, physical therapy, behavior management therapy). Therefore, knowledge of the disorder becomes pertinent for provision of appropriate services.

**Polygenic Inheritance**

The preceding discussion has focused on single-gene anomalies, reflecting the mechanism by which one gene controls one trait (or a given condition). Many traits, however, do not fit simple rules but are transmitted through polygenic inheritance. Polygenic (i.e., multiple genes) inheritance has particular importance for potential contributions to the etiology of the so-
called psychosocial causes of retardation. Unlike the one-gene/one-trait Mendelian pattern of numerous disorders (e.g., PKU), in polygenic inheritance, the interaction of multiple genes and networks influences individual intellectual functioning. Since the complexity of this phenomenon makes precise evaluation difficult in single cases, researchers depend on statistical data from population samples in seeking to understand polygenetic inheritance. That is, “genetic predictions ... have to be based on empirical data from population statistics. Simple genetic models just do not apply” (Scarr & Carter-Saltzman, 1982, p. 804).

While polygenic considerations relate solely to the inheritance of traits based on the impact of multiple genes, it should also be considered within the context of multifactor disorders. As Percy, Lewkis, and Brown (2007) noted, multifactor considerations should be distinguished from polygenic disorders because they refer to conditions that may be as a consequence of genetic contributions (including potentially from multiple genes) as well as environmental factors. For example, spina bifida is thought to be the consequence of certain genes that control metabolism as related to folic acid; maternal diet high in folic acid represents an environmental response that can prevent occurrence of the disorder.

**CHROMOSOMAL DIFFERENCES**

A second major source of biological causes of disabilities is chromosomal anomalies. Although these disorders are rare in the general population, their numbers are significant among cases of developmental disabilities in which cause can be specified. More than 60 chromosomal anomalies have been identified, for a total of about 7 in 1,000 live births, but in addition they are also indicated as the reason for a significant number of abortions. Dependent upon the specific research study, 4%-8% of persons with intellectual disabilities have chromosomal anomalies (Harris, 2006).
The intensive research on chromosomes that began in the late 1950s and early 1960s has yielded a detailed portrait of both typical and atypical chromosomal patterns. These patterns are clarified through the use of karyotypes. The process of karyotyping includes taking a picture of the chromosomes in a human cell, enlarging it, cutting out the pictures of individual chromosomes, and then arranging the chromosomes by pairs from the largest (numbered as pair 1) to the smallest (pair 22), followed by the sex chromosomes (XX or XY).

Approximately 10% of pregnancies begin with some chromosomal imbalance, but most of these abort spontaneously during the first 3 months of pregnancy. A small number of these pregnancies proceed to full term, and the children born illustrate the potential effects of irregularities in the arrangement or alignment of autosomes or sex chromosomes. Chromosomal errors can be identified in approximately 1 in 200 live births.

While genetic disorders are classified as hereditary, chromosomal problems are often more accurately termed innate, since an abnormal chromosome arrangement is present at conception but is not the product of hereditary exchange. Disorders of this type usually result from abnormalities occurring during the stage of cell division called meiosis. During meiosis, individual reproductive cells divide and then pair up to form the genetic foundation of the embryo. The normal process includes 23 chromosomes from each parent, which are paired to form the new organism’s complement of 46 chromosomes. Figure 3 illustrates the karyotypes for a male and a female with typical chromosomal patterns.

Several specific abnormalities that occur during the process of chromosomal arrangement and alignment result in either too much or too little chromosomal material being present. In nondisfunction, a given parental pair of chromosomes fails to split at conception, causing the formation of a group of three chromosomes (a trisomy) in lieu of the normal pair. A trisomy on
chromosome 21 is the most common cause of Down syndrome; trisomies on 18 and 13 have also been noted in the literature. In translocation, a fragment of chromosomal material is located across from or exchanged with another chromosomal pair. For example, a translocation that results in Down syndrome occurs when a fragment broken off from chromosome pair 21 attaches to a chromosome from group 15. In deletion, a portion of the original genetic material is absent from a specific chromosome pair. Finally, mosaicism is an uneven pattern of dissimilar cells (such as of some cells with 46 and some with 47 chromosomes).

Before the 1950s, causes of the disorders classified under chromosomal anomalies were unknown. Seminal research published by Lejeune and his colleagues (e.g., Lejeune, Gautier, & Turpin, 1959) and other geneticists then led to a much clearer understanding of the nature of chromosomal abnormalities. As mentioned earlier, aberrations in the number or arrangement of chromosomes are likely to damage the developing organism. Down syndrome and cri-du-chat syndrome are examples of autosomal disorders; Klinefelter and Turner syndromes come from sex chromosome abnormalities. As a broad generalization, disorders in autosomes are more often associated with mental retardation, whereas anomalies associated with sex chromosomes are more commonly associated with learning disabilities (Bender, Puck, Salbenblatt, & Robinson, 1986; Smith, Polloway, Patton & Dowdy, 2007).
FIGURE 3

Typical Chromosomal Karyotypes

**Down Syndrome**

Down syndrome (DS) is the best known and most frequently researched biologically caused condition associated with intellectual and developmental disabilities. In fact, Dykens et al. (2000), indicated that as many research articles have addressed Down syndrome as for all other genetic etiologies combined. For many laypersons, the concept of a person with intellectual disabilities historically has often been synonymous with a Down syndrome individual. A reasonable estimate of the prevalence of the syndrome is about 1 in 800-1,000 births (Lovering & Percy, 2007), which amounts to roughly 5%–6% of all persons identified as intellectually disabled.

Study of the disorder has revealed three separate chromosomal causes. The first and most common, trisomy 21 is due to the failure of one pair of parental chromosomes to separate at conception, resulting in the child’s having 47 chromosomes (Figure 4). Lovering and Percy (2007) reported that research indicates that 85% of these cases come when the mother contributes the extra chromosome while in 15% of the cases the third chromosome comes from the father. Trisomy 21 accounts for 92 - 95% of children born with Down syndrome (Dykens et al., 2000; Lovering & Percy, 2007). This abnormality has historically been found more often in children born to older mothers, or fathers, and researchers have suggested a variety of reasons.

Specific factors that have been suspected of causing trisomy 21 include: medication and drugs; exposure to radiation, chemicals, or hepatitis viruses; and the possible absence of a mechanism in the mother to abort the fetus spontaneously. Chapman, Scott, and Mason (2002, p. 54) hypothesized that “increased risk for Down syndrome among older, less-educated women may be due to deterioration of the ovum associated with the cumulative effects of chronic stress burden” (p. 54).
Although risk is related to age and increases to approximately 1 in 30 births at 45 years old, age itself is a *correlate* and not the *cause*. With the increased public awareness of the correlation between age and risk of occurrence, many older parents undergo prenatal screening for Down syndrome and may then consider abortion. This fact, plus the reality that births to parents over 40 are relatively rare, results in the large majority of births of children with Down syndrome actually being to younger parents.

A second form of Down syndrome (DS) is caused by a translocation transmitted hereditarily by carriers. Although this translocation is usually to chromosome pairs 13 or 15, the
extra material comes from pair 21 and forms, in a sense, a partial trisomy. It is found in 3-5% of cases of DS (Dyken et al., 2000). Mosaicism, the uneven division that creates cells varying in chromosome numbers (some 47 and some 46), is a third and rarer form of the condition.

Down syndrome is frequently associated with a variety of medical challenges (see Table 4) and also a number of specific physical traits, with the latter including the following:

- Short stature
- Flat, broad face with small ears and nose
- Short, broad hands with incurving fingers
- Upward slanting of the eyes with folds of skins (epicanthic folds) at the inside corner of the eye
- Small mouth and short roof, which may cause the tongue to protrude and contribute to articulation problems
- Single crease across the palm
- Reduced muscle tone (hypotonia) and hyperflexibility of joints
- Incomplete or delayed sexual development
Medical Concerns in Persons with Down syndrome

<table>
<thead>
<tr>
<th>Medical concern</th>
<th>Percentage affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital heart defects</td>
<td>50</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>66-89</td>
</tr>
<tr>
<td>Ophthalmic conditions (e.g., strabismus, refractive errors)</td>
<td>60</td>
</tr>
<tr>
<td>Gastrointestinal conditions</td>
<td>5</td>
</tr>
<tr>
<td>Endocrine conditions (e.g., hypothyroidism)</td>
<td>50-90</td>
</tr>
<tr>
<td>Dental conditions (e.g., crowding, periodontal disease)</td>
<td>60-100</td>
</tr>
<tr>
<td>Orthopedic anomalies (e.g., subclinical atlanoaxial subluxation)</td>
<td>15</td>
</tr>
<tr>
<td>Obesity</td>
<td>50-60</td>
</tr>
<tr>
<td>Skin conditions (e.g., eczema, dry skin)</td>
<td>50</td>
</tr>
<tr>
<td>Seizure disorders</td>
<td>6-13</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.6</td>
</tr>
</tbody>
</table>


These traits vary greatly from one individual to another. Thus, no overgeneralizations should be made according to the defining characteristics that must or may be associated with Down syndrome. Many of the behavioral characteristics traditionally associated with Down syndrome have not been documented in research or require some further explication. For example, the stereotype of the child with Down syndrome who is cheerful, affectionate, rhythmic, and unusually dexterous has not been empirically established. Furthermore, while children with Down syndrome may exhibit more frequent and intense, repetitive behaviors, Evans and Gray (2000) report that they did not differ from young children (matched on mental age) who were nondisabled in terms of the numbers of compulsive behaviors in which they engaged.

A significant area of research on DS has been cognitive and intellectual functioning. Traditionally, the syndrome was assumed to result most often in moderate retardation, with rare
cases reaching a ceiling IQ of 70. Occasional anecdotal reports of ability and special talents, such as in the classic diary of Nigel Hunt (1967), were considered more interesting and unusual than typical.

The first comprehensive study that altered views on this issue was reported by Rynders, Spiker, and Horrobin (1978). Their review of 15 studies provided data on the intelligence test scores of children with Down syndrome that indicated a significant range in level of functioning and refuted the alleged ceiling IQ of 70. Optimistic data on the abilities of children with Down syndrome then continued to accumulate with early intervention viewed as the key. Rynders and Horrobin (1990) and Rynders (2005) provided further support in subsequent research and analyses supporting higher expectations for academic achievement in students with Down syndrome. They cautioned that IQs frequently diminish over time and, therefore, achievement levels should be stressed in assessing level of functioning and designing educational programs.

Individual case histories often support the positive views of the intellectual potentialities of persons with Down syndrome. The success of the 1990s television show *Life Goes On* was due in large part to the character portrayed by Chris Burke, a teenager with Down syndrome.

Language development has also been researched extensively in persons with Down syndrome. Both in terms of speech intelligibility and expressive language, individuals with Down syndrome tend to show differences or delay when compared to other individuals, including those of similar mental age as well as those with other conditions associated with intellectual disabilities. A noteworthy difference appears to be in the area of syntax; Lovering and Percy (2007) summarized their review of the literature by noting that particular difficulties occurred with noun-verb agreement and the use of pronouns.
The story in **BOX 4** provides another such case study.

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**BOX 4  Fighting Back**

Arlington – Kathleen Schermer, a special education specialist at Yorktown High School, can recall vividly the day Sara Miller gently and kindly told off the slackers in her U.S. History class.

“One day, when the vast number of students weren’t doing their homework, Sara turned around to the entire class and said, ‘You know, I have Down syndrome and I am getting this work done and I know you can too,’ Schermer said. “The boys, if they could have slithered into the floor and evaporated, they would have.”

Miller had lobbied long and hard to take the class, convincing administrators ….. she could handle the shift from her special education curriculum. In the end, she graduated from Arlington’s Yorktown High in 2002 with a 3.2 GPA, two years on the swim team and a reputation for bringing positive energy to any situation.

Her teachers were so impressed they nominated her for a national award – and weren’t too surprised when Miller ….. [was] one of three students with disabilities who won the 2003 “Yes I Can” award for self-advocacy by the Council for Exceptional Children. “The reason we chose Sara is because she … basically put her future in her hands and gained the confidence and support in her school,” said Jess Forr, a program development specialist with the Council.

Today, Miller is participating in an extended education program at the Arlington Career Center where she is being trained to become an assistant in early childhood education. “I want to work with kids who have special needs… I just like being there for them, being their companion and their friend… I believe in determination. When I get something done, I’m happy with my life.”

“She was our only child,” said her mother. “We didn’t have anything to compare her against, and we didn’t consider there were things she shouldn’t do.”

She came to Yorktown High with a determination that she could do anything and a fear that other students would think she couldn’t. She was the only student with Down syndrome at the school.

“It scared me that they might think, ‘she is so slow, she can’t do that …. I wanted to slap them in the face (and say) ‘No, I’m not like that. I’m very kind, very smart’.” As the years passed, she overcame her fears and grew to know many people at the school. She developed a few close friends in her special education classes but felt most comfortable with adults…

High school “transformed me into a new person, more loose, comfortable,” Miller said. “I felt safe there.” Miller became an integral part of the swim team and Yorktown’s Fellowship of Christian Athletes chapter, according to senior Jenny Varuska, 17.

She competed in races but also was one of the team’s biggest motivators and made a point of congratulating members on their swims. “She gave us advice and told us we can trust God with anything and that’s how she got through life,” Varuska said. “A lot of people admired her. She had a lot to overcome but never showed a sign of being upset.”

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Abbeduto et al. (2003) noted that:

the comprehension of syntax is more challenging than the comprehension of vocabulary for adolescents and young adults with Down syndrome…. These results suggest that language intervention for adolescents and young adults with Down syndrome must devote considerable attention to increasing the syntactic capabilities of affected individuals and that such interventions may need to be more intense than those targeting lexical skills (p. 156).

An important area of research is life expectancy. In 1929, expectancy for individuals with Down syndrome was only 9 years; by 1990, that average had increased to over 50 years (Eyman, Call, & White, 1991). As age increases, there may be evidence of increased incidence of early onset dementia (Alzheimer type) in persons with Down syndrome. However, there also are variations regarding the age of onset of specific clinical signs (Bush & Beail, 2004). The association is not unexpected, given the identified locus of two genes associated with Alzheimer’s on chromosome pair 21. Epstein (1988) pointed out that the loss of intellectual functioning associated with advanced age will be seen even more often in individuals with Down syndrome because life expectancies have increased.

Several overriding points must be made clear. First, individuals with Down syndrome are primarily and foremost people who have needs, desires, and rights similar to those of other people. Thus while a substantial amount of attention has focused on intellectual considerations, of at least comparable importance is research on socioemotional considerations such as developing friendships (Freeman & Kasari, 2002), emotional development (Kasari, Freeman, & Hughes, 2001), and family relationships (Cuskelly & Gunn, 2003). Dykens (2007) noted several
positive features including: fewer externalizing problems noted with increased age; a sense of humor; and, kindness, caring and forgiveness.

Second, the effects of intensive interventions with young children who have Down syndrome have only been evaluated since the late 1970s; thus, historical descriptions of the syndrome are no longer accurate. For example, as reported in the popular press, Charles de Gaulle had a daughter with Down syndrome. At the time of her early death in 1948, he reflected the sentiments of parents of an earlier historical era when he comforted his wife by saying of their deceased daughter “Come ... now she is like everybody else.” The perspective for this quote in the new millennium would rather much more clearly focus on the similarity and equality of people with Down syndrome in life rather than death.

**Prader-Willi Syndrome**

Another condition that has been linked to an autosomal abnormality is Prader-Willi syndrome (PWS). Most cases (i.e., approximately 70%) of Prader-Willi syndrome appear to be caused by deletion of a portion of the long arm of the paternal chromosome on pair 15. For a significant portion of the remaining 30%, the condition appears to be the result of maternal uniparental disomy of the 15th chromosome; that is, both chromosomes are contributed by the mother with none from the father. A third cause is mutation of paternal chromosome 15 (Percy et al., 2007). Epidemiological data on PWS indicate an incidence of approximately one in 10-20,000, a population prevalence of about one in 53,000, and 3% mortality rate per year (related primarily to increased obesity, see below) (Einfeld et al., 2006; Harris, 2006; Whittington & Holland, 2004).

Persons with PWS often have small features and stature and the condition has also been associated with intellectual and learning disabilities. However, the most significant
characteristics of PWS include insatiable appetite (and hence often obesity) and a pattern of obsessive-compulsive disorder (OCD) (Holsen & Thompson, 2004), often interacting with efforts to obtain food (Joseph, Egli, Koppekin, & Thompson, 2002). The biological mechanism underlying the syndrome brings about a preoccupation with eating that has prompted observers to suggest that, for a Prader-Willi child, “life is one endless meal.” In fact, recent research points to the fact that individuals with Prader-Willi syndrome were more likely than a comparison group of individuals (including those both retarded but not Prader-Willi and nonretarded) to indulge in eating food that was contaminated as well as to eat highly unusual combinations of edible and inedible foods (e.g., cake with grass) (Dykens, 2000; Dykens et al., 2000).

The characteristics associated with Prader-Willi syndrome generally become evident in two stages: an infantile hypotonic phase and a childhood/adulthood obesity phase (Donaldson et al., 1994). Initially, a major paradox is their failure-to-thrive condition, given that failure to thrive subsequently turns into excessive eating and obesity as the child increases in age. In addition, babies with Prader-Willi generally experience hypotonia; thus, the term “floppy baby” has frequently been used to describe them during infancy. After age 3, the characteristics of the second phase of the syndrome begin to become apparent. This phase may include hyperphagia (i.e., an insatiable appetite) and constant preoccupation with food. Also noted during this phase are delayed psychomotor development, signs of cognitive impairment, and delayed and/or abnormal pubertal development.

As persons with Prader-Willi syndrome develop, a pattern of significant behavioral difficulties often emerges including temper tantrums, compulsive and obsessive behaviors, impulsivity, aggression, and stubbornness (Dimitropoulos, Feurer, Butler, & Thompson, 2001). In addition, some research indicates that individuals with Prader-Willi syndrome are more likely
to engage in self-injurious behavior, with skin picking being the most prevalent manifestation being reported (Dimitropoulos et al., 2001; Symons, Butler, Sanders, Feurer, & Thompson, 1999).

Based on research by Dykens and Rosner (1999), individuals with PWS (as compared to those with non-specified mental retardation), are more likely to enjoy eating, think about food, be upset with changes in routine, be impatient with delays, and have a low frustration tolerance while, they are less likely to have many friends and be energetic. Further, as Joseph et al. (2002) noted, the likelihood of OCD effectively distinguishes individuals with PWS from other persons with eating disorders. However, according to Gerschwind and Dykens (2004), PWS manifests in older adults as diminished occurrence of maladaptive and compulsive behaviors (perhaps due to ongoing behavioral and dietary interventions). Dykens (2007) indicated the positive traits for PWS as including interest in the caretaking of others and facility with puzzles and word searches.

Intervention strategies that involve early intervention, exercise, monitoring of caloric intake, and education about appropriate food choices, environmental controls, and specialized transition planning are indicated (Scott, et al., 1997). Length and the quality of life are likely to be closely related to the success and management of weight (Percy et al., 2007).

**Williams Syndrome**

Williams syndrome (WS) was poorly understood until its genetic base was identified in 1990s. As such the syndrome provides an apt example of the continued research on the genetic basis of specific syndromes and the efforts to derive treatment and educational implications from syndrome identification. The literature (e.g., Dykens et al., 2000; Dykens, Rosner, & Ly, 2001; Einfeld, Tonge, & Rees, 2001; Mervis, Klein-Tasman, & Mastin, 2001) on Williams syndrome highlights the fact that it has an incidence of approximately one in 20,000 births. It is caused by
the microdeletion of chromosome #7 with multiple genes involved (i.e., missing), which impacts elastin, a connective tissue protein.

Semel and Rosner (2003) spoke to the enigmas of Williams syndrome when they asked: “How is it possible to conceptualize a group of children who tests as though intellectually disabled, speaks as though gifted, behaves sometimes as though emotionally disturbed and functions like <the> learning disabled.” (p. 1). Specific characteristics of WS include:

- Overly friendly in their interactions.
- Highly anxious.
- An average IQ of 40-90 but with marked unevenness in patterns (according to Searcy et al., 2004, 46% had IQs between 85-70, 45% 69-66, and 9% 54-40).
- Developmental delays in speech/language, motor and academic skills but with unique patterns of development.
- Well-developed vocabulary coincidental with difficulty in maintaining reciprocal conversation.
- An ability to learn to read over time and with strength in phonics-based spelling.
- Limited visual-spatial development and poor visual-motor skills (e.g., handwriting problems).
- Limited mathematical and numerical knowledge.
- Identified medical concerns including cardiac, digestive, and feeding difficulties.
- Positive traits (Dykens, 2007) including often excellent musical, language, interpersonal skills, zest for life, and empathy for others.
**Cri du Chat Syndrome**

Cri du chat syndrome is a chromosomal disorder caused by a partial deletion of the short arm of chromosome 5 (Maas et al., 2009). The cause of this rare chromosomal deletion is unknown. The chromosomal deletion usually occurs as a random event during the formation of reproductive cells or in early fetal development. People with cri du chat typically have no history of the condition in their family. About 10 percent of people with cri du chat syndrome inherit the chromosome with a deleted segment from an unaffected parent (National Human Genome Research Institute, 2013).

The estimated incidence of this syndrome range from 1: 15,000 to 1:50,000 live-born infants (Griffith et al., 2011; Kristoffersen, 2008; Teixeira et al., 2011; Wu, Niebuhr, Yang & Hansen, 2005). The symptoms of cri du chat syndrome vary among individuals. It is characterized by a distinctive, high-pitched, catlike cry in infancy with growth failure, microcephaly, facial abnormalities, and intellectual disability (ID) throughout life (Wu et al., 2005). The degree of ID ranges from moderate to severe (Cornish & Munir, 1998; Maas et al., 2009). However, the severity of symptoms and developmental delays may be associated to the size of the deletion of the 5p arm. Other symptoms include:

- **Developmental difficulties**: poor mobility, dexterity, and verbal communication skills
- **Maladaptive behaviors**: self-injurious behaviors, receptive movements, obsessive attachment to objects, head banging, stereotyped movements, destructive and aggressive behavior, tantrums, hypersensitivity to sensory stimuli, feeding problems, mood disorders, sleep problems, stubbornness, clumsiness (Cornish & Pigram, 1996; Teixeira et al., 2011)
• Problems with daily-living: difficulties feeding self, changing clothes, bathing, cooking, setting the table (Cornish, Munir & Bramble, 1998)

Kristoffersen (2008) reported that the existing literature shows that speech, language and communication skills vary among individuals with cri du chat. Some have spoken language that ranges from one word to multi-word utterances. Their receptive language is generally better than their expressive language (Cornish & Munir, 1998; Cornish et al., 1998; Cornish & Pigram, 1996; Maas et al., 2009). In a study conducted by Cornish and Munir (1998), they reported that although receptive skills improved slightly with the chronological age, expressive skills remained significantly low. Additionally, many individuals with cri du chat experience severe writing problems (Cornish et al., 1998).

The diagnosis of cri du chat syndrome is made at birth through chromosome analysis and/or the genetic test called fluorescent in situ hybridization (FISH) analysis. There is no specific treatment for cri du chat as brain damage resulting occurs at the early stages of the embryonic development. However, individuals benefit from rehabilitative programs, such as physical therapy and speech therapy. Children with cri du chat will most likely require ongoing support from a team made up of the parents, therapists, and medical and educational professionals.

**Sex Chromosomal Differences**

Anomalies in the sex chromosomes also affect development adversely. According to Tartaglia et al. (2007), abnormalities in X chromosomes have an incidence rate of approximately 1 in 400 births, with great variance in terms of the effects both within and between the specific conditions. While autosomal disorders, as discussed earlier, often lead to intellectual disabilities,
sex chromosomal disorders are more often associated with learning disabilities. Two such conditions are discussed next; their karyotypes are shown in Figure 5.

*Klinefelter syndrome* is a condition initially described in 1942 by Dr. Harry Klinefelter, in which males receive an extra X chromosome so that they have an XXY configuration. The clinical pattern includes frequent social retardation, sterility and underdevelopment of the male sex organs, and the acquisition of female secondary sex characteristics. The syndrome may infrequently be associated with mild levels of intellectual disability (Percy et al., 2007) though the risk of such deficits increases with the number of X chromosomes (i.e., XXXY, XXXXY). Because some children with the XXY pattern may not develop the formal syndrome, the term Klinefelter syndrome has often been replaced by describing individuals as *XXY males* (Bock, 1997). The incidence of XXY males is relatively high with approximately 1 in 500 to 1,000 births (Percy et al., 2007). Although no specific cure exists, physical aspects of the condition can be alleviated through surgery and testosterone treatment (with the latter often focused on infertility).

Specific characteristics aspects of XXY syndrome have been identified by Gerschwind and Dykens (2004): rarely intellectually disabled; near or above average intelligence; poor school performance and occupational difficulties; common occurrence of a verbal learning disability; and occurrence of dyslexia, with phonological processing problems.
FIGURE 5  
Sex Chromosomal Abnormalities


Individuals with XXY syndrome are also prone to difficulties in the formation of positive social relationships, depression, and significant mood changes (Bock, 1997). Although often discussed in relation to intellectual disabilities, XXY in males is more commonly associated with
learning disabilities (consistent with the earlier note that sex chromosomal disorders are more often associated with learning disabilities).

A sex chromosomal disorder in females, *Turner syndrome*, results from an absence of one of the X chromosomes (often shown as 45, X or XO). It is the only syndrome with a true monosomy (i.e., one chromosome) and thus the only one in which individuals with the syndrome show fewer than 46 chromosomes. It is a rare condition, occurring in about 1 in 2500-5000 female births. (Percy et al., 2007).

Rovet (1993) noted that over 95% of fetuses conceived with the XO pattern are spontaneously aborted. Further, an estimated 1 in 15 of the total number of spontaneous abortions are 45, X and thus only a small number survive to birth (Rovet, 2004). Turner syndrome produces numerous deviations from normal development, with lack of secondary sex characteristics, sterility, short stature, and varied health problems as particularly common features (Rovet, 2004).

Although Turner syndrome (TS) is not usually a cause of intellectual disabilities, it is noteworthy because it is often associated with learning disabilities. Some data indicate that the pattern includes lower performance scale and full-scale IQ scores (but not lower verbal scores) and with somewhat lower educational and occupational attainments than their peers. Common problems are in spatial relations and hence mathematical abilities, memory, attention, self-esteem, and social competence rather than in language ability (Rovet, 1993; Tartaglia et al., 2007).

According to Rovet (2004), math is a particular important area of research in Turner syndrome. Approximately 55% of individuals with TS are LD with 85% having math LD.
Specific problems noted were multi-digit operations, calculations, procedural problems and problem solving, while facts recall was not a key problem.

CRANIAL MALFORMATIONS

Several conditions associated with retardation manifest themselves as cranial malformations. The most dramatic is anencephaly—literally, the absence of major portions of the brain. Although anencephaly, for obvious reasons, is not associated with any treatments, it has been the subject of exciting research. A major type of neural tube defect (i.e., a defect occurring in the brain or spinal cord), it has been associated with the federal requirements (1998) that food manufacturers of grain products must add the nutrient folic acid to their products because of the positive effects of folic acid on the appropriate development of the fetal neural tube (American Association of Mental Retardation, 1996). This change in the dietary complement of folic acid has proved to have a significant reductive effect on this disorder as well as on spina bifida (i.e., a collection of disorders related to a malformation of the spinal cord that may or may not be related to intellectual disabilities).

Two cranial malformations may be indirectly associated with intellectual disabilities. In both cases, these conditions are most often related to a combination of genetic mutations as well as the possible influence of environmental factors during gestation (Harris, 2006).

Children who have microcephaly are characterized by a small, conical skull, a curved spine that typically leads to a stooping posture, and significant disabilities. In rare cases, the condition can be transmitted genetically, as an autosomal recessive disorder (Harris, 2006), but it is more commonly a secondary consequence of such conditions as congenital rubella or fetal alcohol syndrome (discussed later), or it may be the result of environmental exposure (e.g.,
radiation). Individuals affected by microcephaly have been characterized as imitative, good-natured, and lively. There is no known cure.

*Hydrocephalus* consists of at least six types of problems associated with interference in the flow of cerebrospinal fluid within the skull. The terms hydrocephalus and hydrocephaly are often used interchangeably. Technically, the former refers to the actual blockage of cerebrospinal fluid that result in enlargement of the head and increased pressure on the brain. The latter refers enlargement that is the result of an abnormal accumulation of fluid, related to an imbalance between the reduction and the absorption of fluid. The two primary categories are congenital that is typically related to some combination of environmental influences during the prenatal period along with potential genetic disposition and acquired, which would occur postnatal and typically would be related to some injury or disease after birth (Wooldridge, 2005). The most common type of blockage results in progressive enlargement of the cranium and subsequent brain damage.

Physical manifestations of this condition differ widely; however, an enlarged skull is not present in all cases. Hydrocephalus may result from polygenic inheritance or as a secondary effect of maternal infections or intoxications. The effects of this condition can be reduced in many infants by draining off the fluid, using shunts to decrease the cranial pressure. (*Shunts* are valves or tubes surgically inserted under the child’s skin to pump the fluid away from the brain and maintain proper flow.) The results of shunt treatment have been very encouraging in preventing head enlargement, the symptom most often associated with an increase in the probability of retardation.
OTHER CONGENITAL FACTORS

In addition to cranial malformations, other congenital factors include a variety of conditions that may be associated with harmful factors called teratogens. These can significantly affect prenatal (and, in some cases, postnatal) development. The first widespread public exposure to the awesome power of teratogenic agents came from the thalidomide tragedy in England in the 1960s. Intended as a relaxant during pregnancy, this drug caused severe physical deformities (e.g., missing and/or shortened limbs) in many fetuses. This discussion below focuses on some of the specific factors that have been identified as having teratogenic effects.

Maternal Disorders

The brain is especially susceptible to damage through maternal disease during the first three months of pregnancy. Infection of the mother by rubella (i.e., German measles) early in pregnancy has been found to result in fetal defects in up to 50% of these cases. This is particularly significant because rubella has historically been a disease of epidemic occurrence although immunization procedures developed over thirty years ago helped to limit its incidence. In addition to retardation, congenital rubella can result in heart disease, blindness, and deafness. It previously has been one of the primary causes of severe multiple disabilities among children.

One other cause of intellectual disabilities that may function as an insult to the fetus is blood-group incompatibility between mother and unborn child or Rhesus disease. Most commonly, the condition occurs as a result of the Rh factor, a protein on the surface of some red blood cells. Rh-positive blood cells contain this protein; Rh-negative cells do not. When an Rh-positive male and an Rh-negative female do not conceive an Rh-positive child, mother nor fetus is adversely affected. At birth, however, the mother’s immune system will react to the fetus’s
Rh-positive blood by forming antibodies to the Rh factor. These antibodies remain in the mother’s system and will enter the bloodstream of the next Rh-positive baby conceived, attacking its central nervous system and possibly resulting in intellectual disability, epilepsy, and cerebral palsy. Treatment of this immune response focuses on preventing the destructive antibodies from forming. One technique is to vaccinate the mother with Rh immunoglobulin serum midway through each suspected Rh-positive pregnancy and within 72 hours of its termination (whether by birth, miscarriage, or abortion). This serum destroys the Rh-positive cells that pass from the infant’s to the mother’s bloodstream, inhibiting the development of antibodies that would otherwise attack the next fetus carried. This procedure does not alter the mother’s immune response mechanism but can remove the stimuli that trigger it.

Substance Exposure

A great deal of research has addressed the effects of drugs and industrial chemicals on fetuses. The discussion below focusses on the effects of alcohol and drug exposure during the prenatal period.

Fetal Alcohol Spectrum Disorder: The first significant breakthrough of understanding in this domain was with alcohol consumption. Problems associated with alcohol have been generally acknowledged for years. For example, Haggard and Jellinek (1942) noted that “infants born to alcoholic mothers sometimes had a starved, shriveled and imperfect look” (p. 165). But despite this long-standing suspicion of teratogenic effects, only since the 1970s has the nature of fetal alcohol syndrome (FAS) been documented. Jones, Smith, Ulleland, and Streissguth (1973) coined the term fetal alcohol syndrome after studies of eight unrelated offspring born to chronically alcoholic mothers showed a recognizable pattern of major and minor malformations,
growth deficiencies, and developmental disabilities. More recently, the varied outcomes associated with fetal alcohol have led to the coining of the term fetal alcohol syndrome (or spectrum) disorder (FASD). This range includes from mild impact in the case of fetal alcohol effects (FAE, now clinically referred to as alcohol–related neurological disorders or ARND), which may include characteristics associated with learning disabilities, to the more significant fetal alcohol syndrome (FAS), with association with more significant disabilities.

FASD is among the leading known causes of intellectual disability. The range and estimate for fetal alcohol spectrum disorder is approximately 4-5 in 1,000 births, with estimates of near 1% of births (Harris, 2006) especially when both FAS and ARND are considered (Nulman, Ickowizz, Koren, and Knittel-Keren, 2007). In a study by May et al, (2009), the prevalence of the full spectrum of FASD in the general population was estimated at 9.1 per 1,000 children. This study suggests that FASD may be far more common, as the prevalence may be closer to 4% (Substance Abuse and Mental Health Services Administration (SAMHSA), 2014).

In FAS, the mother’s heavy alcohol consumption has direct toxic effects on the fetus. Exact levels of consumption that cause FAS are not known, but those mothers who are alcoholic, who have several drinks per day, or who engage in binge drinking run a confirmed, significant risk of damaging their unborn children. It was estimated that the prevalence rates for 2001-2003 were 1.9% for binge and 11.0% for any use of alcohol among pregnant women (Tsai, Floyd, Green & Boyle, 2007). The number of pregnant women who drank alcohol between the years 2002 and 2007 is fairly static (Substance Abuse and Mental Health Services Administration [SAMHSA], 2008). Risk rates are particularly high during the first trimester of pregnancy. Research continues on the risks of light or moderate drinking.
An important area of study has been FAE, a more subtle disorder associated with learning and attentional problems. Given the risk of FAE, the contemporary recommendation is for total abstinence from alcohol drinking during pregnancy. The official US government warning related to alcohol consumption is that “women should not drink alcoholic beverages during pregnancy because of the risk of birth defects” (Office of the Surgeon General, 2005).

The characteristics of FASD can be separated into three primary features: central nervous system dysfunction (e.g., disabilities), craniofacial malformations (e.g., cleft palate, microcephaly), and prenatal and postnatal growth development (e.g., low birth weight). A diagnosis of FAS is warranted when a child has a cluster of disorders within these three areas in the presence of maternal use of alcohol during pregnancy (Ryan & Ferguson, 2006).

The impact of fetal alcohol syndrome can be broad-based and influence key functional domains. Miller (2006) presented an analysis of key characteristics and the relationship to the areas of language communication, social and behavioral, academic and cognitive, and adaptive behavior domains. In Table 5, this analysis is presented.

Fetal alcohol syndrome has frequently been associated with lower levels of functioning and hence intellectual disability in 15-20% of the cases (Harris, 2006). In addition; there also is evidence of difficulties associated with retention, abstract thinking, and mathematics. The results of a study conducted by Rasmussen and Bisanz (2011) indicated that children (between the ages of 4-6) with FASD, when compared with typically developing peers, faced significant difficulties in mathematics, in the areas of problem solving, and recalling math terms, concepts, symbols, number patterns, and sequences.

Kerns, Don, Mateer, and Streissguth (1997) reported on a group of adolescents and young adults identified as having FAS who were not intellectually disabled. They confirmed the
presence of learning-related challenges in this population. As they noted, “cognitive impairments of this nature and degree might account, in part, to the widespread reports and observations of functional difficulties that individuals with FAS manifest in school, home, and community” (p. 691).

**TABLE 5**
Fetal Alcohol Spectrum Disorder Impact of Fetal Alcohol Syndrome Characteristics on Functional Domains

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Language/ Communication</th>
<th>Social/Behavioral</th>
<th>Academic/ Cognitive</th>
<th>Adaptive Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social communication/ language difficulties</td>
<td>Interprets cues incorrectly; difficulty with nonverbal communication</td>
<td>Interpersonal and peer problems; social skills deficits (e.g., lacks skills in sharing, cooperating)</td>
<td></td>
<td>Doesn’t follow or understand rules in social games in sports; difficulty communicating needs and wants</td>
</tr>
<tr>
<td>Conceptual reasoning/ thinking skills</td>
<td>Doesn’t use language to reason and analyze; understands at literal level</td>
<td>Lacks understanding of consequences of behavior; attention difficulties; hyperactive</td>
<td>Difficulty understanding abstract concepts; lack of judgment and reasoning skills; difficulty understanding time and sequence; challenged by meaning of cause and effect</td>
<td>Doesn’t understand time-sensitive tasks; difficulty with decision-making skills in home and community; difficulty following directions and problem-solving around functional issues</td>
</tr>
<tr>
<td>Emotional/social</td>
<td>May be chatty, talkative, with adequate or above vocabulary</td>
<td>Temper tantrums and angry outbursts; impulsive; unpredictable behavior and/or moods; mood swings; depression; poor self-esteem; aggressive; noncompliant</td>
<td>Unmotivated; unorganized</td>
<td>Immature behavior</td>
</tr>
<tr>
<td>Independence/ self-sufficiency</td>
<td>Expressive or receptive language deficits</td>
<td>Difficulty regulating behavior</td>
<td>Deficits in short/long-term memory</td>
<td>Lacks independent living skills; problems with age-appropriate hygiene tasks</td>
</tr>
</tbody>
</table>

Ryan and Ferguson (2006) stressed the importance of increased public awareness in general, the need for differentiated instruction in the classroom, and the need for supports from families. US Surgeon General Richard Carmona (2005, cited in Insight, 2005) stated: “we must prevent all injury and illness that is preventable in society, and alcohol-related birth defects are completely preventable, we do not know what, if any, amount of alcohol is safe. But we do know that the risk of a baby being born with any of the fetal alcohol spectrum disorders increases with the amount of alcohol a pregnant woman drink, as does the likely severity of the condition. And when a pregnant woman drinks alcohol, so does her baby. Therefore, it’s in the child’s best interest for a pregnant woman to simply not drink alcohol.” (p.14)

**Prenatal Drug Exposure:** Attention also has extended to other drugs, because of common reports of children exposed to drugs in utero. However, significant problems persist in determining the actual number, with estimates of 500,000-750,000 exposed children born each year (King, 2004). Although the research base is by no means clear, a number of possible characteristics have been noted for children who are at risk due to prenatal exposure to drugs. Such judgments must be made cautiously because the research base is confounded by, for example, lack of control for other factors; wide variance in substances, dosage and purity; multiple drug exposures; and variant levels of prenatal care (King, 2004). Therefore, prenatal drug exposure is a challenging area for research and the accurate determination of cause and effect.

Vincent, Poulsen, Cole, Woodruff, and Griffith (1991), in their review, indicated that problem areas could include:

- exhibition of behavioral extremes
- being easily overstimulated
• low tolerance for changes
• constant testing of limits set by adults
• difficulty in reading social cues
• difficulty in establishing and maintaining relationships with peers
• language delays
• sporadic mastery of skills
• inconsistent problem-solving strategies
• auditory processing and word retrieval difficulties
• decreased capacity to initiate and organize play
• decrease in focused attention and concentration

Considerations of substance exposure must always be set in a broader environmental context. Brady, Posner, Long, and Rosati (1994, cited by King, 2004, p. 5) stressed this in noting:

The long-term effects which will be found within the general population of drug-exposed children will not be explained by drug exposure alone. Before we can predict the developmental outcomes for these high-risk children we need further research into the additive and interactive effects of the multiple risk factors to which they are exposed, including in many cases the global effects of poverty, multigenerational substance abuse, and the impact of growing up in a drug-seeking environment.

POSTNATAL CONCERNS

A variety of postnatal traumatic events leading to disabilities can occur throughout early childhood. Head injuries account for the greater part of such cases. It has been estimated that 1
in 30 children will experience a serious brain injury by the end of the teen years (Allison, 1992). Most of these of these injuries are caused by falls, bicycle and motor vehicle accidents, and sports-related activities. The highest risk years are between 15 and 25, with boys far more likely to be affected than girls. The relationship of auto accidents to brain injury spurred the passage by all states of mandatory child restraint and seat belt laws.

*Child abuse* is a special concern, particularly because of its relationship to disabilities. Child abuse can result from and aggravate primary disabilities. Zantal-Weiner (1987) noted in her review that children with disabilities are less able to defend themselves from abuse, have greater difficulty determining appropriate and inappropriate contact and telling anyone of the abuse once it has occurred, are more dependent on those who abuse them, are less likely to report abuse, and are seen as less credible when they do report it. In addition to striking, other negative so-called disciplinary actions like violent shaking can potentially play a role in brain hemorrhage and retardation. Signs of a “shaken baby” include vomiting, seizures, blood pooling in the eyes, apnea (spells of interrupted breathing), irritability, sleeping difficulties, and drowsiness; outcomes may include hypertension, cerebral palsy, subcranial or subdural hemorrhages, coma, and death.

*Lead poisoning*, which may lead to encephalitis, is permanently and progressively damaging to the central nervous system because of lead’s role as a neurotoxicant. It can cause seizures, cerebral palsy, and intellectual disabilities. Other effects of lead poisoning include gastrointestinal disturbances (e.g., anorexia, vomiting), central nervous system manifestations (e.g., convulsions, drowsiness, irritability), lower intelligence, reading disabilities, hyperactivity, attention deficits, and physical and sensory impairments.
Lead poisoning is typically caused by a process in which lead is inhaled, ingested, or absorbed through the skin. The levels of toxicity are in range from headaches, cramps, and limited appetite to significant impact on behavior, convulsive disorder, and death (Ylvisaker, 2005); although commercial paints used for homes have not contained lead since 1978 (Gaultier, 2005), poisoning is still a factor in residences where a child has access to old, peeling paint. Conscious urban renewal has reduced the scope of this problem through repainting with unleaded paints. In older homes, lead paint can also enter the body through inhalation of dust or fumes, such as during renovation or from the soil around the houses. The existence of high lead levels remains most serious in inner-city areas where abatement efforts have not been fully implemented. Elevated lead blood levels can also be caused by water from lead water pipes, by prolonged breathing of polluted air, as in towns with lead smelters and heavy traffic congestion, and by the young child’s mouthing and eating objects containing lead (see Table 6). Government estimates place the prevalence of preschool children exposed to lead at unacceptable levels up to 5% (Gaultier, 2005).
### TABLE 6

**Increased Risks for Lead Poisoning**

- Residence built before 1978
- Residence with chipped, cracked, or peeling paint
- Residence with lead pipes or lead-soldered copper pipes
- Residence near waste sites and lead industry
- Lead present in water above 500 ppm
- Leaded ceramics and leaded crystal, especially those imported from Mexico, Italy and China
- Residence adjacent to major highways built before 1986
- Family members who work in industry using lead (battery plants, electronics, stained glass, and mining)
- Hobbies using lead (ammunition, molding, and fishing weights)
- Food from cans soldered with lead
- History of eating nonfood substances (e.g., paint chips, pencils, crayons, ashes, and dirt)
- History of poor nutrition, especially low iron, calcium, or Vitamin C
- Playing with old or imported lead toys and old keys
- Elevated lead level, above 10 micrograms per deciliter
The list below summarizes some key blood lead level screening questions for parents. The instructions are: “If you answer yes to any of these questions, your child’s blood lead level needs to be checked by your health care provider.

- In the past six months has your child lived in a house or apartment built before 1950?
- Is there recent remodeling being done in your home? Are there surfaces with peeling or chipped paint?
- Do you have other children who have been diagnosed or treated for lead poisoning?
- Does anyone in your household have a job or hobby that involves exposure to lead?
- Do you live in an area where there is industry release of lead, such as a lead smelter, or battery recycling plant?” (Davis & Sattler, 2004, p.22 – 24).

**PREVENTION**

The purpose of this section on prevention is to highlight selected tools, techniques, and procedures that assist in the process of preventing intellectual disability. Inspired by a 1970s government commitment to prevent the occurrence of 50% of all cases of retardation by the end of the twentieth century (President’s Committee on Mental Retardation, 1976b), researchers tackled virtually all causes of ID. In every known case, a specific preventive measure was identified.

There are three levels of prevention: (a) primary- risk conditions can be eliminated so that a condition never comes into existence, (b) secondary- preventive efforts can reduce or eliminate the effects of an existing risk factor, and (c) tertiary- interventions may assist a child who has a
disability. To illustrate the three types of prevention, Nulman et al. (2007) applied the model to fetal alcohol spectrum disorder. In this instance, primary prevention focuses on societal awareness of the risks associated with alcohol consumption during pregnancy. Secondary prevention focuses on informing women during pregnancy who have been engaging in heavy alcohol consumption to cease alcohol use in order to avoid increased risks. Tertiary prevention then becomes a focus on the identification of children who have fetal alcohol syndrome or alcohol-related neurological disorders and providing them with education and treatment in order to reduce the impact of the learning and behavioral difficulties associated with FASD. Crocker (1992) and Polloway and Rucker (1997) have identified the specific activities associated with a comprehensive prevention program. These considerations are outlined in Table 7 and are implicit in the discussions that follow.
### Elements of a Comprehensive Prevention Program

#### Prenatal strategies
- Ensure family planning and timing of pregnancies
- Provide genetic counseling
- Test for genetic carriers
- Provide adequate prenatal care and diagnostics
- Reduce teenage pregnancy rates
- Reduce births out of wedlock
- Avoid alcohol and other teratogenic substances during pregnancy

#### Perinatal strategies
- Screen newborns for disorders
- Screen newborns for diseases (e.g., HIV)
- Provide early intervention for at-risk infants (e.g., those born prematurely)

#### Preschool strategies
- Enroll children in early intervention programs
- Provide parental education and support
- Avoid lead in environment
- Avoid hazards associated with brain injury
- Reduce occurrences of child abuse and neglect
- Use safety restraints in vehicles

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</tbody>
</table>
Immunize for diseases
Provide proper medical care and treatment
Plan for appropriate transition to school

School preventive strategies
Provide effective instruction and relevant curriculum
Involve parents in education
Provide a family life curriculum to future parents

Federal and state policy strategies
Commit to a reduction in poverty
Reduce the prevalence of homelessness
Provide public information about prevention
Support comprehensive prevention programs
Develop and provide universal health-care programs

Preconception
Preventive measures taken before conception can avert hereditary, innate, congenital, and other constitutional disorders. One basic tool is genetic counseling, an attempt to determine risks of occurrence or recurrence of specific genetic or chromosomal disorders. The tools of the genetic counselor include the family history and personal screening. Study of the persons’ genetic and medical history is particularly concerned with evidence of spontaneous abortions or stillbirths, relatives’ age at death and causes of death, and the existence of any interfamily marriages that might bear on the presence of specific genetic disorders. Screening is primarily for carriers of recessive trait disorders. Blood samples can be analyzed easily and inexpensively. Based on an
understanding of the mathematical probabilities associated, for example, with recessive, dominant, or sex-linked inheritance, prospective parents can make an informed decision about the risks of having a child who may have a developmental disability.

An unusual side effect has emerged from genetic research. With the significant advances associated with Human Genome Project, increasingly some see genetics as business. Advertising is now becoming more common as related to soliciting donors for sperm, marketing donor eggs, and providing services that enable individuals to access their own genetic information through analysis of their genome.

Other specific means of prevention are also available during this period. Immunization for maternal rubella can prevent women from contracting this disease during pregnancy. Blood tests can identify the presence of venereal diseases. Adequate maternal nutrition can lay a sound metabolic foundation for later childbearing. Family planning in terms of size, appropriate spacing, and age of parents can also affect a variety of specific causal agents.

**During Gestation**

Two general approaches to prevention during pregnancy are prenatal care and analysis for possible genetic disorders. Numerous prenatal precautions can be taken to avert congenital problems. Adequate nutrition, fetal monitoring, and protection from disease are certainly the grounding of prenatal care. Avoidance of teratogenic substances resulting from both exposure (e.g., radiation) and personal consumption (e.g., alcohol and drugs) also relate specifically to this period.

Analysis of the fetus for the possible presence of genetic or chromosomal disorders is another key component of genetic counseling. Prenatal diagnosis is typically recommended under the following circumstances: when the mother is 35 or older; when the risk of the disorder
is greater than the risk of the procedure; and/or when couples are known to be at risk (e.g., have had a previous child with the condition; are genetic carriers; have an established risk due to familial patterns).

Prenatal screening may include the triple test (or triple screen), amniocentesis, chorionic villi sampling, fetoscopy, fetal biopsy, and ultrasound. The *triple screen* is a procedure that provides an analysis of three chemicals (i.e., maternal serum alpha-feto protein (AFP), unconjugated estriol, and human chorionic conadotropin) to provide an initial assessment of at-risk pregnancies (Dykens et al., 2000). As Apolloni (1998, p. 34-5) noted, with the triple screen “each of these three analyses are derived from blood samples and considered in conjunction with related information (i.e., age and weight of the mother, ethnic group, gestational age of the fetus and the number of fetuses)…. [It is] cheaper to perform, it is faster (results available in 1–3 days versus 2 weeks for amniocentesis), and there is no risk to the fetus, it provides an initial direction for determining whether further diagnostics should be performed.”

Usually performed during the 14th to 16th week of pregnancy (i.e., mid-trimester), *amniocentesis* involves drawing amniotic (embryonic sac) fluid for biochemical analysis of fetal cells. In the majority of cases where amniocentesis is used, its primary purpose has been the detection of chromosomal errors. Generally, the technique is safe. However, parents should be informed of certain considerations, including the risk of about 0.5% or less of a miscarriage, the possibility of an unsuccessful culture of fetal cells, and the possibility of disorders remaining undiagnosed by the procedure. The procedure may be used earlier in gestation, but the risks are slightly increased.

Another technique for prenatal diagnosis is *chorionic villus sampling* (CVS), which can also provide information on chromosomal and biochemical anomalies. In CVS, chorionic tissue
(the fluffy material that forms the placenta) is withdrawn. The test can be performed after approximately 9 weeks of gestation, with initial results (chromosomal analysis) available within 2 days and a full culture (for analysis) available within two weeks after sampling. The most significant advantage of the process is that it allows an earlier analysis of fetal status. It has been estimated that CVS is associated with a risk rate for miscarriage and other complications slightly higher than that for amniocentesis (about 1%-2%; Harris, 2006).

One other technique that has contributed to an understanding of the prenatal environment is ultrasound, or sonography. This technique can be used for possible determination of hydrocephalus, some central nervous system disorders, and limb anomalies. The technique is also used to determine the location for amniocentesis, to assist in delivery, and as a common adjunct to fetal therapy, which seeks to correct conditions existing in utero. Ultrasound is a non-invasive, safe and accurate procedure (Machalek, Percy & Brown, 2007).

These analytical techniques have three purposes. Most encouraging, of course, is that negative tests assuage parental fears or anxieties. Second, the result can confirm suspicions of disorders and give the parents a chance to determine what to expect. They may also alert physicians to the need for careful monitoring prenatally, perinatally, and postnatally. Finally, the information can be used as a basis for decisions about termination of pregnancy. The use of these techniques along with elective abortion has significantly reduced the birth rates of a number of specific disorders (e.g., for cases when DS is confirmed, studies range from 80-95% of those receiving these data consequently report a decision to terminate; Roberts, Strough, & Parrish, 2002; American Journal of Obstetrics and Gynecology, 2005, as cited by Porske, 2007), although obviously it has also generated much controversy. It has also been questioned as a personal level as well (see Box 5).
Roberts et al. (2002) researched the responses of mothers to the role of genetic counseling in the process of deciding whether to terminate pregnancy. They surveyed 69 women at risk for carrying a fetus with disability. A series of questions were asked including: would you terminate if a disorder were confirmed? (65%: yes); were you encouraged to talk with a parent of a child with disability? (91.3%: no); and was genetic counseling helpful? (91% for information on prenatal disorders; 13% for information on quality of life issues; and 17.4% in terms of being provided with positive and negative aspects of giving birth to a child with a disability).

<table>
<thead>
<tr>
<th>BOX 5</th>
<th>Down Syndrome</th>
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<tbody>
<tr>
<td>To the Editor: “It was with an increasingly heavy heart that I read about yet another refinement in genetic testing. Twenty-four years ago we began an unexpected journey for which we had no preparation: our daughter was born with Down syndrome. Then, as now, a genetic test could have forewarned us. What the test could not have revealed, however, was the person that she eventually became. Her delight in life and extraordinary capacity for love and forgiveness enrich the lives of those who know her. Years ago a friend, sensing an absence of the pretense that plagues so many “normal” people, described her as “a rose with the thorns removed.” Tragically, a genetic test may lead one to find thorns with no hope of experiencing the rose.”</td>
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Percy, Lewkis, and Brown (2007, p. 103) noted that the “availability of technology that could detect genetic defects causing intellectual and developmental disabilities is a blessing to many parents. Knowing the exact cause of the problem helps parents to understand the likely outcome for the child and to choose the best intervention. Such information is absolutely
essential for researchers to develop rational treatments or even cures. It also provides choices for family planning”. At the same time, they noted that these are always related to ethical concerns. Will they consider an abortion? Will they inform other biological family members about the disorder? How does it influence the way the professionals deal with parents and families? Is it ethical for children to be tested for genetic disorders? Will this information be made available to insurance companies through health records? Will health insurance be difficult to obtain after diagnoses have been made?

Perske (2007, p.6) summarized responses received from parents of young children with Down syndrome that speak to these concerns:

- Most expectant mothers only learn about the painful side of such a birth from clinicians.
- Many admitted that they felt pressure from physicians to terminate the birth.
- Almost never did they receive the latest information on Down syndrome.
- Almost never did they receive information about organizations for persons with Down syndrome.
- Most young expectant mothers carry such hope and joy regarding the baby within them, they refuse all offers of prenatal testing.

Given the controversial nature of abortion at this time, it is worth noting the following key policy issues that continue to receive public scrutiny and debate: funding for prenatal screening research, parental consent, trimester/length of term (when abortion can/can not be considered), federal funding for abortions, and maternal health and safety.

At Delivery

Prevention at delivery is based on anticipating possible problems. Pregnancies deserving of special attention include those involving very young or older mothers, inconsistent prenatal
care, prematurity, preterm delivery, lower birth weight, closely spaced pregnancies, drug exposure during pregnancy, and a history of previous children with genetic disorders.

Several specific measures are associated with the perinatal period. The most common is the Apgar test of vital signs (Apgar, 1953), an evaluation routinely given at 1 and 5 minutes after the birth of a child. The physician rates each of the following factors on a scale of 0 to 2: heart rate, respiratory effort, muscle tone, skin color, and reflex response. An Apgar score of 8 to 10 suggests the newborn is healthy and responsive; scores of 5 to 7 and 0 to 4 indicate moderate and severe concerns for further attention, respectively. Initially, screening using such a scale can assist in preliminary decision making about children who may be at risk for specific disorders, and a more comprehensive assessment then follows. Intensive intervention can begin almost immediately for premature and other infants identified as having a particular difficulty.

Computer-assisted obstetric measures aid in the close monitoring of both mother and child. Another helpful measure for Rh incompatibility during the first 3 days after birth is injection of immunoglobulin serum, as described earlier. If a child is born to a mother who did not have the necessary series of injections in the course of a previous pregnancy, a complete transfusion of the newborn’s blood can prevent the destruction of its blood cells by the mother’s antibodies.

A third focus is on screening for specific genetic disorders (e.g., PKU). Federal guidelines call for newborn screening for PKU, congenital hypothyroidism, and sickle cell anemia. Related state guidelines range from 4-36 disorders (across states) for which screening is to occur. All states require subsequent notification of the health care provider, while less than half require direct notice to the parents.
McNab and Blackman (1998) provided an important summary of the challenges facing infants with birth complications and their families when they noted:

Despite the ability of neonatologists to provide life-saving measures for very sick babies, allowing them to be discharged from the hospital, significant obstacles often face many of these infants and their families once they are home. Ongoing health problems in these children can hamper or delay the normal course of motor, cognitive, language, and social development. Community early intervention professionals such as educators, social workers, and physical, occupational and speech therapists can improve these children’s’ long-term outcomes by being knowledgeable about these health problems and devising creative family-centered early intervention strategies (p. 198).

These concerns are clearly important but nevertheless caution should be used with any generalizations. It is important to note that babies having one or several risk factors may experience no ill effects.

**Early Childhood**

Several types of intervention are important during early childhood. Proper nutrition is critical throughout development, but particularly so during the first 6 months of infancy. Dietary restrictions for specific metabolic disorders should be maintained until no longer required. Avoidance of hazards in the child’s environment can prevent head injury, and avoidance of exposure to substances such as lead and mercury are mandatory to proper development.

Finally, key issues related to prevention during the early childhood period fall most appropriately within the psychosocial arena. The preceding discussion has highlighted a variety of preventive measures that relate to various causes of disability discussed earlier in this chapter.
For such biological causes, the advances of the last 40 years have been breathtaking. In terms of psychosocial causes, the successes that have been achieved are tempered by the obvious need for greater commitment. Whether society is willing to devote the necessary resources to breaking the poverty cycle and altering the effects of psychosocial causes, with the goal of reducing the prevalence of retardation, is still an unanswered question.

It is clear that, regardless of whether or not a child already has a disability, growing up in restricting conditions interferes with a child’s opportunity to develop and mature as well as his or her more privileged peers. The negative consequences of an unstimulating environment must be diminished through the most promising intervention strategies. As Baroff (1974) wrote over 40 years ago, “Equality of opportunity is a ghastly charade if individuals are so stunted by early experiences” that they do not take advantage of opportunities for treatment that are available (p. 116). By facilitating children’s cognitive, academic, social, and emotional development, we increase the chances of having a future population of healthy, self-sufficient, mature adults. Intervention strategies with a preventive aim must work to identify children at risk and establish strategies designed to facilitate the development of each of them.

**ETHICAL ISSUES**

Remarkable developments in molecular biology and genetic engineering are reported daily in the popular press. Further advances in genetic science and medical technology will almost certainly change the course of the human experience. The eradication of what are now considered diseases, disorders, and defects may become possible before the end of the new century. As medicine advances, however, a critical question may be how diseases, disorders, and defects are defined. Is an intellectual disability, in this context, a disease, a defect, or a human
difference? Should intellectual disability be prevented in all circumstances, or is it part of the spectrum of human variation? Depending on the answer, what does this say about the status of people with this condition in a society that values human equality? What does it say about their fundamental value as people?

The danger that people with intellectual disabilities will be further devalued as genetic interventions proliferated and become more accessible, is illustrated by remarks by James Watson. Winner of the Nobel Prize and codiscoverer of DNA, Watson was also the first director of the Human Genome Project. In his capacity as leader of the effort to map and sequence the genetic makeup of human beings, Watson also advocated careful consideration of the ethical, legal, and social implications of the project. Yet, in an article entitled “Looking Forward,” Watson questioned the value of the lives of people with significant disabilities. He spoke of the decisions faced by “prospective parents when they learn that their prospective child carries a gene that would block its opportunity for a meaningful life” (Watson, 1993, p. 314). In this article he spoke of parents who do not undergo genetic testing. “So we must also face up to the ethical and practical dilemma, facing these individuals who could have undergone genetic diagnosis, but who for one reason or another declined the opportunity and later gave birth to children who must face up to lives of hopeless inequality” (p. 315).

Later Watson spoke to the German Congress of Molecular Medicine and condemned the eugenic philosophy that resulted in the atrocities of the Nazi era. Then, in a seeming contradiction, he advocated what might be termed “parental eugenics.” He asserted that the “truly relevant question for most families is whether an obvious good will come from having a child with a major handicap.” From this perspective, Watson said, “seeing the bright side of being handicapped is like praising the virtues of extreme poverty” (Lee, 1998, p. 16).
As it becomes possible to identify virtually all persons at risk for having a child affected by a genetic disorder (Moser, 2000), the excitement over prevention must be sobered by the ethical aspects of this capacity. It is therefore critical to consider carefully the actions that can be taken, versus those that should be taken, once a specific disability, or risk of a disability, has been identified.

Skotko (2005) reported on his study of mothers noted that historically “prenatal screening and diagnosis have almost exclusively existed to allow women the option of terminating their pregnancy. Knowing this, health care providers have historically operated under the assumption that if a woman consents to prenatal screening or diagnosis, she must believe that having a child with DS would be an undesired outcome and wish to terminate her pregnancy if such a diagnosis were made prenatally” (p. 676). Skotko (2005) further explained that the results of his study “indicate that this is not true for all women. Consequently, health care providers should appreciate that many women consent to prenatal testing with ambivalence or no intent whatsoever to terminate” and that “women who chose to continue their pregnancy after a prenatal diagnosis of DS do so primarily because of religious or personal reasons” (Skotko, 2005, p.675- 676).

Another major ethical concern is the question of the right to life after birth of children who are disabled. Newspaper accounts of the cases of a newborn at Johns- Hopkins Hospital in Baltimore, Baby Doe in Indiana, Baby Jane Doe in New York, Phillip Becker (a California teenager with Down syndrome) and Baby Gabriel in Canada sensitized the public to issues that for years had been quietly debated in professional circles (Perske, 2007). In most cases, the question was whether a child’s disability should be a primary factor in the decision to provide optimum medical care. These cases, and the public response, led to litigation and legislation to
protect the rights of citizens with disabilities (in these cases, most often with Down syndrome) (Perske, 2007).

An additional ethical issue is that of “do not resuscitate orders” (DNR) for persons with special needs. Given the complexity of the medical needs of some individuals, this area promises to be of great concern in the future. Smith’s (1995) discussion of John Lovelace, an adult with intellectual disability who was deinstitutionalized, provides a vivid discussion of this issue. Lovelace, at risk for a stroke due to a vascular abnormality in his brain, was deemed to be not a candidate for emergency treatment in the event of a health crisis. This decision was reached based on his disability, absence of family and his dependency on governmentally funded medical care. It was decided without his informed consent. (For further information on DNR orders and special education, see Sewall & Balkman, 2002).

Increasingly complex ethical issues require the scrutiny and advocacy of professional educators. As Smith (1989) noted, special educators may often be better informed than physicians concerning the possibilities and potentialities in the lives of children with disabilities. They are in a unique position to act as advocates.

**FINAL THOUGHTS**

Hundreds of specific etiological factors have been identified as causes of intellectual disabilities and developmental disabilities. Nevertheless, in the vast majority of individual cases, a specific cause cannot be identified.

To understand etiology, we must first understand the principles of genetics, since a large percentage of biological causes stem from recessive, dominant, and sex-linked inheritance and from chromosomal abnormalities. Other causes include prenatal infections and intoxications,
brain injury, malnutrition, cranial malformations, disorders related to pregnancy, and environmental influence.

Prevention of intellectual and developmental disabilities requires an intensive program that begins before conception and continues throughout the developmental period. Every specifiable cause has a preventive measure of one type or another.

Advances in medical technology have created ethical problems that society must face. Each professional must accept the responsibility of becoming informed on these ethical issues and developing her or his own informed position.

Summary

Introduction

- The causes of intellectual disability are many and varied.
- Professionals in the field need to have a general awareness of causes.
- Terminology used to describe various etiologies comes from three sources: conventional wisdom, names of specific people, and biomedical vocabulary.

Genetic and Chromosomal Considerations

- Genetics is the study of heredity with a focus on genes and chromosomes.
- Intellectual disabilities can result from problems with genetic material on either autosomes or sex chromosomes.
- Genetic transmission can occur through autosomal dominant or recessive means or through X-linked recessive or dominant patterns.
- Karyotypes are charts of chromosomes.
• The most recognizable condition associated with chromosomal anomalies is Down syndrome.

*Other Etiological Considerations*

• Cranial malformations involve conditions such as hydrocephalus.
• Many different toxic substances can significantly affect prenatal and postnatal development.
• Events such as head injuries and child abuse can also contribute to intellectual disabilities.

*Prevention*

• Prevention requires an intensive program that begins before conception and continues throughout the developmental period.
• Every specifiable cause can be matched with one or more preventive measure.

*Ethical Issues*

• Advances in medical technology have created ethical problems that society must face.
• Special educators are uniquely qualified and professionally positioned to act as advocates for children with disabilities when ethical issues arise.
References


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