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A Comprehensive Guide to Intellectual and Developmental Disabilities

Second Edition

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Factors Causing or Contributing to Intellectual and Developmental Disabilities

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WHAT YOU WILL LEARN

- Importance of education about factors that cause or contribute to intellectual and developmental disabilities (i.e., risk factors)
- Overview of causal or contributing factors
- Biomedical, social, behavioral, and educational risk factors
- Prevention of intellectual and developmental disabilities
- Comorbid sensory impairments and mental health disorders
- Future directions in the field

The purpose of this chapter is to draw awareness to different factors that can cause or contribute to intellectual and/or developmental disabilities. There are several reasons why this chapter is important. First, obtaining an explanation for why a person has been diagnosed with intellectual disability as early as possible (i.e., an early diagnosis) provides relief to families and others who care for the child. Second, an early diagnosis facilitates access to supports and services earlier than in the absence of a diagnosis; in some cases, these may prevent actual or further impairment from developing. Third, an early diagnosis may help to prevent recurrences of certain types of intellectual and developmental disabilities within an affected individual's family. Fourth, having information about the causes of intellectual and developmental disabilities helps administrators and policy makers allocate funding for supports and services, because these often are geared to specific types of disabilities. Finally, before an explanation is sought for what may have caused intellectual or developmental impairments, professionals and families should consider any negative consequences that might arise from a child becoming "labeled." Sometimes, complex ethical, legal, and social issues can arise that might interfere with obtaining medical or life insurance or with employment, or labels might upset family members. Should such concerns arise, it is important that appropriate guidelines, laws, policies, or strategies be developed and implemented to guard against them (Percy, 2007; Percy & Brown, 2011).

OVERVIEW

Using criteria in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR),* intellectual disability has been estimated to affect approximately 2%–3% of the general population worldwide, the prevalence being lower in developed than developing countries (American Psychiatric Association [APA], 2000). On the basis of *DSM-5* criteria, the prevalence is approximately 1% (APA, 2013). However, in a study of 1997–2008 data representative of U.S. households, as many as 1 in 6 children in the United States is affected by some type of developmental disorder,

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including attention-deficit/hyperactivity disorder (ADHD), intellectual disability, cerebral palsy, autism spectrum disorder (ASD), seizures, stuttering or stammering, moderate to profound hearing loss, blindness, learning disorders, and/or other developmental delays (Boyle et al., 2011). Most cases of intellectual disability are mild, with less than 0.5% being severe (Rauch et al., 2012).

Intellectual disability is sometimes classified as syndromic (in which intellectual impairments associated with other medical and behavioral signs and symptoms are present) and nonsyndromic (in which intellectual impairments appear without other medical and behavioral signs and symptoms). Syndromic intellectual impairments account for 30%–50% of cases (Kaufman, Ayub, & Vincent, 2010; Rauch et al., 2012; Srour & Shevell, 2014.)

Many different factors that cause or contribute to intellectual and developmental disabilities have been identified. One quarter to one half of intellectual or developmental disability diagnoses are associated with genetic factors (Srour & Shevell, 2014). Although some publications report that the cause of intellectual disability is unknown in up to half of cases, a population study in a middle-income country identified causal factors in approximately 90% of a birth cohort (Karam et al., 2015). Studies of children indicate that 1.5 times as many males are affected with intellectual disability as females, but the male-to-female proportion decreases with increasing severity of intellectual impairment (McLaren & Bryson, 1987). In autism spectrum disorder (ASD), the most widely reported male-to-female ratio is 4-5:1 (Lai, Lombardo, Auyeung, Chakrabarti, & Baron-Cohen, 2015).

The American Association on Intellectual and Developmental Disabilities (AAIDD) focuses on four different types of factors that cause or contribute to intellectual disability (biomedical, social, behavioral, and educational) and on the timing of exposure to these factors (prenatal, perinatal, and postnatal) (AAIDD, 2010). Biomedical factors include genetic disorders and various factors adversely affecting health. Social factors include adverse family social interactions, lack of access to health care, and parental neglect. Behavioral factors include any behavior that adversely affects functioning, such as maternal alcohol or substance abuse. Educational factors include lack of accessibility to educational experiences that support adaptive skills, such as family support and/or special education, especially early in life. Sometimes the term *environmental* is used to denote health-related, social, behavioral, and educational factors. *Prenatal* means occurring before birth; *perinatal* relates to the period shortly before and after birth (traditionally, from the 20th week of gestation to the 28th day of newborn life). *Postnatal* means after birth (traditionally, the first 6 weeks after birth). Nongenetic factors are sometimes referred to as environmental factors.

Factors involved in intellectual and developmental disabilities are often referred to as risk factors. Many forms of intellectual and developmental impairment are thought to result from more than one factor (McLaren & Bryson, 1987). Risk factors can be causal or contributing. The term *causal* implies that the factor (or factors acting in combination) actually causes the intellectual impairment or developmental delay (i.e., that the probability of causing the intellectual impairment or developmental delay is 100% or close to this). *Contributing* implies that the factor(s) in question is/are not sufficient on its/their own to cause the intellectual impairment or developmental delay. Conversely, some factors can help to prevent intellectual impairment or developmental delay or reduce its severity. The study of factors involved in intellectual and developmental disabilities is complex and challenging. For example, having an extra chromosome 21 is known to cause Down syndrome, and Down syndrome is associated with intellectual disability. However, the degree of intellectual disability in people with Down syndrome is highly variable, and the nature of this variability is not yet understood. This may involve multiple biomedical and/or psychosocial factors. Susser (2002) noted that ideas of what are causal factors in human disease have "changed over the years as societies, understanding of disease, and technical resources have changed." Furthermore, this field of study continues to evolve (Xiang et al., 2015).

An introduction to risk factors for intellectual and developmental disabilities should include a brief review of genetics, the "nature versus nurture" debate, the subspecialty of genetics called epigenetics, and brain plasticity.

A Brief Review of Genetics

Every cell in the human body contains 46 chromosomes: 23 from the mother and 23 from the father. Chromosomes are structures in the nucleus of the cells made up of tightly coiled strands of DNA.

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Along these strands are sections referred to as genes. Genes contain information that both enables the body to grow and work and determines how the body grows and works. Genes are passed from parents to children. Twenty-two of the 23 chromosome pairs are called autosomes; these are not involved in sex determination. The chromosomes that determine sex (the sex chromosomes) are the X in females and the Y in males. Females have two X chromosomes; males have one X and one Y. DNA is also present in mitochondria, the energy-producing organelles of cells. Mitochondrial DNA is inherited from the mother. When the first cell is formed from the mother and father, mitochondria from the father are destroyed. In this first cell, very occasionally a chromosome (or more) is structurally not normal, or there can be too many or too few of them, or they can be changed in very minor ways. Sometimes genetic abnormalities are inherited from one parent or from both parents, but sometimes they are not and occur de novo (i.e., spontaneously; Nussbaum, McInnes, & Willard, 2015). Inheritance of a genetic disorder can be dominant (a mutation in just one of two copies of a gene is sufficient to cause a problem) or recessive (mutations are needed in both copies of a gene to have an effect). There is no controversy that eye and hair color are specified by variants of specific genes encoded in each human cell.

A Brief Review of Nature versus Nurture

The nature theory supports the idea that even more abstract traits such as intelligence, personality, aggression, and sexual orientation are encoded in a person's DNA. The nurture theory, on the other hand, proposes that behavioral aspects of humans originate only from the environmental factors of upbringing. There was considerable debate over several decades about whether nature or nurture predominates in matters of child development. It is now generally agreed that both play important roles, that they interact in sometimes complex ways, and that the relative importance of nature or nurture varies considerably from one person to another.

A Brief Review of Epigenetics

Epigenetics is the study of changes in gene activity that are caused by things other than the makeup of the genes themselves. From conception to the end of life, genes are coded to function in specific ways that determine growth and changes over the lifespan, but genes are not always active. Through biochemical processes collectively known as genetic imprinting, genes can be turned "on" or "off"—something like a light switch–or they can be "dimmed"—something like a light-switch dimmer. One imprinting process involves the addition of methyl groups to particular cytosine residues in DNA, a process called methylation. This is often a good thing. For example, during the early adolescent years, genetic imprinting permanently turns off certain growth genes so that the body stops growing taller; otherwise, a person would continue to grow taller and taller throughout life. A second example of imprinting involves silencing of many genes on one of the two X chromosomes in females at an early stage in development. This is so that females have approximately the same number of active genes on their two X chromosomes as males do on their one X. An interesting aspect of epigenetic research that has emerged in recent years is showing that life's events, positive or negative, can also influence genes being turned on or off. For example, prenatal exposure to alcohol has been found to result in unique DNA methylation changes in offspring, both in mice and humans (Laufer et al., 2015). Thus, although understanding of epigenetics is in its infancy, epigenetic research is helping to resolve the nature versus nurture debate. Environmental factors and experiences can indeed shape who people are and have profound consequences about how they live (Percy & Brown, 2011).

A Brief Review of Brain Plasticity

The term *brain plasticity* (or *neuroplasticity*) refers to changes in neural connections that occur in the brain when people learn new things or memorize new information (see Chapter 12). Using the brain in new and different ways causes it to create new "pathways" that did not previously exist. These changes can occur throughout life, which makes clear the importance of mental exercise at all life stages. Studies point to the involvement of epigenetic processes in these brain changes. For example, whereas DNA methylation (addition of methyl groups to DNA) is necessary to inhibit genes involved in memory suppression, DNA demethylation (removal of methyl groups from DNA) is important in activating genes whose expression is positively correlated with memory formation (Miller & Sweatt, 2007).

The next four main sections highlight different risk factors that cause or contribute to intellectual

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and developmental disabilities. The first three main sections deal with factors that are biomedical in nature, and the fourth deals with social, behavioral and educational risk factors.

BIOMEDICAL RISK FACTORS FOR INTELLECTUAL AND DEVELOPMENTAL DISABILITIES: INTRODUCTION

This risk factors introductory section explains why the developing fetus is particularly susceptible to damage by certain risk factors and provides an overview of biomedical risk factors.

Fetal Vulnerability

The developing fetus is particularly susceptible to damage at certain developmental stages (Table 13.1). Substances and agents that induce the production of physical deformities in the fetus, including the central nervous system, are called teratogens. See also Chapter 9.

Biomedical Risk Factors

Biomedical risk factors for intellectual and developmental disabilities, based on the AAIDD system for classifying risk factors, are presented in Table 13.2. Involvement of factors other than biomedical ones is difficult to substantiate. Hence, it is not surprising that factors identified from research studies are primarily biomedical in nature.

BIOMEDICAL RISK FACTORS FOR INTELLECTUAL AND DEVELOPMENTAL DISABILITIES: GENETIC CAUSES

This main section, which is divided into several subsections, provides details about the genetic basis of intellectual and developmental disabilities.

Table 13.1. Fetal vulnerability at different stages of development

Developmental stage[a]	Developmental features	Potential issues
Fertilization	Restoration of diploid number, establishment of sex, triggering of first cleavage division	
First week	Embryo is transported from site of fertilization to site of implantation in the uterus; formation of blastula	50%–70% of pregnancies end in spontaneous abortions within the first 2 weeks due to • Chromosomal abnormalities, which result in 60% of miscarriages • Failure of zygote to implant • Maternal immune response • Physical teratogens such as heat and ionizing radiation (e.g., x rays, gamma rays)
Second week	Embryo implants into lining of uterus; amniotic cavity and primitive yolk sac are formed	
Third through eighth weeks	Organogenesis—beginning of the development of body form	Chemical teratogens (e.g., alcohol) and maternal metabolic upsets (e.g., obesity, diabetes, thyroid malfunction) may produce major malformations.
Second trimester	Multiplication of neurons	
Third trimester to 18–24 months after birth	Brain growth spurt: glial cell multiplication, dendritic arborization, synaptogenesis, and myelination	The brain is very vulnerable to malnutrition, endogenous and environmental poisons, and hormonal imbalances; in utero effects of teratogens may include minor malformations and neurobehavioral and neurocognitive effects.

Sources: Brent (2004), Dobbing (1981), Guze (2005), D. Laslo personal communication (April 25, 1999), and Rice and Barone (2000).

[a]Pregnancy is measured from the start of a woman's last menstrual period. It usually lasts 40 weeks or about 9 calendar months. The first trimester lasts from 0 to 13 weeks, the second from 14 to 27 weeks, and the third from 28 to 40 weeks.

Table 13.2. Biomedical risk factors for intellectual and developmental disabilities

	Associated developmental period(s)		
Risk factor	Prenatal	Perinatal	Postnatal
Genetic	Chromosomal disorders (changes in number or structure)		
	Transmitted single gene defects (autosomal, X- or Y-linked)		
	De novo mutations (including known syndromes and nonsyndromic intellectual and developmental disabilities)		
	Copy number variants		
	Complex or multifactorial disorders		
	Mitochondrial disorders (defects in mitochondrial DNA)		
Health related	Maternal infections (e.g., cytomegalovirus, rubella, Zika virus)	Infections acquired from the mother during birth or shortly afterward (e.g., cytomegalovirus, herpesvirus types 1 and 2, HIV, streptococcus B)	Infections acquired after birth (e.g., whooping cough, measles, meningitis, HIV, influenza Haemophilus b)
	Maternal malnutrition from poor diet, including iodine deficiency	Malnutrition (e.g., resulting from poor quality or insufficient quantity of breast milk or infant formula)	Malnutrition (e.g., resulting from poor or inadequate diet)
	Maternal metabolic disorders (e.g., obesity, diabetes, thyroid dysfunction, phenylketonuria [PKU])		
	Traumatic brain injury (e.g., from physical assault, motor vehicle accidents, falls)	Traumatic brain injury (e.g., from birth complications, child battering, motor vehicle accidents, falls)	Traumatic brain injury (e.g., from child battering, motor vehicle accidents, accidents, falls)
	Maternal exposures to teratogens (e.g., alcohol, drugs)	Conditions resulting in lack of oxygen (asphyxia)	Stroke (mainly from sickle cell anemia) Brain tumors Conditions resulting in lack of oxygen
	Maternal exposures to toxins and toxic metals (e.g., lead, mercury, aluminum)	Exposures to toxins and toxic metals	Exposures to toxins and toxic metals
	Rh disease of the fetus	Prematurity for any reason	Seizure disorders
	Maternal stress	Caregiver stress	Caregiver stress
	Lack of prenatal screening for potentially treatable conditions (e.g., diabetes, thyroid disorders, Rh disease, maternal PKU)	Lack of neonatal screening for potentially treatable conditions (e.g., congenital hypothyroidism, PKU)	Lack of neonatal screening for potentially treatable conditions (e.g., congenital hypothyroidism, PKU)
	Parental age effects (refers to the statistical relationship between the age of a parent and effects on the child; see the chapter text for examples)		
	Abnormal maternal microbiome effects[a]	Abnormal maternal and/or infant microbiome effects[a]	Abnormal infant microbiome effects[a]

(continued)

Table 13.2. *(continued)*

	Associated developmental period(s)		
Risk factor	Prenatal	Perinatal	Postnatal
Congenital brain anomalies	Anencephaly, encephalocele, spina bifida (bifida occulta, meningocele, and myelomeningocele), lissencephaly, hydranencephaly		
Other	Consanguinity (having offspring from union to a second cousin or closer)		

Sources: American Association on Intellectual and Developmental Disabilities (2010), Percy (2007), and Percy and Brown (2011).

[a]The term *microbiome* refers to the collection of microorganisms that inhabit various places in or on one's body, primarily in the gut. The microbiome carries out various functions which are thought to be vital for human development, health, and survival. See text of this chapter as well as Chapters 9 and 11.

Overview

Genetic causes of intellectual and developmental disabilities are often subdivided into a number of different categories, as shown in Table 13.2. In 2004, approximately 7,500 different genetic disorders were known. As of 2015, more than 18,000 single-gene disorders had been identified. Of these, more than 6,000 are known to be heritable (i.e., passed down through generations; R. R. McInnes, personal communication, January 18, 2015). As of 2014, 450 genes were implicated in intellectual impairments and developmental disorders, with 400 attributed to syndromic intellectual impairments and developmental disorders and 50 to nonsyndromic intellectual impairments and developmental disorders (Srour & Shevell, 2014).

Variability of Expression of Genetic Disorders

Genetic disorders associated with intellectual and developmental disabilities are variable in their expression. For example, although some people with a given genetic disorder have intellectual impairments or developmental disorders, others do not. Noonan syndrome is an example of a common genetic disorder in which only approximately one third of affected children have mild intellectual disability (see Chapter 21). The reason a disorder can vary so much in the way it is expressed is thought to be the result of the nature and severity of the mutation causing the condition, effects of background genes (i.e., genes not carrying the abnormality that causes the genetic disorder but that modify the effects of the mutant gene), and other biomedical factors and differing life experiences (see Table 13.2).

The Most Common Genetic Disorders

Worldwide, the most common intellectual and developmental disabilities with a genetic basis are Down syndrome, 22q11.2 deletion syndrome (which includes previously identified syndromes such as DiGeorge syndrome and velocardiofacial syndrome; see Chapter 17), and fragile X syndrome (FXS). The estimated birth incidence of Down syndrome is between 1 in 1,000 and 1 in 100. The birth incidence of 22q11.2 deletion syndrome is approximately 1 in 2,000. One in 3,600 to 1 in 4,000 males and 1 in 4,000 to 1 in 6,000 females have FXS. Down syndrome is the most common etiology for intellectual disability resulting from an aberration of chromosome number. It is usually caused by the presence of an additional chromosome 21 and is referred to as trisomy 21 (i.e., having three copies of chromosome 21 instead of the usual two copies). Most cases of Down syndrome are not inherited and occur spontaneously without a family history. The birth incidence of Down syndrome increases markedly after a maternal age of 35 years (see Chapter 14). 22q11.2 deletion syndrome is a chromosomal disorder resulting from a missing piece of chromosome 22. Expression of this disorder is very variable and may include delayed growth and speech development and learning disabilities. Affected children are at risk of also having ADHD or ASD. Later in life, people with this syndrome are at increased risk of developing other mental health problems (see Chapter 17). FXS is the most common inherited etiology resulting in intellectual or developmental disability. FXS is an X-linked single gene disorder caused by unstable mutations in the FMR1 gene. Though both men and women can carry X chromosomes with FMR1 mutations, mutated FMR1 is

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transmitted only by females, and the mutations tend to get larger as they are passed on from one generation to the next. Males are affected more severely by FXS than females because they have only one X chromosome; females with FXS tend to be spared because they carry one normal X as well as the X with a mutation (see Chapter 15).

Inborn Errors of Metabolism

As of 2014, 89 potentially treatable genetic disorders called inborn errors of metabolism (i.e., genetic disorders in which the body cannot properly turn food into energy) had been identified (van Karnebeek, 2014). These disorders include phenylketonuria (PKU), galactosemia, Hunter syndrome, and Lesch-Nyhan syndrome (see Chapter 21). Effects of PKU can be prevented if this disorder is identified by genetic screening at birth and a special diet lacking in phenylalanine is adopted. Mothers who carry a PKU gene should adhere to a strict diet during pregnancy. Effects of galactosemia can be attenuated by adherence to a diet lacking in galactose. The U.S. Food and Drug Administration approved a treatment for Hunter syndrome that involves intravenous administration of the enzyme that is deficient in this disorder (da Silva, Strufaldi, Andriolo, & Silva, 2016). Quite a number of different disorders, including Hunter syndrome and Lesch-Nyhan syndrome, are being treated on an experimental basis with cord blood stem cell transplants.

Sex Chromosome Disorders and Imprinting Disorders

Turner syndrome and Klinefelter syndrome are disorders involving abnormalities in the number of sex chromosomes. These syndromes are sometimes, but not always, associated with mild intellectual impairment and physical anomalies (see Chapter 21).

Two very different but related genetic conditions resulting in intellectual impairment or developmental disorder are Prader-Willi syndrome and Angelman syndrome. These are both caused by small deletions in exactly the same region of chromosome 15 or by duplication of one chromosome 15 and loss of the other. Prader-Willi syndrome is often caused by deletions in the paternal chromosome 15 or by duplication of the maternal chromosome 15. Angelman syndrome is often caused by deletions in the maternal chromosome 15 or by duplication of the paternal chromosome 15 (see Chapter 21). (This parent of origin phenomenon arises because genes on chromosome 15 are expressed only if they have not been marked by the imprinting process; maternal and paternal chromosome 15s have different imprinting patterns.)

Other Disorders

Congenital hypothyroidism is a disorder resulting from thyroid hormone deficiency that is easily treated. This affects approximately 1 in 4,000 newborns in North America. Congenital hypothyroidism can result from genetic mutations or from iodine deficiency (see Chapter 21).

De novo single nucleotide mutations and loss of function mutations (i.e., small genetic changes not transmitted by parents that can occur in individuals with intellectual and developmental disabilities) have emerged as possible risk factors for moderate and severe levels of intellectual impairment (Hamdan et al., 2014) and ASD (Gamsiz et al., 2015). Copy number variants (CNVs) also are associated with intellectual disability and ASD (Kaminsky et al., 2011). CNVs are specific types of alteration in genomic DNA that result in the cell having an abnormal number of copies of a DNA segment equal to or greater in size than 1,000 base pairs. A CNV can refer to the addition or deletion of such a segment. These may be transmitted by parents or arise de novo. Because de novo mutations and CNVs are common in the general population, establishing that they are pathologically involved in intellectual disability or ASD, and how, remains challenging.

ASD has a prevalence that is an order of magnitude larger than Down syndrome. ASD is multifactorial, meaning that it is thought to result from a variety of factors. Suspected risk factors include complex genetic interactions, nutritional deficiencies (e.g., vitamin D deficiency) or overloads, pre- and postnatal exposure to chemicals or viruses, errors during the embryonic neural tube closure process, dysfunctional immune systems, a dysfunctional gut microbiome, maternal diabetes in the first 26 weeks of pregnancy, and even allergies (see Chapter 16). Furthermore, a number of different genetic disorders associated with features similar to those seen in ASD sometimes are incorrectly diagnosed as ASD. These include PKU, FXS, tuberous sclerosis, Williams syndrome, Prader-Willi and Angelman syndromes, Rett syndrome, and 22q11.2 deletion syndrome (see Chapter 21). In a recent analysis of U.S. medical records, counties with higher rates of

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genital deformities in newborn males had higher rates of ASD and intellectual disability. This highlights the possibility of congenital exposure to harmful environmental factors such as pesticides in both disorders (Rzhetsky et al., 2014).

Mitochondrial disorders resulting from mutations in mitochondrial DNA are not common. Overall, they affect approximately 1 in 5,000 individuals across all ages. Mutations can be maternally inherited (see previous discussion) or occur sporadically. Mutations in mitochondrial DNA often affect multiple organ systems that require a lot of energy (e.g., heart, brain, muscles). Two examples of mitochondrial disorders that affect brain function are myoclonic epilepsy with ragged-red fibers—a disorder affecting many parts of the body—and mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke syndrome—a progressive neurodegenerative disorder (Nussbaum et al., 2015).

Other Factors that Affect Genetic Causes of Disabilities

Two other factors that affect genetic causes of intellectual and developmental disabilities are ethnic origin and survival advantage. Ethnic origin may influence the chances of a child being affected by, or being a carrier of, a genetic disability. Disorders that have a high prevalence in certain ethnic groups, regardless of where individuals from those groups live now, result from probable common ancestry. This explains why there are many more people in these groups who carry a gene for the disorder than in the general population. This phenomenon is sometimes referred to as a founder effect. For example, there is a high frequency of Tay-Sachs disease (a fatal genetic disorder in which harmful quantities of a fatty substance called a ganglioside accumulate in the nerve cells of the brain) among Ashkenazic (central, northern, or eastern European) Jews but not among Sephardic (Spanish, Portuguese, or Middle Eastern) Jews. In contrast, PKU is mostly found in Caucasians and is rare in people of (or descended from) African or Asian ethnic groups. FXS is reported to be particularly common in Finland and in Quebec (Percy, 2007; Percy & Brown, 2011). Consanguineous parentage (i.e., union of closely related kin) increases the risk for conditions with autosomal recessive inheritance.

Survival advantage is a phenomenon associated with some recessive mutant genes. In such cases, mutant genes that are harmful when present in two copies have some survival advantage when only one copy has been inherited. Sickle-cell anemia (a condition in which red blood cells are sickle-shaped rather than round) and beta thalassemia (a disorder in which the body cannot make the beta chains of hemoglobin, the red cell protein that carries oxygen and carbon dioxide in the blood) are two recessive genetic disorders that are sometimes associated with intellectual and developmental disabilities and in which being the carrier of one mutant gene has an advantage. The trait for sickle-cell anemia, found in many people of African origin, is connected with a resistance to malaria; two sickle-cell genes result in the expression of anemia and resistance to malaria, whereas a carrier possessing a single sickle-cell gene is resistant to malaria and lacks the anemia. The trait of beta thalassemia, found in people of Mediterranean origin, similarly is connected with a resistance to malaria (Mount Sinai Hospital, 2013). Treatment for the anemia in both disorders requires blood transfusions, which leads to iron overload and organ failure if the body iron load is not normalized by treatment with drugs that remove iron from the body.

BIOMEDICAL RISK FACTORS FOR INTELLECTUAL AND DEVELOPMENTAL DISABILITIES: HEALTH-RELATED FACTORS

Numerous health-related factors are risk factors for intellectual and developmental disabilities (see Table 13.2). The following sections elaborate on some of these factors. Some of these factors are largely preventable.

Malnutrition

Malnutrition is suspected of being a cause of or contributing factor to intellectual impairment in a large proportion of affected individuals. Maternal malnutrition prior to conception may be the largest culprit. Although adults are remarkably resistant to the effects of malnutrition, the developing fetal brain is very susceptible. Protein-energy undernutrition and deficiencies of certain vitamins (e.g., folic acid, vitamin B_{12}, vitamin A) and minerals (e.g., iodide, iron, zinc) are problems not only in underdeveloped countries but in developed countries, including the United States and Canada (Bailey, West, & Black, 2015). As of 2010, one quarter of the world's population younger than 5 years of age was found to be

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underweight (UNICEF, 2010). About one in 12 newborns in the United States is underweight (March of Dimes Foundation, 2016). In North America, *underweight* is defined as having a birth weight of less than 2,500 grams (or 5.5 pounds). For couples planning pregnancy, there are many regional programs to address the challenge of how to prevent low birth weight infants (CDC, 2015; March of Dimes Foundation). The following subsections discuss several specific factors that contribute to malnutrition.

Protein-Energy Undernutrition Protein-energy undernutrition refers to a reduced protein intake over an extended period of time (Scheinfeld, 2015). This reduced intake eventually leads to depletion of the tissue protein reserve and lowering of blood protein levels, compromising proper function of nerve, muscle, and intellectual function. The latter may be irreversible if protein deprivation occurs during periods of brain development. Economic, social, and cultural factors (e.g., poor feeding habits, superstitions, belief in incorrect information about health and nutrition) all contribute to protein malnutrition in many countries. Infants and young children are very vulnerable. There are two disorders of protein-calorie malnutrition: marasmus and kwashiorkor (Scheinfeld, 2015). Which form develops depends upon the relative availability of nonprotein and protein sources of energy. In marasmus, there is severe deficiency of calories in the diet, including calories from protein. This results in severe growth failure and emaciation. Kwashiorkor results from premature abandonment from breast feeding, usually when a second child is born and replaces the first born at the mother's breast. Children with kwashiorkor have an odd reddish-orange color of the hair as well as a characteristic red skin rash. In kwashiorkor, the total calorie intake may be adequate but there is a deficiency of protein in the diet. Kwashiorkor often is associated with a maize-based diet. Protein-calorie malnutrition results in more severe infections than would occur in a state of adequate nutrition.

Folic Acid and Vitamin B_{12} Deficiencies Folate (or folacin) is a water-soluble B vitamin that all people need in order for their bodies to make new cells. A folic acid deficiency may result from low dietary intake of folic acid (eating the wrong foods) and/or as the result of one's genetic makeup. Folic acid deficiency is a risk factor for neural tube defects such as spina bifida (a birth defect in the bony encasement of the spinal cord) and anencephaly (a birth defect characterized by missing or a very reduced amount of brain tissue). Pregnant women (especially women who have diabetes, epilepsy, or a family history of neural tube defects) should take a daily folic acid supplement before and during pregnancy to reduce the risk of having an infant with a neural tube defect. The United States, Canada, and some other countries fortify grain products, such as bread and pasta, with folic acid. As of this writing in 2016, there is concern that excessive synthetic folic acid intake may be associated with certain adverse health effects. Folic acid supplementation masks and exacerbates effects of vitamin B_{12} deficiency. Prenatal folic acid supplement may be associated with an increased risk of unilateral neuroblastoma in a subset of the population homozygous for a particular variant of the dihydrofolate reductase gene. Finally, high maternal red cell folate in pregnancy has been associated with insulin resistance in offspring (Selhub & Rosenberg, 2016).

Vitamin B_{12} is a water-soluble vitamin found in animal products, including fish, meat, poultry, eggs, milk, and milk products. Vitamin B_{12} deficiency during pregnancy also is a risk factor for neural tube defects (Thompson, Cole, & Ray, 2009). Though confirmation is needed, it is prudent for women considering pregnancy to be B_{12} replete and have a serum value not below 300 nanograms per liter at the time of conception.

Vitamin A Deficiency and Excess Vitamin A (retinol) is a fat-soluble vitamin that is found mainly in fish liver oils, liver, egg yolks, butter, and cream. Vitamin A precursors (e.g., carotene) are found in green leafy and yellow vegetables. Vitamin A is crucial for normal nervous system development and is important for proper function of the immune system. Vitamin A deficiency (VAD) is the leading cause of preventable blindness in children and raises the risk of disease and death from severe infections accompanied by diarrhea and measles. In pregnant women, VAD causes night blindness and may increase the risk of maternal mortality. For pregnant women in high-risk areas, VAD can occur during the last trimester, when demand by both the unborn child and the mother is highest. VAD may also be associated with elevated mother-to-child transmission of human immunodeficiency virus (HIV). Secondary VAD results when vitamin A precursors cannot be converted into vitamin A; from problems with absorption, storage, or transport of vitamin A (as in celiac disease, a disorder

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resulting from intolerance to a protein called gluten that is found in wheat and many other grains); or from intestinal infections. VAD is a public health problem in 118 countries, especially in Africa and Southern and Eastern Asia. It is common in protein-energy malnutrition.

More of vitamin A is not necessarily better. Too much is toxic and can result in death. Women of child-bearing age need to be very careful. Women who are pregnant should carefully check the amount of vitamin A in their multivitamins and consult with their doctor to make sure the dose is safe.

Vitamin D Deficiency Vitamin D is a fat-soluble substance that is called a vitamin, although it is actually a prohormone. It is known as the "sunshine vitamin" because it is produced in the body as the result of mild sun exposure. It also is consumed in certain foods (e.g., fatty fish, fish oil) and supplements. Vitamin D sufficiency is essential for preventing rickets in children and for good bone health (National Institutes of Health, n.d.). Vitamin D deficiency is unusually common in people with intellectual and developmental disabilities, partly because of insufficient exposure to sunlight (Frighi et al., 2014). In addition to involvement in bone health, vitamin D deficiency is suspected of contributing to abnormal fetal development (Hart et al., 2015), to ASD (Fernell et al., 2015), and to a wide range of neurological and neuropsychiatric disorders (Dursun, 2010; Groves, McGrath, & Burne, 2014). Furthermore, there is evidence that the vitamin D system is regulated by epigenetic mechanisms and is important in maintenance of the epigenome (Fetahu, Höbaus, & Kállay, 2014). These issues must be addressed in prospective research studies, and the importance of maintaining vitamin D sufficiency must be communicated to professionals and the public.

Iodine Deficiency Iodine is a trace mineral used by the thyroid gland to produce the important thyroid hormone called thyroxine. Thyroid dysfunction resulting from iodine deficiency disorder is the single most common cause of preventable developmental disability and brain damage in the world; more than 54 countries are still iodine deficient (World Health Organization [WHO], 2015). In North America, salt is usually iodized. Nevertheless, in the United States, mild iodine deficiency may still be problematic (Stagnaro-Green, Dogo-Isonagie, Pearce, Spencer, & Gaba, 2015). Iodine deficiency is also still problematic in some other developed countries, such as Switzerland and Germany. Iodine deficiency in children can cause stunted growth; apathy; difficulty with movement, speech, and hearing; and intellectual impairment. Iodine deficiency in pregnant women causes miscarriages and stillbirths; if the fetus survives, severe maternal iodine deficiency retards fetal growth and brain development. Infants with iodine deficiency are usually given L-thyroxine for a week plus iodide to quickly restore a normal thyroid state. Iodide supplementation is then continued.

More iodine is not necessarily better. Chronic iodine toxicity results when iodine intake is 20 times greater than the daily requirement. Paradoxically, too much iodine can lead to hypothyroidism, as can too little (Vitti, 2014).

Iron Deficiency Iron, a trace metal that is essential for life, is absorbed in the intestines. It comes in two forms: heme iron (found in meats), which is well absorbed, and nonheme iron (found in leafy vegetables–e.g., spinach), which is not as well absorbed. Most of the consumed iron goes to form hemoglobin, the substance that helps red blood cells transport oxygen from the lungs to the rest of the body. The rest of the iron is stored for future needs and mobilized when dietary intake is inadequate. Because iron also plays a key role in helping to prepare the immune system to do its job, a deficiency may lead to colds. Low iron levels can also cause fatigue, pallor, and listlessness—hallmarks of anemia.

Iron deficiency affects more than 2 billion people in the world; 30% of the population is anemic. In developing countries, approximately 50% of pregnant women and 40% of children are iron deficient (WHO, 2015). Iron deficiency anemia during the third trimester of fetal development affects one third of the pregnancies in the United States and has been associated with adverse postnatal behavioral outcomes. Complications of iron deficiency anemia in infants and children include developmental delays; behavior disturbances such as decreased motor activity, social interaction, and attention to tasks; compulsive eating of nonfood items (pica) and ice; and irreversible impairment of learning ability. In adults, iron deficiency anemia can result in a low capacity to perform physically demanding labor. Iron deficiency anemia also contributes to lead poisoning in children by increasing the gastrointestinal tract's ability to absorb heavy metals, including lead. (A common source of lead overload is exposure to dust from lead-based paint in old houses.) Iron deficiency anemia is

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associated with conditions that may independently affect infant and child development. Iron deficiency during pregnancy contributes to maternal mortality and fetus/infant mortality in the perinatal period. During the first two trimesters of pregnancy, it is associated with increased risk for preterm delivery and for delivering a low birth weight infant.

Iron deficiency can result from poor diet (e.g., a poor vegetarian diet), parasitic diseases (e.g., from worm and malaria infections), and abnormal uterine bleeding. Iron therapy in anemic children can often, but not always, improve behavior and cognitive performance, lead to normal growth, and hinder infections. Researchers at Guelph University in Canada created replicas of a small river fish—associated with luck in village folklore—to be put into iron cooking pots. When put into cooking pots in a village in Cambodia, these fish supplied up to 75% of the daily iron requirement and resulted in an enormous decrease in anemia, dizziness, and headaches in village women (Dalal, 2014). Of note, however, is that excessive iron can be damaging. Too much supplemental iron in a malnourished child or in people from certain ethnic backgrounds promotes fatal infections, because the excess iron is available for pathogen use. Also, excessive body iron resulting from excessive iron therapy, repeated blood transfusions, or iron overload resulting from a genetic condition called hemochromatosis is problematic (Moalem, Weinberg, & Percy, 2004).

Toxic Threats

Toxic threats to a child's environment during prenatal, neonatal, or postnatal development can have adverse outcomes ranging from severe intellectual impairment or developmental delay to more subtle changes, such as problems with attention, memory, learning, social behavior, and intellectual ability, depending on timing and dose of the toxic threat. Furthermore, infants and children have unique patterns of exposure and special vulnerabilities to pesticides (Landrigan, Kimmel, Correa, & Eskenazi, 2004). Toxic threats include exposures to methylmercury, polychlorinated biphenyls (PCBs), ethanol, lead, arsenic, toluene, manganese, fluoride, chlorpyrifos (a pesticide), tetrachloroethylene (PERC), polybrominated diphenyl ethers (PBDEs), and dichlorodiphenyltrichloroethane (DDT/DDE) (Grandjean & Landrigan, 2014). Additional toxic threats include exposures to aluminum, dioxins, ionizing radiation (i.e., x rays, gamma rays), and environmental tobacco smoke, as well as maternal use of alcohol, tobacco, marijuana, and cocaine. Other exposures suspected of being a threat include maternal consumption of antidepressants and antianxiety drugs and maternal exposure to dental x rays (Percy & Brown, 2011). By learning about different types of toxic threats and their sources, by taking efforts to avoid them, and by promoting hand washing and good dietary habits, parents and caregivers can play an important role in reducing exposures to toxicants present in consumer products. Many places are undertaking initiatives to reduce sources of toxic threats in the environment. (For more information, see Hamblin [2014], Mercola [2008, 2010], and Winneke [2011].)

Maternal Metabolic Effects

Certain metabolic abnormalities in the mother may have harmful effects on the developing fetus. Such effects are called gestational programming (Ross & Desai, 2005). Examples are described in the following subsections.

Maternal Obesity and Diabetes Being overweight during pregnancy is associated with a greatly increased risk of neural tube defects such as spina bifida and anencephaly (Stothard, Tennant, Bell, & Rankin, 2009). Obesity is becoming a worldwide epidemic. Associated with obesity is the occurrence of type 2 diabetes, a disorder in which the level of blood sugar is excessively high. Some women have diabetes before they become pregnant. Others develop it during pregnancy, a form called gestational diabetes. About 3% of pregnant women have problems with their blood sugar. Presently, it is not clear whether it is obesity or high blood sugar that results in the neural tube defects. Infants born to mothers with diabetes tend to be very large. This poses risks to their health and to the mothers, who may require delivery by caesarean section. Furthermore, infants born to diabetic mothers may have cognitive dysfunction and also develop diabetes themselves. Maternal diabetes diagnosed at 26 weeks of gestation or earlier was recently established as a significant risk factor for ASD (Xiang et al., 2015). It is very important that pregnant women control their blood sugar levels.

Abnormal Thyroid Function Abnormal thyroid function in a pregnant mother, in the fetus, or in the newborn all have repercussions on neuropsychological development. There are three sets of clinical thyroid disorders that affect fetal development:

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those that affect the infant only, those that affect only the maternal thyroid gland, and iodine deficiency that affects maternal and fetal thyroid function. Hypothyroidism (a condition in which the thyroid does not make enough thyroid hormone) in pregnant women is associated with an increased risk of miscarriage, preeclampsia (i.e., high blood pressure sometimes with fluid retention and loss of protein in the urine), abruptio placentae (premature separation of the placenta from the uterus), low birth weight infants, still births, and fetal distress in labor. Children born to mothers with untreated hypothyroidism during pregnancy score lower on IQ tests than children of healthy mothers. Thus, it is important for pregnant mothers with hypothyroidism to be adequately treated during their pregnancies. Congenital hypothyroidism of the fetus affects approximately 1 in 4,000 newborn infants, resulting in permanent developmental delay and growth defects (see Chapter 21). In the United States, Canada, and other developed countries, newborns are screened for hypothyroidism and are given early thyroid replacement therapy, when necessary, to prevent severe intellectual and developmental disabilities. Causes of this congenital hypothyroidism can be genetic or environmental (e.g., caused by iodine deficiency). (For more information, see Gruters & Krude, 2012, & LaFranchi, 2016.)

Maternal Stress

Prospective studies have revealed that a mother's depression, anxiety, or emotional stress while pregnant increases the risk for her child having adverse outcomes that include emotional problems, symptoms of ADHD, ASD, or impaired cognitive development. Based upon information from animal models, the mechanisms underlying these changes are being explored (Glover, 2015).

Infections

Infections with various microorganisms and viruses are known to be causal or contributing factors for intellectual and developmental disabilities. This subsection provides some detail about such risk factors, including human immunodeficiency virus (HIV) and Zika virus.

Intrauterine and Perinatal Infections The acronym TORCH stands for toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus, and herpesvirus infections. These infections used to cause a large percentage of intellectual impairments and developmental disorders in children (Stegman & Carey, 2002). However, with the availability of improved vaccines, prevention methods, and early identification, these infections in many instances can now be prevented or treated early enough to prevent damage to the central nervous system of the fetus. The application of antibiotics to cut umbilical cords prevents much newborn infection. However, there has been an unfortunate resurgence of some vaccine–preventable diseases in North America because some families deliberately refuse vaccination. New challenges also include pediatric HIV, and perinatal bacterial infections with Group B *streptococcus* and *Listeria monocytogenes*. There is also concern that unidentified multiple organisms causing bacterial vaginal infections may be causing intellectual and developmental disabilities in some children (Smith, 2014).

Human Immunodeficiency Virus Infection Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate fluid, or breast milk. It is spread mostly through unprotected sexual contact. Mother-to-child transmission of HIV occurs when an HIV-positive mother passes the virus to her child during pregnancy, labor, delivery, or breastfeeding. New HIV infections among children have declined by 50% worldwide since 2010 (UNAIDS, 2016). This has resulted because of effective voluntary testing and counseling services, access to antiretroviral therapy, safer delivery practices, and the widespread availability and safer use of breast milk substitutes, especially in the developed world. However, there are unique challenges in the developing world—HIV infection is rampant, especially among teenagers, and many people are not aware that they are infected. Also, there are many barriers that need to be overcome with respect to HIV prevention and treatment. One is the very high cost of antiretroviral drugs; a second is lack of health infrastructure to effectively provide essential public health services (Maartens, Celum, & Lewin, 2014).

Zika Virus In April, 2016, the CDC declared prenatal infection with Zika virus, carried by a particular type of mosquito, to be a teratogen causing microcephaly as well as other serious neurological

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diseases (Rasmussen, Jamieson, Honein, & Petersen, 2016; see also Chapter 9). First identified in Brazil early in 2015, the virus has spread rapidly throughout the Americas. Efforts are being mounted to find ways of preventing adverse outcomes especially from virus infection during pregnancy.

Rh Disease in the Newborn

Rh factor is an inherited protein found on the surface of red blood cells. Most people have this protein (i.e., they are Rh positive), but some do not (i.e., they are Rh negative). Rh-negative pregnant women who carry an Rh-positive infant sometimes become sensitized to Rh protein and make antibodies to the Rh protein that destroy fetal red blood cells. Rh disease was once a leading cause of fetal and newborn death as well as of intellectual disability. Fortunately, Rh disease can be prevented by giving mothers a purified blood product called Rh immune globulin (RhIG) to prevent sensitization. These shots are given to the mother at 28 weeks of pregnancy and again within 72 hours of giving birth if a blood test shows that her infant is Rh positive (March of Dimes Foundation, 2016).

Preterm Delivery and Low Birth Weight

Preterm delivery (birth occurring before 36 weeks of gestation) is associated with increased risk for intellectual impairment or developmental delay. The more premature or underweight the newborn, the greater the risks of illness (e.g., infection, respiratory distress), impairments such as cerebral palsy and learning problems, hearing and vision problems, and death. Factors that predispose to prematurity are multiple births, regardless of the cause, placental failure, and excess amniotic fluid. Preterm delivery is known to place the immature brain at risk of hemorrhage, which can result in tissue damage. Low birth weight is also associated with increased risk for intellectual impairment or developmental delay, even if an infant is full term. The frequency of preterm and low birth weight infants is increasing in North America. This increased frequency may, in part, be related to the use of in vitro fertilization and/or to women having children at a later age than in previous decades (Jarjour, 2015).

Premature Cutting of the Umbilical Cord

For more than 200 years, there has been an awareness that the umbilical cord should be cut after the infant has drawn its first breath and after the cord stops pulsating. However, since 1980, cords are often clamped as soon as possible after birth or following delivery of the fetal head in order to obtain cord blood samples for diagnosis of asphyxia. There is increasing support for delayed cord clamping because it increases the baby's hemoglobin levels and iron stores, thereby countering anemia, which can result in altered behavioral and neural development. Such consequences are considered beneficial as long as an infant does not have severe, untreated jaundice. Severe, untreated jaundice can result in permanent brain damage called kernicterus. Jaundice in newborns is treated by phototherapy (i.e., exposure to ultraviolet light) (McDonald, Middleton, Dowswell, & Morris, 2013).

Advanced Parental Age

Studies of parental age are providing new information about factors that cause or contribute to intellectual and developmental disabilities and to ASD. Trisomy 21, 13, and 18 are three syndromes associated with intellectual and developmental disabilities that increase in frequency with increasing maternal age as the result of mistakes in cell division that occur during the time of conception. General cognitive impairment also is associated with advanced maternal age (Cohen, 2014). Evidence from multiple sources supports the hypothesis that paternal and maternal advancing age are risk factors for ASD but that different mechanisms are involved. Higher rates of de novo mutations in older fathers may account for the paternal effect, but the mechanism underlying the maternal effect is different (Lee & McGrath, 2015). However, it should be noted that ASD is considered to be a multifactorial and heterogeneous disorder and that factors as esoteric as the gut microbiome may be involved in affected individuals.

Brain Injury

As detailed in Table 13.2, brain injury can result from various factors. Brain injury resulting from head injury is a common cause of intellectual disability and cerebral palsy. Many circumstances can lead to head injury, including falls; child battering; bicycle, scooter, and sports accidents; accidents with guns, and car accidents. Surveillance and intervention activities could prevent many cases of brain injury.

SOCIAL, BEHAVIORAL, AND EDUCATIONAL RISK FACTORS FOR INTELLECTUAL AND DEVELOPMENTAL DISABILITIES

Biomedical factors are important in the etiology of intellectual and developmental disabilities; however, they do not always act alone. Various other factors can interact with such factors or independently of them over the lifetime of individuals and even act across generations (AAIDD, 2010; Emerson, 2010). By understanding intergenerational causes, appropriate supports can be used to prevent and reverse the effects of risk factors. Some examples of social, behavioral, and educational risk factors contributing to intellectual and developmental disabilities are given in Table 13.3.

Table 13.3. Examples of social, behavioral, and educational risk factors for intellectual and developmental disabilities

	Associated developmental period(s)		
Etiological classification	Prenatal	Perinatal	Postnatal
Social	Adverse family social interactions • Negative or stressful interactions with spouse/ partner, children, other family, friends, or caregivers • Social isolation • Low socioeconomic status	Adverse family social interactions (same as for prenatal)	Adverse family social interactions (same as for perinatal)
	Lack of access to health care • No insurance • Lack of a regular health care provider • Travel to health care services is difficult	Lack of access to health care (same as for prenatal)	Lack of access to health care (same as for perinatal)
	Parental neglect • Family poverty	Parental neglect • Family poverty • Leaving a baby unattended	Parental neglect • Family poverty • Leaving a baby unattended • Inadequate stimulation • Institutionalization
Behavioral	Behaviors that adversely affect functioning • Parental alcohol and drug abuse • Parental smoking • Parental immaturity	Behaviors that adversely affect functioning • Parental rejection of caregiving • Parental abandonment of child • Child abuse and neglect • Domestic violence • Inadequate safety measures • Social deprivation • Difficult child behaviors • Institutionalization	Behaviors that adversely affect functioning (same as for perinatal)
Educational	Lack of access to educational experiences • No or poor information about good prenatal care	Lack of access to educational experiences • No or poor information about good neonatal care and parenting • No information about family support services	Lack of access to educational experiences • No information about good postnatal care and parenting • No information about family support services • No information about educational supports • No knowledge of developmental milestones

Sources: American Association on Intellectual and Developmental Disabilities (2010) and Kaderavek (2014).

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The following examples illustrate how sociological, behavioral, and educational factors are involved in intellectual and developmental disabilities. We have discussed how certain prenatal and genetic risk factors can result in the emergence of intellectual and developmental disabilities. Of importance, research has shown that the developmental trajectories of children with an early diagnosis of intellectual and developmental disabilities can be altered by a favorable early environment (e.g., positive interactions with their mothers) and that such interactions can promote resilience (i.e., ability to cope with stress and adversity) (Fenning & Baker, 2012).

It is known that parents do much more than ensure that their offspring are adequately nourished and sheltered. Deprivation and neglect from living in an orphanage can result in odd behaviors, delayed language, and various other challenges, including intellectual and developmental disabilities. However, children who are placed into foster care or adopted by about age 2 are more likely to grow up with "typical brains" than those who are not (Marshall, 2015; Powell, 2010; Sheridan, Drury, McLaughlin, & Almas, 2010).

ASD is a neurodevelopmental disorder characterized by impaired social interaction, impaired verbal and nonverbal communication, and restricted and repetitive behavior that may or may not be associated with intellectual disability. There is evidence that early intensive behavior intervention is beneficial for some young children with ASD and has positive effects on the clinical manifestations compared to other interventions available in the community (Reichow, Bartin, Boyd, & Hume, 2014).

Advanced maternal age and chromosomal nondisjunction are known risk factors for having a child with Down syndrome. Meiosis I is responsible for approximately 77% and meiosis II for 23% of maternal nondisjunction, but why this happens is not clear. Hunter et al. (2013) found that low socioeconomic status is significantly associated with chromosome 21 nondisjunction occurring during meiosis II in mothers of children with Down syndrome, independently of their age. Further studies are needed to explore which aspects of low maternal socioeconomic status, such as environmental exposures or poor nutrition, may account for these results.

CO-OCCURRENCE OF SENSORY IMPAIRMENTS, CHALLENGING BEHAVIORS, AND MENTAL HEALTH DISORDERS IN PEOPLE WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES

Sensory impairments (impairments in vision or hearing), challenging behaviors, and mental health disorders are unusually common in people with intellectual and developmental disabilities. Because sensory impairments are underrecognized among people with intellectual and developmental disabilities, changes in behavior or challenging behaviors are often attributed to the intellectual impairment or to mental health disorders rather than to sensory impairment and resulting communication difficulties. Sensory impairments and challenging behaviors exacerbate one another. Because sensory impairments limit sensory stimulation, learning opportunities, and social interaction, they can result in underdevelopment of learning and brain activity. In turn, this can lead to more challenging behavior. To provide the best quality of life, it is imperative that hearing and vision be evaluated at as early an age as possible and at regular intervals throughout life and that appropriate supports are provided.

Co-occurring Sensory Impairments and Intellectual and Developmental Disabilities

The prevalence of sensory impairments (visual and hearing) is much greater in adults with intellectual and developmental disabilities than in the general population. The prevalence of hearing loss is approximately 1 in 1,000 in the general population and is about 40 times higher in people with intellectual and developmental disabilities. The prevalence of visual impairment is approximately 0.5%–2% in the general population and at least 8.5 times higher in people with intellectual and developmental disabilities. Comorbidity (i.e., the presence of both) of hearing and vision impairment also is more common in people with intellectual and developmental disabilities. The frequency of sensory impairments increases with severity of intellectual impairment and increasing age (Kiani & Miller, 2010).

Vision loss in people with intellectual and developmental disabilities may be congenital, arise

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Table 13.4. Factors resulting in vision loss in people with intellectual and developmental disabilities

Time of onset	Factor
Congenital (genetic in nature)	Down syndrome (predisposes to early age cataracts and later onset vision problems)
	Inborn errors of metabolism (e.g., mucopolysaccharidoses)
	Other specific syndromes (e.g., Leber congenital amaurosis, Batten disease, Bardet-Biedel syndrome)
Pregnancy or at birth (acquired)	Intrauterine infection (e.g., rubella, cytomegalovirus, syphilis, toxoplasmosis, herpes)
	Fetal alcohol spectrum disorder (associated with anatomical abnormalities of the eye and various vision problems)
	Asphyxia
	Prematurity (e.g., resulting in cerebral hemorrhage, resulting in the need for artificial respiration)
Later onset ophthalmological problems (acquired)	Self-injurious behavior, directed at or near the eyes
	Advanced age
Later onset cerebral conditions (acquired)	Meningitis
	Significant head trauma
	Brain tumor
	Asphyxia by near drowning or near sudden infant death

From the Rehabilitation Research and Training Center on Developmental Disabilities and Health (RRTCDD). (2015b). *Visual Impairment.* Retrieved from http://www.rrtcadd.org/resources/Resources/Topics-of-Interest/Health-Promotion/visual-imp.PDF, p. V7; adapted by permission. For additional resources, please visit the Rehabilitation Research and Training Center on Developmental Disabilities and Health (www.RRTCDD.org).

during pregnancy or birth, or stem from later onset ophthalmological problems or cerebral conditions (Table 13.4). Similarly, hearing loss may be congenital, arise during pregnancy or birth, or be of later onset (Rehabilitation Research and Training Center on Developmental Disabilities and Health, 2015a).

At least 50% of cases of congenital hearing loss are caused by genetic disorders, which are primarily a result of inheriting recessive genes (Kiani & Miller, 2010). Congenital hearing loss is associated with procreation within a close family network, poverty, and inadequate access to health care and immunization in the general population. Cytomegalovirus infection plays a major role in acquired hearing loss (Deltenre & Van Maldergem, 2013). In Down syndrome, structural anomalies of sensory organs are common (e.g., narrow ear canals, keratoconus—a degenerative disorder of the eye in which structural changes within the cornea cause it to thin and change to a more conical shape than the more normal gradual curve), and sensory impairments may occur several decades earlier than in the general population (Kiani & Miller, 2010; see also Chapters 14 and 49). Certain syndromes or conditions are associated with intellectual and developmental disabilities and combined hearing and vision loss. These include prematurity, congenital rubella syndrome, meningoencephalitis, and Usher syndrome, among others. (For information about Usher syndrome, see Mathur & Yang, 2015.) Many individuals with congenital deafblindness have some degree of intellectual impairment.

Co-occurring Challenging Behaviors, Mental Health Disorders, and Intellectual and Developmental Disabilities

The prevalence of challenging behaviors, including mental health disorders, is three to four times more common in people with intellectual and developmental disabilities than in the general population. People with ASD, severe disabilities, and sensory impairments and communication disorders are more likely to demonstrate these behaviors. Moreover, as mentioned earlier, quite a number of genetic disorders are associated with behaviors resembling those seen in individuals with ASD. People with intellectual and developmental disabilities also are at increased risk of having comorbid mental health disorders, including ADHD, schizophrenia, depression, and bipolar disorder. As already noted, sensory impairments can exacerbate challenging behaviors and mental health disorders. Because challenging behaviors often serve as a form of communication, efforts should be made to identify the cause of these and implement supports

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to subdue them (see Chapter 23). Ideally, a sensory impairment team, care pathway, and clinical network should be developed within every disability support service to work across the professional and organizational boundaries and in close collaboration with audiology and ophthalmology services (Kiani & Miller, 2010).

INTELLECTUAL AND DEVELOPMENTAL DISABILITIES AND PREVENTION

Since the mid-1980s, advances in research and public education endeavors have reduced the incidence of intellectual and developmental disabilities (The Arc, n.d.). In particular, newborn screening programs have prevented the development of intellectual impairment and developmental disorder from PKU, congenital hypothyroidism, and other causes by early and appropriate therapy. Rh disease resulting in severe jaundice in the newborn has been prevented by the use of anti-RhIG in the mother. Immunization programs can reduce intellectual impairment or developmental delay resulting from infectious causes. For example, vaccination programs in young children have prevented many cases of *Haemophilus influenzae* type b, measles, encephalitis, and rubella (German measles). Other interventions also reduce occurrences of intellectual impairment or developmental disorders (Percy & Brown, 2011); examples follow.

- Having access to early comprehensive prenatal care and preventive measures prior to and during pregnancy increases a woman's chances of not having a child with intellectual impairment or developmental disorders.
- Counseling women with PKU to use a restricted phenylalanine diet for 3 months prior to pregnancy and during pregnancy prevents intellectual impairment or developmental disorders in their infants.
- Removal of lead from the environment reduces the chances of brain damage in children.
- Safe storage of toxins prevents accidental exposures.
- Use of child safety seats, bicycle helmets, and sports helmets reduces occurrences of head trauma in children.
- Installation of pool fencing prevents asphyxia from near drowning.
- Measures to avoid drunk driving help prevent accidents that result in brain injury and intellectual impairment.
- Enrolling high-risk infants and toddlers into early intervention programs has positive effects on intellectual functioning.
- Identifying children's special educational needs and providing appropriate supports and services helps enable them to develop to their full potential.

For more information, see chapters for specific disorders (e.g., Chapters 14–20) as well as ones with broader perspectives (e.g., Chapters 21, 33, and 34).

SUMMARY

Since 2000, tremendous technical advances have been made with respect to the ability and feasibility of detecting abnormalities in DNA of individuals. In particular, complete sequencing of genomic DNA is becoming economically as well as practically feasible. This latter technique is leading to new information about the involvement of genetic mutations in intellectual and developmental disabilities and ASD and to new strategies for obtaining a genetic diagnosis (Ellison, Rosenfeld, & Shaffer, 2013). New approaches are being developed to determine whether new mutations are pathologically associated with particular disorders (Xiong et al., 2015). The recognition that life experiences and different bacteria in the gut (i.e., the microbiome), via epigenetic mechanisms, can modify brain function as well as infant development in positive and negative ways has created awareness of the probable complexity of the mechanisms that cause variation in intellectual and developmental disability phenotypes (see Chapters 11 and 23). The potential involvement of vitamin D deficiency in intellectual and developmental disabilities and associated mental disorders warrants particular attention. Also, insights about what aspects of cognitive function and behavior are genetic and what are not also are coming from comparison studies of "identical" twins (who were once thought to be exact genetic photocopies of one another but are not) and of fraternal twins (whose genes are different but upbringings are very similar). Because epigenetic processes are potentially

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reversible and theoretically amenable to manipulation, there is optimism that changes in lifestyle and environment (including physical exercise, social activity, and exercises to develop brain function), and also new forms of pharmacological intervention directed at modification of epigenetic processes, may be fruitful avenues for intervention in intellectual and developmental disorders and certain disorders of mental health. Finally, much can be learned about risk factors for intellectual and developmental disabilities from detailed longitudinal studies of individuals in families including the prenatal, neonatal, and postnatal stages of development as well as the transition to adulthood and aging.

FOR FURTHER THOUGHT AND DISCUSSION

1. What can be done to target and educate prospective mothers about the dangers of folic acid and vitamin B_{12} deficiencies, drinking, smoking, preterm birth, low birth weight infants, as well as other preventable causes of developmental disabilities?
2. What actions might be taken to curb brain injury due to drunk driving, accidental falls, and child battering?
3. What actions might policy makers take to ensure that health professionals are appropriately paid for providing services to people with intellectual and developmental disabilities?
4. What strategies should be undertaken to create awareness of toxic threats to the health of infants and children?

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