NCC Pediatrics Continuity Clinic Curriculum:
Down Syndrome for the PCM
Faculty Guide

Goals & Objectives: *To manage healthcare of a child with Down Syndrome from birth to adolescence and, then, transition to adult care.*

- Recognize and identify principle features of Down Syndrome.
- Anticipate common medical and behavioral issues associated with Down Syndrome.
- Know the recommended screenings and interventions at different ages.
- Understand the AAP and the Special Olympics guidelines for Atlantoaxial Instability.

Pre-Meeting Preparation:

Please read the following enclosures:

- Smith's Patterns of Human Malformation (Chapter 1)
- "Health Supervision for Children with Down Syndrome" *(Pediatrics, 2011)*
- "Atlantoaxial Instability" *(Peds-in-Review, In Brief, 2003)*

Conference Agenda:

- *Review* Down Syndrome Quiz
- Complete Down Syndrome Cases

Post-Conference: *Board Review Q&A*

Additional Resources:

- National Down Syndrome Society Website
- "Clinical Report— Supporting the Health Care Transition from Adolescence to Adulthood in the Medical Home" *(Pediatrics, 2011)*
- *"Growth Charts for Children with Down Syndrome"* Zemel et al. *Pediatrics,* Vol 136:5. Nov 2015

1 Recognizable Patterns of Malformation

A Chromosomal Abnormality Syndromes

DOWN SYNDROME
(TRISOMY 21 SYNDROME)

Hypotonia, Flat Facies, Slanted Palpebral Fissures, Small Ears

Down's report of 1866 on the ethnic classification of idiots stated that a "large number of congenital idiots are typical Mongols," and he set forth the clinical description of the Down syndrome. The textbook by Penrose and Smith provides an overall appraisal of this disorder that has an incidence of 1 in 660 newborns, making it the most common pattern of malformation in man.

ABNORMALITIES

General. Hypotonia with tendency to keep mouth open and protrude the tongue, diastasis recti, hyperflexibility of joints, relatively small stature with awkward gait, increased weight in adolescence.

Central Nervous System. Mental deficiency.

Craniofacial. Brachycephaly with relatively flat occiput and tendency toward midline parietal hair whorl; mild microcephaly with upslanting palpebral fissures; thin cranium with late closure of fontanels; hypoplasia to aplasia of frontal sinuses, short hard palate; small nose with low nasal bridge and tendency to have inner epicanthal folds.

Eyes. Speckling of iris (Brushfield spots) with peripheral hypoplasia of iris; fine lens opacities by slit lamp examination (59%); refractive error, mostly myopia (70%); nystagmus (35%); strabismus (45%); blocked tear duct (20%); acquired cataracts in adults (30% to 60%).

Ears. Small; overfolding of angulated upper helix; sometimes prominent; small or absent earlobes; hearing loss (66%) of conductive, mixed, or sensorineural type; fluid accumulation in middle ear (60% to 80%).

Dentition. Hypoplasia, irregular placement, fewer caries than usual. Periodontal disease.

Neck. Appears short.

Hands. Relatively short metacarpals and phalanges; fifth finger: hypoplasia of midphalanx of fifth finger (60%) with clinodactyly (50%), a single crease (40%), or both; simian crease (45%); distal position of palmar axial triradius (84%); ulnar loop dermal ridge pattern on all digits (35%).

Feet. Wide gap between first and second toes, plantar crease between first and second toes, open field dermal ridge patterning in hallucal area of sole (50%).

Pelvis. Hypoplasia with outward lateral flare of iliac wings and shallow acetabular angle.

Cardiac. Anomaly in approximately 40%; endocardial cushion defect, ventricular septal defect, patent ductus arteriosus, auricular septal defect, and aberrant subclavian artery, in decreasing order of frequency; mitral valve prolapse with or without tricuspid valve prolapse and aortic regurgitation by 20 years of age; risk for regurgitation occurs after 18 years of age.

Skin. Loose folds in posterior neck (infancy); cutis marmorata, especially in extremities (43%); dry, hyperkeratotic skin with time (75%);

infections in the perigenital area, buttocks, and thighs that begin as follicular pustules in 50% to 60% of adolescents.

Hair. Fine, soft, and often sparse; straight pubic hair at adolescence.

Genitalia. Relatively small penis and decreased testicular volume; primary gonadal deficiency is common, is progressive from birth to adolescence, and is definitely present in adults; although fertility has rarely been reported in females, no male has reproduced.

OCCASIONAL ABNORMALITIES.

Seizures (less than 9%); keratoconus (6%); congenital cataract (3%); low placement of ears; webbed neck; two ossification centers in manubrium sterni; funnel or pigeon breast; tracheal stenosis with hourglass trachea and midtracheal absence of tracheal pars membranacea; gastrointestinal tract anomalies (12%) including tracheoesophageal fistula; duodenal atresia; omphalocele, pyloric stenosis, annular pancreas, Hirschsprung disease, and imperforate anus. Incomplete fusion of vertebral arches of lower spine (37%); only 11 ribs; atlantoaxial instability (12%); posterior occipitoatlantal hypermobility (8.5%); abnormal odontoid process (6%); hypoplastic posterior arch C1 (26%). Hip abnormality (8%) including dysplasia, dislocation, avascular necrosis, or slipped capital femoral epiphyses; syndactyly of second and third toes; prune belly anomaly. The incidence of leukemia is approximately 1 in 95, or close to 1%. Thyroid disorders are more common, including athyreosis, simple goiter, and hyperthyroidism. Fatal perinatal liver disease has been reported.

PRINCIPAL FEATURES IN THE NEONATE.

The diagnosis can generally be made shortly after birth, and therefore, the following ten features of Down syndrome in the neonate are presented as set forth by Hall, who found at least four of these abnormalities in all of 48 neonates with Down syndrome and six or more in 89% of them.

Hypotonia	80%
Poor Moro reflex	85%
Hyperflexibility of joints	80%
Excess skin on back of neck	80%
Flat facial profile	90%
Slanted palpebral fissures	80%
Anomalous auricles	60%
Dysplasia of pelvis	70%
Dysplasia of midphalanx of fifth finger	60%
Simian crease	45%

NATURAL HISTORY.

Muscle tone tends to improve with age, whereas the rate of developmental progress slows with age. For example, 23% of a group of Down syndrome children under 3 years had a developmental quotient above 50, whereas none of those in the 3- to 9-year group had intelligence quotients above 50. Though the IQ range is generally said to be 25 to 50 with an occasional individual above 50, the mean IQ for older patients is 24. Fortunately, social performance is usually beyond that expected for mental age, averaging 3⅓ years above mental age for the older individuals. Generally "good babies" and happy children, individuals with Down syndrome tend toward mimicry, are friendly, have a good sense of rhythm, and enjoy music. Mischievousness and obstinacy may also be characteristics, and 13% have serious emotional problems. Coordination is often poor, and the voice tends to be harsh. Early developmental enrichment programs for Down syndrome children have resulted in improved rate of progress during the first 4 to 5 years of life. Whether such training programs will appreciably alter the ultimate level of performance remains to be determined.

Sleep-related upper airway obstruction occurs in approximately one third of cases.

Growth is relatively slow, and during the first 8 years, secondary centers of ossification are often late in development. However, during later childhood, the osseous maturation is more "normal," and final height is usually attained around 15 years of age. Adolescent sexual development is usually somewhat less complete than normal. Because thyroid dysfunction is common and can be easily missed, periodic thyroid function studies should be performed.

The median age at death increased from 25 years in 1983 to 49 years in 1997. The major cause for early mortality is congenital heart defects. Mortality from respiratory disease, mainly pneumonia, as well as other infectious diseases is much higher than in the general population. Although leukemia has frequently appeared on death certificates of affected individuals, other neoplasms were listed less than one-tenth as often as expected. Low-grade problems that occur frequently are chronic rhinitis, conjunctivitis, and periodontal disease, none of which are easy to "cure." Immunologic dysfunction including both T-cell and B-cell derangement, has been demonstrated, as has the

frequent occurrence of hepatitis B surface antigen carrier state. Therefore, HBV vaccination is advised.

Although asymptomatic atlantoaxial dislocation occurs in 12% to 20% of individuals with Down syndrome, symptoms referable to compression of the spinal cord are rare. Unfortunately, the literature regarding radiographic screening for this finding is controversial. No study to date has documented that radiographic findings can predict which children will develop neurologic problems. Any child with Down syndrome who develops changes in bowel or bladder function, neck posturing, or loss of ambulatory skills should be evaluated carefully with plain roentgenograms of the cervical spine. The majority of patients develop symptoms before 10 years of age, when the ligamentous laxity is most severe. The Committee on Genetics of the American Academy of Pediatrics has published health supervision guidelines for children with Down syndrome that offer recommendations for follow-up of affected children.

ETIOLOGY. The etiology of Down syndrome is trisomy for all or a large part of chromosome 21. The combined results of 11 unselected surveys totaling 784 cases showed the following relative frequencies of particular types of chromosomal alteration for Down syndrome:

Full 21 trisomy	94%
21 Trisomy/normal mosaicism	2.4%
Translocation cases (with about equal occurrence of D/G and G/G translocations)	3.3%

Faulty chromosome distribution leading to Down syndrome is more likely to occur at older maternal age, as shown in the following figures of incidence for Down syndrome at term delivery for particular maternal ages: 15 to 29 years, 1 in 1500; 30 to 34 years, 1 in 800; 35 to 39 years, 1 in 270; 40 to 44 years, 1 in 100; and over 45 years, 1 in 50.

Though the general likelihood for recurrence of Down syndrome is 1%, the principal task in giving recurrence risk figures to parents is to determine whether the Down syndrome child is a translocation case with a parent who is a translocation carrier and thereby has a relatively high risk for recurrence. The likelihood of finding a translocation in the Down syndrome child of a mother under 30 years of age is 6%, and of such cases only one out of three will be found to have a translocation carrier parent. Therefore, the estimated probability that either parent of a Down syndrome patient born of a mother under 30 years is a G/D or G/G translocation carrier is 2% versus 0.3% when the Down syndrome patient is born of a mother over 30 years of age. Having excluded a translocation carrier parent, the risk for recurrence may be stated as about 1%. Although a low figure, it is enough to justify prenatal diagnosis for any future pregnancy. The recurrence risk for the rare translocation carrier parent will depend on the type of translocation and the sex of the parent. Mosaicism usually leads to a less severe phenotype. Any degree of intellectual ability from normal or nearly normal to severe retardation is found, and this does not always correlate with the clinical phenotype. Patients with the features of Down syndrome and relatively good performance are likely to have mosaicism (which is not always easy to demonstrate).

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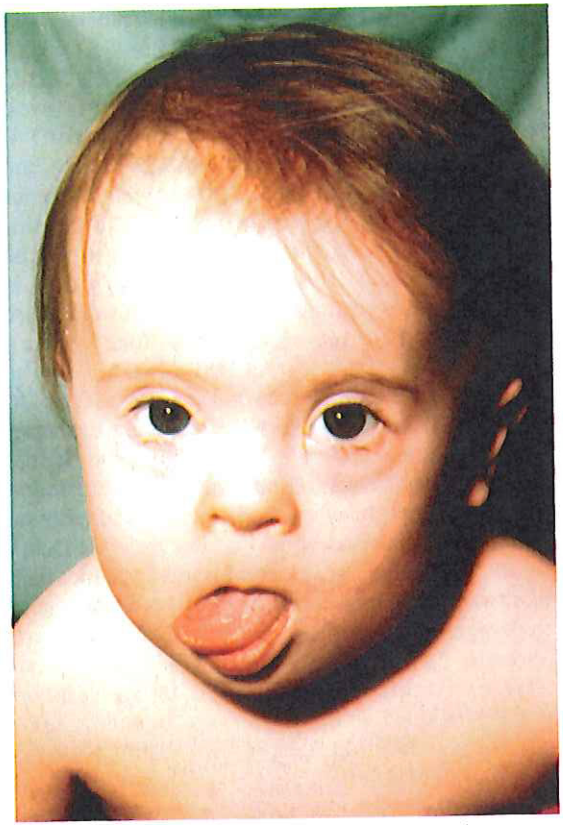

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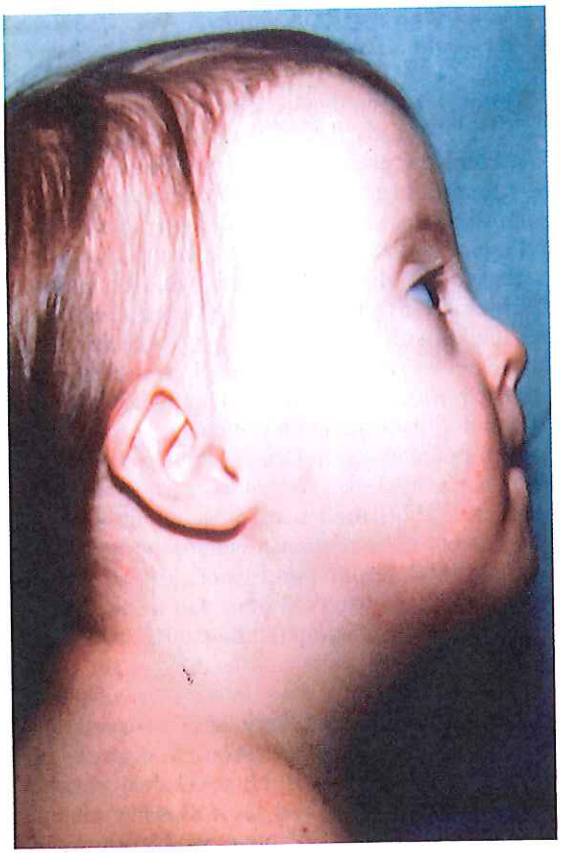

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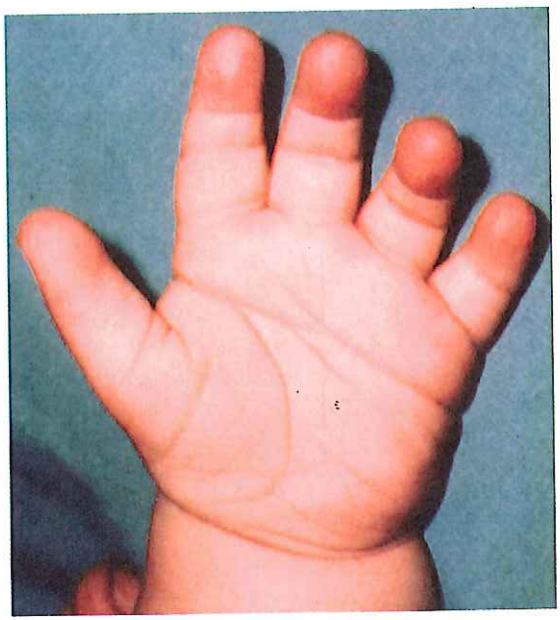

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FIGURE 1. Down syndrome. **A–C,** Young infant. Flat facies, straight hair, protrusion of tongue, single crease on inturned fifth finger.

A

B

FIGURE 2. **A** and **B,** Upslanting palpebral fissures. Low nasal bridge with upturned nares. (Courtesy of Dr. Lynne M. Bird, Children's Hospital, San Diego.)

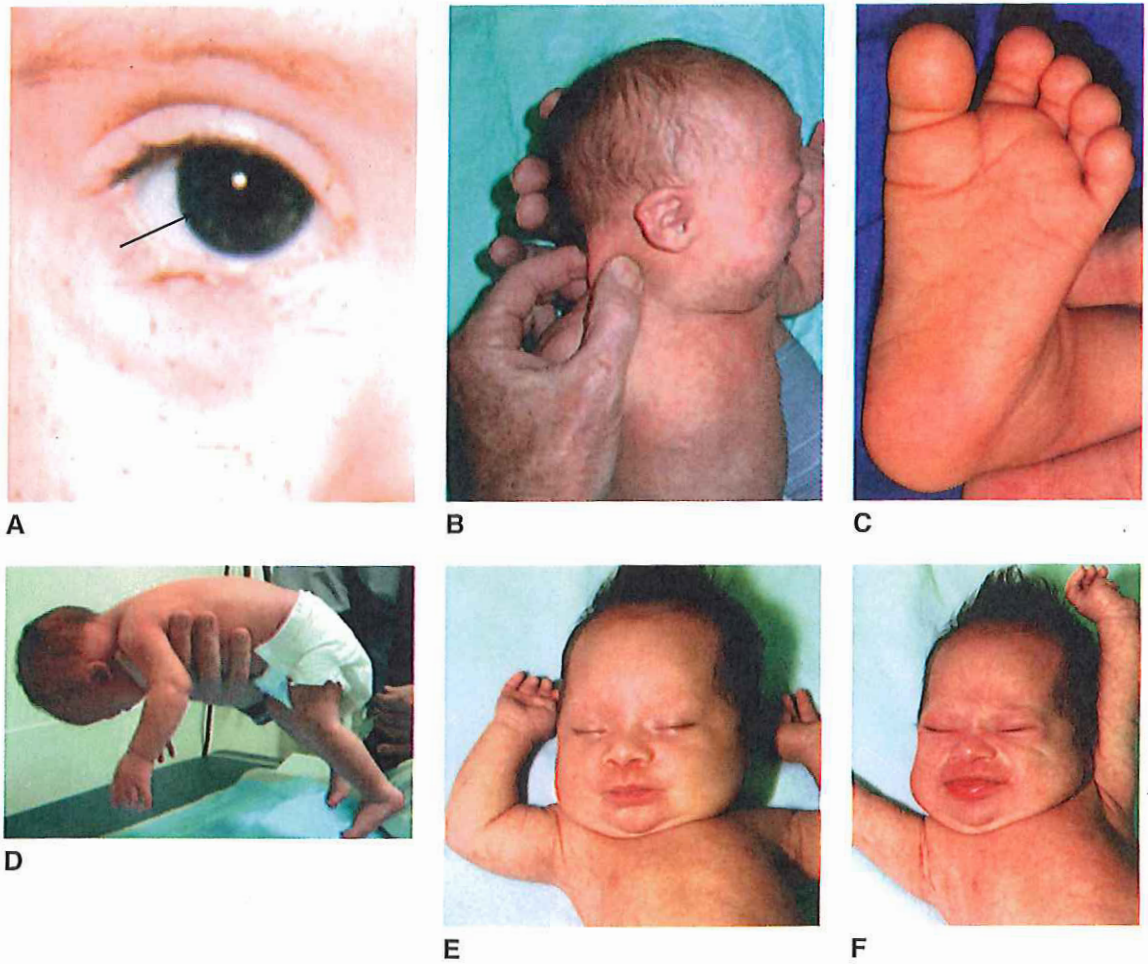

FIGURE 3. **A,** Brushfield spots. **B,** Loose nuchal skin. **C,** Wide space between toes 1 and 2. **D,** Poor tone. **E** and **F,** Accentuation of typical face when crying. (**E** and **F,** Courtesy of Dr. Marilyn C. Jones, Children's Hospital, San Diego.)

American Academy of Pediatrics
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FROM THE AMERICAN ACADEMY OF PEDIATRICS

Guidance for the Clinician in Rendering Pediatric Care

Clinical Report—Health Supervision for Children With Down Syndrome

Marilyn J. Bull, MD, and the COMMITTEE ON GENETICS

ABBREVIATIONS

BAER—brainstem auditory evoked response
TSH—thyroid-stimulating hormone
CRP—C-reactive protein

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abstract

FREE

These guidelines are designed to assist the pediatrician in caring for the child in whom a diagnosis of Down syndrome has been confirmed by chromosome analysis. Although a pediatrician's initial contact with the child is usually during infancy, occasionally the pregnant woman who has been given a prenatal diagnosis of Down syndrome will be referred for review of the condition and the genetic counseling provided. Therefore, this report offers guidance for this situation as well. *Pediatrics* 2011;128:393–406

INTRODUCTION

Children with Down syndrome have multiple malformations, medical conditions, and cognitive impairment because of the presence of extra genetic material from chromosome 21.[1,2] Although the phenotype is variable, there typically are multiple features that enable the experienced clinician to suspect the diagnosis. Among the more common physical findings are hypotonia, small brachycephalic head, epicanthal folds, flat nasal bridge, upward-slanting palpebral fissures, Brushfield spots, small mouth, small ears, excessive skin at the nape of the neck, single transverse palmar crease, and short fifth finger with clinodactyly and wide spacing, often with a deep plantar groove between the first and second toes. The degree of cognitive impairment is variable and may be mild (IQ of 50–70), moderate (IQ of 35–50), or occasionally severe (IQ of 20–35). There is a significant risk of hearing loss (75%); obstructive sleep apnea (50%–79%); otitis media (50%–70%); eye disease (60%), including cataracts (15%) and severe refractive errors (50%); congenital heart defects (50%); neurologic dysfunction (1%–13%); gastrointestinal atresias (12%); hip dislocation (6%); thyroid disease (4%–18%)[3–6]; and, less commonly, transient myeloproliferative disorder (4%–10%) and later leukemia (1%) and Hirschsprung disease (<1%) (Table 1). The social quotient may be improved with early-intervention techniques, although the level of function is exceedingly variable. Children with Down syndrome often function more effectively in social situations than would be predicted on the basis of cognitive assessment results.

In approximately 95% of children with Down syndrome, the condition is sporadic because of nonfamilial trisomy 21, in which there are 47 chromosomes with a free extra chromosome 21 being present. In approximately 3% to 4% of persons with the Down syndrome phenotype, the extra chromosomal material is the result of an unbalanced translocation between chromosome 21 and another acrocentric chromosome, usually chromosome 14. Approximately three-quarters of these

TABLE 1 Medical Problems Common in Down Syndrome

Condition	%
Hearing problems	75
Vision problems	60
Cataracts	15
Refractive errors	50
Obstructive sleep apnea	50–75
Otitis media	50–70
Congenital heart disease	40–50
Hypodontia and delayed dental eruption	23
Gastrointestinal atresias	12
Thyroid disease	4–18
Seizures	1–13
Hematologic problems	
Anemia	3
Iron deficiency	10
Transient myeloproliferative disorder	10
Leukemia	1
Celiac disease	5
Atlantoaxial instability	1–2
Autism	1
Hirschsprung disease	<1

unbalanced translocations are de novo, and the remainder result from familial translocations. If the child has a translocation, a balanced translocation must be excluded in the parents. When there is a translocation in a parent, additional familial studies and genetic counseling should be provided. In the remaining 1% to 2% of persons with the Down syndrome phenotype, a mix of 2 cell lines is present: one normal and the other with trisomy 21. This condition is called mosaicism. Persons with mosaicism may be more mildly affected than persons with complete trisomy 21 or translocation chromosome 21, but this is not always the case, and their condition may include any of the associated medical problems and be indistinguishable from trisomy 21. Recurrence risks for families with an affected child depend on many factors, and families benefit from counseling by a clinical genetic professional.

Medical management, home environment, early intervention, education, and vocational training can significantly affect the level of functioning of children and adolescents with Down syndrome and facilitate their transition to adulthood. The following outline is designed to help the pediatrician provide care for children with Down syndrome and their families in the medical home. It is organized by the issues that need to be addressed in various age groups (see Appendix 1).

Several areas require ongoing assessment throughout childhood and should be reviewed at every physician visit and at least annually. These areas include:

- personal support available to family;
- participation in a family-centered medical home;
- age-specific Down syndrome–related medical and developmental conditions;
- financial and medical support programs for which the child and family may be eligible;
- injury and abuse prevention with special consideration of developmental skills; and
- nutrition and activity to maintain appropriate weight.

THE PRENATAL VISIT

The American College of Obstetricians and Gynecologists recommends that all pregnant women, regardless of age, be offered the option of diagnostic testing for Down syndrome and consider less invasive screening options.[7,8] Screening options have improved significantly with the introduction of first-trimester screening, which incorporates maternal age, nuchal translucency ultrasonography, and measurement of maternal serum human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein A (PAPP-A). Second-trimester screening is available for patients who first seek medical care in the second trimester or in locations where first-trimester screening is not available. The second-trimester screening, often called the quad screen, incorporates maternal age risk with measurement of maternal serum hCG, unconjugated estriol, α-fetoprotein (AFP), and inhibin levels. The detection rate of Down syndrome by first-trimester screening is 82% to 87%, by second-trimester screening is 80%, and by combined first- and second-trimester screening (referred to as integrated screening) is approximately 95%. These screening tests are reported to have a 5% false-positive rate.[9–12]

Pediatricians may be asked to counsel a family whose fetus has been identified with or is at increased risk of Down syndrome. In some settings, the pediatrician may be the primary resource for counseling. At other times, counseling may have been provided for the family by a certified genetic counselor, a clinical geneticist, obstetrician, or developmental-behavioral pediatrician. In addition, parents may have received information from a Down syndrome program, a national Down syndrome organization, or an Internet site. Because the pediatrician often has a previous relationship with the family, he or she should be prepared to review this information and assist in the decision-making process. When asked, the pediatrician should discuss the following topics with the family:

1. The prenatal laboratory studies that lead to the diagnosis and any fetal imaging studies that have been or will be performed.
2. The mechanism for occurrence of the disorder in the fetus and the potential recurrence rate for the family as provided by genetic counseling.
3. The prognosis and phenotypic manifestations, including the wide range of variability seen in infants and children with Down syndrome. Families benefit from hearing a fair and balanced perspective, including the many positive outcomes of

children with Down syndrome and their effect on the family.

4. Any additional studies performed that may refine the estimation of the prognosis (eg, fetal echocardiogram, ultrasonographic examination for gastrointestinal tract malformations). Consultation with an appropriate medical subspecialist, such as a pediatric cardiologist or a pediatric surgeon, should occur prenatally if abnormal findings are detected.
5. Currently available treatments and interventions. This discussion needs to include the efficacy, potential complications and adverse effects, costs, and other burdens associated with treatments. Discuss early-intervention resources, parent support programs, and any appropriate future treatments.
6. The options available to the family for management and rearing of the child should be discussed using a nondirective approach. In cases of early prenatal diagnosis, this may include discussion of pregnancy continuation or termination, raising the child in the family, foster care placement, and adoption.
7. Availability of genetic counseling or meeting with a genetics professional.

If the pregnancy is continued:

1. Develop a plan for delivery and neonatal care with the obstetrician and the family. As the pregnancy progresses, additional studies should be performed if available, if recommended by subspecialty consultants, and/or if desired by the family for modifying this management plan (eg, detection of a complex heart defect by echocardiography).
2. Offer parent-to-parent contact and information about local and national support organizations.
3. Offer referral to a clinical geneticist for a more extended discussion of clinical outcomes and variability, recurrence rates, future reproductive options, and evaluation of the risks for other family members.

HEALTH SUPERVISION FROM BIRTH TO 1 MONTH: NEWBORN INFANTS

Examination

The first step in evaluating a newborn infant for trisomy 21 is a careful review of the family history and prenatal information, particularly if prenatal chromosome studies were performed. Previous children born with trisomy 21 or developmental differences or pregnancies that ended in miscarriage may be significant clues that a family may carry a balanced translocation that predisposes them to having children with trisomy 21. For children who have had the diagnosis made prenatally, a formal copy of the chromosome report should be obtained. This report allows the clinician to confirm the diagnosis, review the results with the family, and add the formal diagnosis to the child's medical record. If the results of prenatal testing are not available, a blood sample should be obtained for postnatal cytogenetic analysis to confirm the diagnosis and rule out a chromosome translocation.

A physical examination is the most sensitive test in the first 24 hours of life to diagnose trisomy 21 in an infant. If the clinician feels that enough criteria are present on physical examination, then a blood sample should be sent for chromosome evaluation. The clinician should alert the laboratory and request rapid results. A study that uses fluorescent in situ hybridization (FISH) technology should be available within 24 to 48 hours to facilitate diagnosis and parent counseling. A FISH study can only indicate that an extra copy of chromosome 21 is present; it cannot detect translocations. Therefore, a positive FISH-test result should be confirmed by a complete chromosome analysis to identify translocations that may have implications for further reproductive counseling for the parents and possibly other family members.

The mother should be allowed to recover from the immediate delivery of the infant and have her partner or support person present before the diagnosis is given. The information should be relayed in a private setting by the physicians involved, optimally by the primary care provider for the infant and the delivering physician.[13] It is recommended that hospitals coordinate the delivery of the information and offer a private hospital room pending confirmation of the diagnosis.

An important aspect of providing information about Down syndrome to families includes first congratulating parents on the birth of their infant. Obstetricians and pediatricians should coordinate their messaging and inform parents of their suspicion immediately, in a private setting and, where appropriate, with both parents together. Physicians should use their experience and expertise in providing support and guidance for families. Clinicians should ensure a balanced approach rather than their personal opinions, give current printed materials, and offer access to other families who have children with Down syndrome and support organizations if locally available. It is important that clinicians be cognizant of the realities and possibilities for healthy, productive lives of people with Down syndrome in society.[13]

Confirm the laboratory diagnosis of Down syndrome and review the karyotype with the parents when the final result is available. Discuss the specific findings with both parents whenever possible, and talk about the potential clinical manifestations associated with the syndrome. These topics

should be reviewed again at a subsequent meeting. Parents should be referred for genetic counseling if it was not conducted prenatally.

Newborn care is often provided in a hospital setting by a physician who will not be the primary care provider, and extreme care is required to be certain that a smooth transition occurs for the family.

Discuss and Review

- Hypotonia.
- Facial appearance, and acknowledge the presence of familial characteristics.
- Feeding issues. Children with Down syndrome can usually nurse, and many can breastfeed successfully. Occasionally, some will need early supplementation until a successful nursing pattern is established. Some infants will also sleep for prolonged periods and need to be awakened to feed to maintain adequate calorie intake.

Evaluate for

- Heart defects (~50% risk). Perform an echocardiogram, to be read by a pediatric cardiologist, regardless of whether a fetal echocardiogram was performed. Refer to a pediatric cardiologist for evaluation any infant whose postnatal echocardiogram results are abnormal.
- Feeding problems. Refer all infants who have marked hypotonia as well as infants with slow feeding, choking with feeds, recurrent pneumonia, or other recurrent or persistent respiratory symptoms and unexplained failure to thrive for a radiographic swallowing assessment.[14,15]
- Cataracts at birth by looking for a red reflex. Cataracts may progress slowly and, if detected, need prompt evaluation and treatment by an ophthalmologist with experience in managing the child with Down syndrome.
- Congenital hearing loss, with objective testing, such as brainstem auditory evoked response or otoacoustic emission, at birth, according to the universal newborn hearing screening guidelines. Complete any needed follow-up assessment by 3 months.[16,17]
- Duodenal atresia or anorectal atresia/stenosis by performing a history and clinical examination.
- Apnea, bradycardia, or oxygen desaturation in a car safety seat for infants who are at increased risk because they have had cardiac surgery or are hypotonic. A car safety seat evaluation should be conducted for these infants before hospital discharge.[18]
- Constipation. If constipation is present, evaluate for restricted diet or limited fluid intake, hypotonia, hypothyroidism, or gastrointestinal tract malformation, including stenoses or Hirschsprung disease, for which there is an increased risk.
- Gastroesophageal reflux, which is usually diagnosed and managed clinically. If severe or contributing to cardiorespiratory problems or failure to thrive, refer for subspecialty intervention.
- Stridor, wheezing, or noisy breathing. If severe or contributing to cardiorespiratory problems or feeding difficulty, refer to pediatric pulmonologist to assess for airway anomalies. Tracheal anomalies and small tracheal size may also make intubation more difficult.
- Hematologic abnormalities. Obtain a complete blood cell count. Leukemoid reactions, or transient myeloproliferative disorder (TMD). TMD is found almost exclusively in newborn infants with Down syndrome and is relatively common in this population (10%).[19] TMD usually regresses spontaneously within the first 3 months of life, but there is an increased risk of later onset of leukemia for these patients (10%–30%).[20] Polycythemia is also common in infants with Down syndrome (18%–64%)[21] and may require careful management. Infants with TMD and polycythemia should be followed according to subspecialty consultation recommendations. Parents of infants with TMD should be counseled regarding the risk of leukemia and made aware of the signs, including easy bruising, petechiae, onset of lethargy, or change in feeding patterns. Leukemia is more common in children with Down syndrome than in the general population but still rare (1%).
- Congenital hypothyroidism (1% risk). Obtain thyroid-stimulating hormone (TSH) concentration if state newborn screening only measures free thyroxine (T4); congenital hypothyroidism can be missed if only the T4 concentration is obtained in the newborn screening. Many children with Down syndrome have mildly elevated TSH and normal free T4 levels. Management of children with abnormal thyrotropin or T4 concentrations should be discussed with a pediatric endocrinologist.

Anticipatory Guidance Given at Least Once Between Birth and 1 Month of Age

- Discuss increased susceptibility to respiratory tract infection. Children with signs and symptoms of lower respiratory tract infection should be evaluated acutely by a medical provider, and in the presence of cardiac or chronic respiratory disease, aggressive treatment should be instituted.[14] Children with comorbid conditions who qualify should have respiratory syncytial virus prophylaxis.[22]

- Discuss with parents the importance of cervical spine-positioning precautions to avoid excessive extension or flexion to protect the cervical spine during any anesthetic, surgical, or radiographic procedure.[23,24]
- Discuss efficacy of early intervention and availability of early-intervention services and therapies in the community. Initiate referral as appropriate.[25]
- Inform the family of the availability of support and advice from parents of other children with Down syndrome.
- Supply names of Down syndrome support groups and current books and pamphlets (see "Resources for Parents").
- Discuss the strengths of the child and positive family experiences.
- Discuss the individual resources for support, such as family, clergy, and friends.
- Talk about how and what to tell siblings, other family members, and friends. Review methods of coping with long-term disabilities.
- Review the recurrence risk in subsequent pregnancies and the availability of prenatal diagnosis as provided in genetic counseling.
- Discuss treatments that are considered complementary and alternative. Parents need an opportunity to learn objectively which therapies are safe and which are potentially dangerous (eg, cell therapy that may transmit slow viruses and fat-soluble vitamins that can cause toxicity). Several articles and Internet sites evaluate the legitimacy of claims that are made.[26–28]
- Renal and urinary tract anomalies have been reported to occur at increased frequency among persons with Down syndrome, and screening for these anomalies for all children with Down syndrome has been suggested.[29] Until studies confirm this finding and document that screening improves outcomes, routine renal and urologic screening is not recommended.

HEALTH SUPERVISION FROM 1 MONTH TO 1 YEAR: INFANCY

Physical Examination and Laboratory Studies

Review the risk of serous otitis media (50%–70%). Review the previous hearing evaluation (brainstem auditory evoked response [BAER, ABR] or otoacoustic emission). If the child passed the screening study, rescreen at 6 months of age for confirmation. If the infant failed to pass screening studies, refer to an otolaryngologist who is comfortable with examining infants with stenotic external canals to determine if a middle-ear abnormality is present. Tympanometry may be necessary if the tympanic membrane is poorly visualized. Middle-ear disease should be treated promptly. Once a clear ear is established, a diagnostic BAER should be performed to accurately establish hearing status. In children with stenotic canals, in which the tympanic membranes cannot be seen, refer to an otolaryngologist for examination under an office microscope. Interval ear examinations should be performed by the otolaryngologist every 3 to 6 months until the tympanic membrane can be visualized by the pediatrician and tympanometry can be performed reliably. A behavioral audiogram may be attempted at 1 year of age, but many children will not be able to complete the study and may need additional testing by BAER.[30,31]

- At least once during the first 6 months of life, discuss with parents symptoms of obstructive sleep apnea, including heavy breathing, snoring, uncommon sleep positions, frequent night awakening, daytime sleepiness, apneic pauses, and behavior problems that could be associated with poor sleep. Refer to a physician with expertise in pediatric sleep disorders for examination and further evaluation of a possible sleep disorder if any of the above-mentioned symptoms occur.[32,33]
- At each well-child visit, discuss with parents the importance of maintaining the cervical spine in a neutral position during any anesthetic, surgical, or radiographic procedure to minimize the risk of spinal cord injury and review the signs and symptoms of myelopathy. Perform careful history and physical examination, and pay attention for myelopathic signs and symptoms.
- Within the first 6 months of life, refer to a pediatric ophthalmologist or ophthalmologist with expertise and experience with infants with disabilities to evaluate for strabismus, cataracts, and nystagmus.[34] Check the infant's vision at each visit and use developmentally appropriate subjective and objective criteria. If lacrimal duct obstruction is present, refer for evaluation for surgical repair of drainage system if not resolved by 9 to 12 months of age.[35]
- Verify results of newborn thyroid-function screen if not previously performed. Because of increased risk of acquired thyroid disease, repeat measurement of TSH at 6 and 12 months of age and then annually.
- Monitor infants with cardiac defects, typically ventricular or atrioventricular septal defects that cause intracardiac left-to-right shunts, for symptoms and signs of congestive heart failure as pulmonary vascular resistance decreases and pulmonary blood flow increases. Tachypnea, feeding difficulties, and poor weight gain may

indicate heart failure. Medical management, including nutritional support, may be needed until the infant can undergo cardiac surgery to repair the defects. For patients with large ventricular septal defects and without obstruction to pulmonary blood flow, repair should be performed before 4 months of age to limit the potential for development of pulmonary hypertension and associated complications. Infants and children with Down syndrome are also at increased risk of pulmonary hypertension even in the absence of intracardiac structural defects.

- Obtain hemoglobin concentration beginning at 1 year of age and annually thereafter. Children with Down syndrome have been shown to have significantly lower dietary intakes of iron than their typically developing peers.[36] Increased erythrocyte mean corpuscular volume (MCV) has been reported in 45% of patients with Down syndrome with and without heart disease, and when MCV is decreased, it occurs at approximately the same time as anemia.[37] Therefore, MCV is not useful in screening for the diagnoses of iron deficiency, lead toxicity, or thalassemia in children with Down syndrome. Serum ferritin concentration is a sensitive parameter for assessment of iron stores in healthy subjects but is an acute-phase reactant and may be increased in the presence of chronic inflammation or infection and should be evaluated together with C-reactive protein (CRP) concentration. An elevated CRP level is an indication that a normal ferritin level may be falsely elevated and is not a reliable indication of normal iron status. Serum ferritin and CRP or reticulocyte hemoglobin (CHr) concentrations should be obtained at annual visits for patients who are at increased risk of iron deficiency on the basis of a history of decreased iron intake.[38–42]
- Monitor for signs of neurologic dysfunction that may occur. Children with Down syndrome have an increased risk of seizures, including infantile spasms (1%–13%)[43,44] and other conditions including Moyamoya disease.[45]
- Administer immunizations, including influenza vaccine and other vaccines recommended for all children, unless there are specific contraindications.[46]

Anticipatory Guidance

- Monitor weight and follow weight-for-height trends at each health care visit. Review the infant's growth and plot it by using the standard growth charts of the National Center for Health Statistics or the World Health Organization.[47] The previously used Down syndrome-specific growth charts no longer reflect the current population styles and body proportion. Until new charts are developed, patterns of growth and weight gain should be followed on the available standard growth charts and should include use of weight for height and BMI.[48]
- Review availability of Down syndrome support groups at least once in the first year of life (see "Resources for Parents").
- Assess the emotional status of parents and intrafamilial relationships at each well-child visit. Educate and support siblings and discuss sibling adjustments.
- Review connection to early-intervention services and their relationship to the strengths and needs of the infant and family at each well-child visit.
- Review the family's understanding of the risk of recurrence of Down syndrome and the availability of prenatal diagnosis at least once in the first year of life and more often if judged necessary by the clinician. Refer for genetic counseling if not already provided.
- Be prepared to discuss and answer questions about treatments that are considered complementary and alternative at each well-child visit.

HEALTH SUPERVISION FROM 1 TO 5 YEARS: EARLY CHILDHOOD

- Obtain a history and perform a physical examination, and give attention to growth and developmental status at every well-child visit.
- Review the risk of hearing loss associated with serous otitis media. For a child who passed diagnostic hearing testing, additional screening or behavioral audiogram and tympanometry should be performed every 6 months until normal hearing levels are established bilaterally by ear-specific testing (usually after 4 years of age). Subsequently, behavioral hearing tests should be performed annually. If normal hearing is not established by behavioral testing, additional screening by otoacoustic emissions or diagnostic BAER should be performed with sedation if necessary. Children who demonstrate a hearing loss should be referred to an otolaryngologist who is comfortable with the examination of children with stenotic ear canals. The risk of serous otitis media between 3 and 5 years of age is approximately 50% to 70%.
- Check the child's vision, and use developmentally appropriate subjective and objective criteria at each well-child visit. Refer the child annually to a pediatric ophthalmologist or ophthalmologist with special expertise and experience with children with disabilities. Children with Down syndrome have a 50%

risk of refractive errors that lead to amblyopia between 3 and 5 years of age. Addressing refractive errors and strabismus at an early age can help prevent amblyopia and encourage normal visual development.[34,49–51]

Atlantoaxial Instability

Discuss with parents, at least biennially, the importance of cervical spine-positioning precautions for protection of the cervical spine during any anesthetic, surgical, or radiographic procedure. Perform careful history and physical examination with attention to myelopathic signs and symptoms at every well-child visit or when symptoms possibly attributable to spinal cord impingement are reported. Parents should also be instructed to contact their physician for new onset of symptoms of change in gait or use of arms or hands, change in bowel or bladder function, neck pain, stiff neck, head tilt, torticollis, how the child positions his or her head, change in general function, or weakness.

The Asymptomatic Child

Children with Down syndrome are at increased risk of atlantoaxial subluxation. However, the child must be 3 years of age to have adequate vertebral mineralization and epiphyseal development for accurate radiographic evaluation of the cervical spine.[52] Plain radiographs do not predict well which children are at increased risk of developing spine problems, and normal radiographs do not provide assurance that a child will not develop spine problems later.[53,54] For these reasons, routine radiologic evaluation of the cervical spine in asymptomatic children is not recommended. Current evidence does not support performing routine screening radiographs for assessment of potential atlantoaxial instability in asymptomatic children.[55–64] Parents should be advised that participation in some sports, including contact sports such as football and soccer and gymnastics (usually at older ages), places children at increased risk of spinal cord injury[65] and that trampoline use should be avoided by all children with or without Down syndrome younger than 6 years and by older children unless under direct professional supervision.[66,67] Special Olympics has specific screening requirements for participation in some sports.[68]

The Symptomatic Child

Any child who has significant neck pain, radicular pain, weakness, spasticity or change in tone, gait difficulties, hyperreflexia, change in bowel or bladder function, or other signs or symptoms of myelopathy must undergo plain cervical spine radiography in the neutral position.[55,65] If significant radiographic abnormalities are present in the neutral position, no further radiographs should be taken and the patient should be referred as quickly as possible to a pediatric neurosurgeon or pediatric orthopedic surgeon with expertise in evaluating and treating atlantoaxial instability. If no significant radiographic abnormalities are present, flexion and extension radiographs may be obtained before the patient is promptly referred.[23,62,63]

- Measure TSH annually or sooner if child has symptoms that could be related to thyroid dysfunction.
- For children on a diet that contains gluten, at each preventative care visit review for symptoms potentially related to celiac disease, including diarrhea or protracted constipation, slow growth, unexplained failure to thrive, anemia, abdominal pain or bloating, or refractory developmental or behavioral problems.[69–71] For those with symptoms, obtain a tissue transglutaminase immunoglobulin A (IgA) level and simultaneous quantitative IgA. The quantitative IgA is important, because a low IgA level will result in a false-negative tissue transglutaminase IgA result. Refer patients with abnormal laboratory values for specialty assessment. There is no evidence showing routine screening of asymptomatic individuals as being beneficial. There are neither data nor consensus that would indicate whether patients with persistent symptoms who had normal laboratory values on initial evaluation should have further laboratory tests.
- Discuss symptoms of obstructive sleep apnea, including heavy breathing, snoring, restless sleep, uncommon sleep positions, frequent night awakening, daytime sleepiness, apneic pauses, and behavior problems, that could be associated with poor sleep at each well-child visit. There is poor correlation between parent report and polysomnogram results.[33,72] Therefore, referral to a pediatric sleep laboratory for a sleep study or polysomnogram for all children with Down syndrome by 4 years of age is recommended. Refer to a physician with expertise in pediatric sleep any child with signs or symptoms of obstructive sleep apnea or abnormal sleep-study results. Discuss obesity as a risk factor for sleep apnea.[34] It is recognized that access to a pediatric sleep laboratory or specialist may be limited for some populations and geographic areas.
- Maintain follow-up with a pediatric cardiologist for patients with cardiac lesions even after complete repair to monitor for recurrent/residual lesions as well as development of pulmonary hypertension.
- Monitor for neurologic dysfunction, including seizures.
- Obtain hemoglobin concentration

annually. Also, obtain serum ferritin and CRP concentrations for any child at risk of iron deficiency.

Anticipatory Guidance

- Review early intervention, including physical therapy, occupational therapy, and speech therapy, at all health maintenance visits.
- Discuss at the 30-month visit the transition from early intervention to preschool, which occurs at 36 months of age. Help the family understand the change from the Individualized Family Service Plan (IFSP) in early intervention to the Individualized Education Plan (IEP) through public education.
- Discuss with caregivers at every visit the child's behavioral and social progress. Refer children who may have autism, attention-deficit/hyperactivity disorder, or other psychiatric or behavioral problems for appropriate evaluation and intervention as soon as suspected. Autism and other behavioral problems occur with increased frequency in children with Down syndrome, and symptoms may manifest as early as 2 or 3 years of age.[73–76]
- Provide influenza vaccine annually. Children with chronic cardiac or pulmonary disease should be given the 23-valent pneumococcal polysaccharide vaccine (PPS23) at 2 years or older.[22]
- Reassure parents that delayed and irregular dental eruption patterns are common and that hypodontia occurs with increased frequency (23%).[77,78]
- Encourage and model use of accurate terms for genitalia and other private body parts (penis, vulva) any time these body parts are discussed or examined. Model respect for body rights by reminding patients that their body is their own and explain to the child what you will do before moving into child's personal space or performing a procedure. Remind patient and family that the only reason anyone should be looking at or touching private body parts is for health (doctor office visits) or hygiene (bathing or showering).[79]
- On at least 1 well-child visit educate parents about increased risk of sexual exploitation, and remind them that likely perpetrators are people their child knows and trusts, not strangers.
- At least once between 1 and 5 years of age, as with discussion in the first year of life, discuss future pregnancy planning and review risk of recurrence of Down syndrome and availability of prenatal diagnosis.
- Assess the child's behavior and talk about behavioral management, sibling adjustments, socialization, and recreational skills.
- Encourage families to establish optimal dietary and physical exercise patterns that will prevent obesity.
- Be prepared to discuss and answer questions about treatments that are considered complementary and alternative.

HEALTH SUPERVISION FROM 5 TO 13 YEARS: LATE CHILDHOOD

- Obtain a history and perform a physical examination with attention to growth and developmental status at each annual well-child visit.
- Monitor growth patterns, especially BMI, and emphasize healthy diet and lifestyle for preventing obesity.
- Obtain annual ear-specific audiologic evaluation.
- Obtain ophthalmologic evaluation every 2 years.
- Measure TSH annually; the risk of hypothyroidism increases with age.
- Individualize cardiology follow-up on the basis of history of cardiac defects.
- Obtain hemoglobin concentration annually and serum ferritin and CRP or reticulocyte hemoglobin concentrations at annual visits for any child at risk of iron deficiency on the basis of history of decreased iron intake.
- For children on a diet that contains gluten, review for symptoms potentially related to celiac disease at every health maintenance visit and evaluate if indicated.
- At each well-child visit, discuss with parents the importance of universal precautions for protection of the cervical spine during any anesthetic, surgical, or radiographic procedure. Perform careful history and physical examination with attention to myelopathic signs and symptoms. Parents should also be instructed to contact their physician immediately for new onset of symptoms of myelopathy.
- Counsel parents that some sports place children at increased risk of spinal cord injury.[65–67]
- Monitor for neurologic dysfunction, including seizures.
- Very dry skin, which may be a sign of hypothyroidism, and other skin problems are particularly common in patients with Down syndrome. Therefore, be attentive to these dermatologic problems and discuss them with the patient and family.
- Discuss symptoms related to obstructive sleep apnea at every well-child visit, including snoring, restless sleep, daytime sleepiness, nighttime awakening, behavior problems, and abnormal sleep position. Refer to a physician with expertise in pediatric sleep any child with signs or symptoms of obstructive sleep apnea or abnormal sleep-

study results. Discuss obesity as a risk factor of sleep apnea.

Anticipatory Guidance at Every Health Maintenance Visit

- Review the child's development and appropriateness of school placement and developmental intervention.
- Discuss socialization, family status, and relationships, including financial arrangements, health insurance, and guardianship.
- Discuss the development of age-appropriate social skills, self-help skills, and development of a sense of responsibility.
- Monitor for behavior problems that interfere with function in the home, community, or school. Attention problems, attention-deficit/hyperactivity disorder, obsessive compulsive behaviors, noncompliant behavior, and wandering off are some of the common behavior concerns reported. Psychiatric disorders seen in typically developing children may also occur. Evaluate for medical problems that can be associated with behavior changes, including thyroid abnormalities, celiac disease, sleep apnea, gastroesophageal reflux, and constipation. Intervention strategies depend on the child's age, the severity of the problem, and the setting in which the problem occurs. Referral to community treatment programs, psychosocial services for consultative care, or behavioral specialists experienced in working with children with special needs may be necessary. The use of medication for behavior management should be discussed between the primary care physician and specialists involved in the child's care, because children with Down syndrome may be more sensitive to certain medications. Although there has been little research to directly address the use of psychotropic medications among children with Down syndrome, anecdotal reports indicate that such children may differ in their response to medications.
- Counsel families regarding the transition from elementary to middle school, when major change often occurs, from 1 to many teachers and from 1 class to changing classes. Prepare them to facilitate adjustment at a time when the academic disparity becomes greater and full inclusion becomes more difficult.
- Refer children who may have autism for appropriate evaluation and intervention as soon as suspected.
- Continue to assess, monitor, and encourage independence with hygiene and self-care. Encourage parents to teach, model, and respect privacy at home and in the community. Discuss appropriate management of sexual behaviors such as masturbation.
- Discuss progression of physical and psychosocial changes through puberty and issues of fertility and contraception.[79,80] Remind parents that physical development usually follows patterns similar to those found in the general population, but the child with Down syndrome will likely need more preparation in understanding and managing them.[81]
- Discuss the need for gynecologic care in the pubescent girl. Talk with the patient and her family about the recurrence risk of Down syndrome (50%) were she to become pregnant.[82,83] Although males with Down syndrome are usually infertile, there have been rare instances in which a male has reproduced.[83–85] Birth control and prevention of sexually transmitted diseases should be discussed with patients and their families. Families may wish to discuss sterilization, and the pediatrician may review the topic in the American Academy of Pediatrics policy statement "Sterilization of Minors With Developmental Disabilities."[86]
- Be prepared to discuss and answer questions regarding treatments that are considered complementary and alternative.

HEALTH SUPERVISION FROM 13 TO 21 YEARS OR OLDER: ADOLESCENCE TO EARLY ADULTHOOD

Physical Examination and Laboratory Values

- Measure hemoglobin concentration annually.
- Measure TSH concentration annually.
- Obtain annual ear-specific audiologic evaluation.
- For children on a diet that contains gluten, review for symptoms potentially related to celiac disease at every health maintenance visit, and evaluate if indicated.
- Individualize cardiology follow-up on the basis of history of cardiac defects. Discuss symptoms related to obstructive sleep apnea, including snoring, restless sleep, daytime sleepiness, nighttime awakening, behavior problems, and sleep position at every health maintenance visit. Refer to a physician with expertise in pediatric sleep any child with signs or symptoms of obstructive sleep apnea or an abnormal sleep-study result. Discuss the risk factor of obesity for sleep apnea.
- Discuss with parents and the patient at every visit the importance of cervical spine-positioning precautions for protection of the cervical spine during any anesthetic, surgical, or radiographic procedure. Perform careful history and physical

examination with attention to myopathic signs and symptoms. Parents and patients should also be instructed to contact their physician immediately for new onset of symptoms of myopathy.

- Counsel parents that some sports place children at increased risk of spinal cord injury.[65–67]
- Monitor for signs of other neurologic dysfunction, including seizures.
- Obtain ophthalmologic evaluation every 3 years. Check for onset of cataracts, refractive errors, and keratoconus, which can cause blurred vision, corneal thinning, or corneal haze and is typically diagnosed after puberty.
- Examine annually for acquired mitral and aortic valvular disease in older patients with Down syndrome. An echocardiogram should be obtained if there is a history of increasing fatigue, shortness of breath, or exertional dyspnea or abnormal physical examination findings, such as a new murmur or gallop. Discuss skin, hair, and scalp care at each preventive health care visit.

Anticipatory Guidance at Every Health Maintenance Visit

- Discuss issues related to transition into adulthood, including guardianship and long-term financial planning from early adolescence. Potential adult morbidities including apparent tendency toward premature aging and increased risk of Alzheimer disease may also be discussed.[87]
- Monitor growth patterns, especially BMI, and counsel regarding healthy diet and a structured exercise program.
- Discuss behavioral and social states and refer patients who have chronic behavioral problems or manifest acute deterioration in function for specialized evaluation and intervention.[88,89]
- Discuss appropriateness of school placement, and emphasize planning for transition to adulthood and adequate vocational training within the school curriculum.[90,91]
- Talk with the female patient and her family about the recurrence risk of Down syndrome should she become pregnant.
- Continue to assess, monitor, and encourage independence with hygiene and self-care. Provide guidance on healthy, normal, and typical sexual development and behaviors. Emphasize the need for understandable information, and encourage opportunities for advancing comprehension of sexuality. Discuss the need for contraception and prevention of sexually transmitted diseases and the degree of supervision required. Advocate for the least invasive and least permanent method of birth control and be familiar with local law and resources to assist the family in their decision-making regarding questions about sterilization.[86]
- Make recommendations and provide or refer for routine gynecologic care if not already provided. Discuss premenstrual behavioral problems and management of menses.[92]
- Discuss group homes and independent living opportunities, workshop settings, and other community-supported employment.
- Discuss intrafamily relationships, financial planning, and guardianship.
- Facilitate transition to adult medical care.[93]

FUTURE CONSIDERATIONS

Many issues related to the development and health of people with Down syndrome remain to be evaluated, and research agendas for addressing both public health and basic science topics have been developed. Knowledge in several topics of great importance to the care of children with Down syndrome could be enhanced through population-based research. A rigorous evidence-based review of screening and treatment for atlantoaxial instability, for example, is needed,[94] and continuing research is critical for directing the care for optimal outcomes of persons with Down syndrome.[1,95,96]

ACKNOWLEDGMENT

The mentoring and contributions of Dr. William Cohen have been sincerely appreciated and were integral to the development of this clinical report. His untimely death is a great loss to his patients and their families, his colleagues, and the greater medical community. This clinical report is dedicated to his memory.

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RESOURCES FOR PARENTS

National Down Syndrome Society: www.ndss.org.

National Down Syndrome Congress: www.ndsccenter.org.

APPENDIX 1 Health Supervision for Children With Down Syndrome

	Prenatal	Birth–1 mo	1 mo–1 y	1–5 y	5–13 y	13–21 y
Counseling regarding prenatal screening test & imaging results	■					
Plan for delivery	■					
Referral to geneticist	■					
Parent-to-parent contact, support groups, current books and pamphlets	■	▨	■	▨		
Physical exam for evidence of trisomy 21		■				
Chromosomal analysis to confirm dx		▨	▨	▨		
Discuss risk of recurrence of Down syndrome			▨	▨		
Echocardiogram		■				
Radiographic swallowing assessment if marked hypotonia, slow feeding, choking with feeds, recurrent or persistent respiratory sx, FTT		■	▨			
Eye exam for cataracts		■	■			
Newborn hearing screen and follow-up		■				
Hx and PE assessment for duodenal or anorectal atresia		■				
Reassure parents delayed and irregular dental eruption, hypodontia are common			▨			
If constipation, evaluate for limited diet or fluids, hypotonia, hypothyroidism, GI malformation, Hirschsprung		**Any visit**				
CBC to R/O transient myeloproliferative disorder, polycythemia		■				
Hb annually; CRP & ferritin or CHr if possible risk iron deficiency or Hb <11 g.				**Annually**		
Hemoglobin						**Annually**
TSH (may be part of newborn screening)		■	**6 and 12 mo**	**Annually**		
Discuss risk of respiratory infection		■				
If cardiac surgery or hypotonic: evaluate apnea, bradycardia, or oxygen desaturation in car seat before discharge		■				
Discuss complementary & alternative therapies		**All health maint. visits**				
Discuss cervical spine positioning, especially for anesthesia or surgical or radiologic procedures		**All health maint. visits**				
Review signs and symptoms of myopathy		**All health maint. visits**				
If myopathic signs or symptoms: obtain neutral position spine films and, if normal, obtain flexion & extension films & refer to pediatric neurosurgeon or orthopedic surgeon with expertise in evaluating and treating atlanto-axial instability		**Any visit**				
Instruct to contact physician for change in gait, change in use of arms or hands, change in bowel or bladder function, neck pain, head tilt, torticollis, or new-onset weakness				**Biennially**		
Advise risk of some contact sports, trampolines				**All health maint. visits**		
Audiology evaluation at 6 mo			■			
If normal hearing established, behavioral audiogram and tympanometry until bilateral ear specific testing possible. Refer child with abnormal hearing to ot				**Every 6 mo**		
If normal ear-specific hearing established, behavioral audiogram				**Annually**		
Assess for obstructive sleep apnea Sx			■	**All health maint. visits**		
Sleep study by age 4 years				■		
Ophthalmology referral to assess for strabismus, cataracts, and nystagmus			■			
Refer to pediatric ophthalmologist or ophthalmologist with experience with Down syndrome				**Annually**	**Every 2 y**	**Every 3 y**
If congenital heart disease, monitor for signs & Sx of Congestive heart failure		**All visits**				
Assess the emotional status of parents and intrafamilial relationships		**All health maint. visits**				
Check for Sx of celiac disease; if Sx present, obtain tissue transglutaminase IgA & quantitative IgA				**All health maint. visits**		
Early intervention: physical, occupational, and speech therapy				**Health maint. visits**		
At 30 months, discuss transition to preschool and development of IEP				■		
Discuss behavioral and social progress				**Health maint. visits**		
Discuss self-help skills, ADHD, OCD, wandering off, transition to middle school					**Health maint. visits**	
If chronic cardiac or pulmonary disease, 23-valent pneumococcal vaccine at age >2 y				■		
Reassure regarding delayed and irregular dental eruption				■		
Establish optimal dietary and physical exercise patterns				**Health maint. visits**		
Discuss dermatologic issues with parents					■	
Discuss physical and psychosocial changes though puberty, need for gynecologic care in the pubescent female					■	■
Facilitate transition: guardianship, financial planning, behavioral problems, school placement, vocational training, independence with hygiene and self-care, group homes, work settings						**Health maint. visits**
Discuss sexual development and behaviors, contraception, sexually transmitted diseases, recurrence risk for offspring						**Health maint. visits**
	■	Do once at this age				
	▨	Do if not done previously				
		Repeat at indicated intervals				

Maint. indicates maintenance; dx, diagnosis; sx, symptoms; FTT, failure to thrive; Hx, history; PE, physician examination; GI, gastrointestinal; CBC, complete blood count; R/O, rule out; Hb, hemoglobin; ot, occupational therapy; CHr, reticulocyte hemoglobin; IgA, immunoglobulin A; IEP, Individualized Education Plan; ADHD, attention-deficit/hyperactivity disorder; OCD, obsessive compulsive disorder.

Atlantoaxial Dislocation

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The joint between the first and second cervical vertebrae, the atlas and axis, is subject to instability and even to dislocation, with backward movement of the odontoid process of the axis, leading to compression of the spinal cord. The underlying instability that can lead to frank atlantoaxial dislocation may arise from laxity of the ligaments that maintain the integrity of the joint, bony abnormalities of the cervical vertebrae, or both. Radiographically, atlantoaxial instability appears as a space larger than 5 mm between the posterior aspect of the anterior arch of the atlas and the odontoid process.

About 15% of children who have Down syndrome have atlantoaxial instability, which also can occur in patients who have rheumatoid arthritis, intrinsic abnormalities of the odontoid process, and various bone dysplasias. Although it is far less common than instability, atlantoaxial dislocation is life-threatening and presents with signs and symptoms of cord compression: abnormal gait, neck pain, limited neck mobility, head tilt, incoordination, clumsiness, and changes in bowel and bladder control. A neurologic examination may reveal sensory deficits, spasticity, hyperreflexia, clonus, and the presence of a Babinski sign.

Our understanding of the natural history of atlantoaxial instability and dislocation is incomplete. Symptomatic instability is rare among patients who have Down syndrome. It is not even clear that radiographically demonstrated asymptomatic instability is a significant risk factor for either symptomatic instability or, worse, for frank atlantoaxial dislocation following an injury to the neck. Even the reproducibility of radiographs for atlantoaxial instability is poor, with the picture often changing over time either from normal to abnormal or, perhaps more confusing, with initial evidence of instability disappearing on later films. Further, no evidence establishes that screening with lateral cervical radiographs is effective in preventing symptomatic atlantoaxial instability.

Given this lack of clarity, the American Academy of Pediatrics (AAP) has abandoned its previous recommendation to screen all children who have Down syndrome radiographically before they participate in sports. Instead, the AAP now recommends careful neurologic evaluation for signs and symptoms consistent with spinal cord injury as the most important clinical predictor of symptomatic atlantoaxial instability and dislocation. Physicians caring for children who have Down syndrome should take a careful history and perform a thorough physical examination, looking for evidence of neurologic involvement. This clinical screening process should be ongoing, with directed histories and examinations at least yearly. In addition, physicians should educate the parents of children who have Down syndrome about the early signs of myelopathy, such as abnormal gait, increasing clumsiness, and changes in bowel and bladder control.

Asymptomatic children who are identified as having atlantoaxial instability, usually because of a cervical neck film, should be followed closely with repeated neurologic examinations. Children who are symptomatic, either with the sudden onset of neurologic findings or with progression of previously noted symptoms, should receive appropriate imaging to determine the extent of neural encroachment and cord compression. If computed tomography or magnetic resonance imaging confirms cord compression, the child should be evaluated immediately by a neurosurgeon or orthopedic surgeon. The goal of surgery is to prevent further injury to the spinal cord by stabilizing the upper segment of the cervical spine.

Despite the revised policy of the AAP, the Special Olympics continues to mandate, in addition to a physical examination, preparticipation radiographic screening of all children who have Down syndrome. If atlantoaxial instability is diagnosed, the child is not allowed to participate in activities that place the neck in extension, including diving, butterfly stroke and diving starts in swimming, gymnastics, high jump, pentathlon, soccer, and any warm-up exercises that place pressure on the head and neck muscles.

Further studies, particularly longitudinal studies, need to be performed to determine what combination of signs, symptoms, and radiographic findings best identify the apparently very few children who have Down syndrome and are at special risk for spinal cord injury from participation in sports.

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Comment: Wouldn't it be nice if medically related policy was based on evidence? Worse things have been done to children than having them undergo a lateral neck film for no supportable reason, but that hardly justifies the anxiety and cost created by an inappropriate screening program.

Henry M. Adam, MD
Editor, In Brief

Down Syndrome Quiz

1. According to Smith's, what are the **10 principal features of Down Syndrome**, and what are their prevalence rates?

Flat facial profile 90%
Poor Moro reflex 85%
Hypotonia 80%
Hyperflexibility of joints 80%
Excess skin on back of neck 80%
Slanted palpebral fissures 80%
Dysplasia of pelvis 70%
Anomalous auricles 60%
Dyplasia of midphalanx 5th finger 60%
Simian/single palmar crease 45%

2. What are the **most common medical problems associated with Down Syndrome**, and what are their prevalence rates? *(See Table 1 from CPG)*

Hearing problems 75%
Obstructive sleep apnea 50–75%
Otitis media 50–70%
Vision problems 60%
Refractive errors 50%
Congenital heart disease 40–50%
Hypodontia/delayed dental eruption 23%
Thyroid disease 4–18%
Cataracts 15%
Gastrointestinal atresias 12%
Seizures 1–13%
Iron deficiency 10%
Transient MPD 10%
Celiac disease 5%
Anemia 3%
Atlantoaxial instability 1–2%
Leukemia 1%
Autism 1%
Hirschsprung disease <1%

3. **True** or **False?**
   A) If a FISH study is positive for Trisomy 21, you do *not* need to obtain a complete chromosome analysis. **FALSE**
   B) A healthy-appearing infant with Down Syndrome, without a heart murmur and growing normally, does not need an Echo. **FALSE**
   C) During the 1st year of life, a behavioral hearing screen is appropriate as the sole source of hearing screening in the child with Down Syndrome. **FALSE**
   D) The growth of children with Down Syndrome should be plotted on Down Syndrome-specific growth charts. **TRUE**
   E) All children and adolescents with Down Syndrome should receive routine screening radiographs for potential atlanto-axial instability. **FALSE**

4. *When is National Down Syndrome Day?* **3:21** (March 21). First official NDSD was in 2012!

Down Syndrome Cases

Case 1

You are working in the newborn nursery, and are asked by the nurses to evaluate a 3-hour old infant. Infant was born via spontaneous vaginal delivery, with routine resuscitation, Apgars 7/8. Infant has made some breastfeeding attempts, but has otherwise transitioned well. The mother had an elevated risk for Trisomy 21 on her prenatal screening, but declined further testing, and wants to know if this infant has Trisomy 21.

Knowing that a physical exam is the most sensitive test in the first 24 hrs to diagnose Trisomy 21, what signs on physical exam should you look for?

Generalized hypotonia

Short metacarpals and phalanges, with 5th finger hypoplasia/clinodactyly, single transverse palmar crease (no longer called simian crease), wide spacing between 1st and 2nd toe – so-called 'sandal-toe deformity'

Note: Other facial features, such as upslanting palpebral fissures, small nose, inner epicanthal folds may not be as evident in newborn, especially when there may be facial swelling from birth

Based upon physical findings, you relay to the parents that you strongly suspect their infant has Trisomy 21, and order confirmatory testing.

What problems in the early newborn period should you be concerned about, and what screening or testing needs to be performed prior to discharge?

Feeding problems – usually related to hypotonia

Hyperbilirubinemia

Apnea/bradycardia/desaturation – consider car seat testing prior to discharge

Risk of cataracts – needs bilateral red reflex

Heart defects – need screening EKG and screening pulse oximetry. If normal, can wait and have echocardiogram performed as outpatient within 1 month of life. Still needs echo performed even if had normal fetal echo

Hearing testing

Duodenal atresia – needs careful physical exam

Hirschsprung disease – evaluation if delayed passage of meconium

Transient myeloid proliferative disorder – order screening CBC

Congenital Hypothyroidism – order TSH and free T4 in addition to routine newborn screening – should be trended over first month of life

> Note – Many children with Down syndrome have mildly elevated TSH and normal free T4 levels and should be referred to Pediatric Endocrinology for further evaluation – most children will end up on replacement synthroid

Your patient, Brent Lee, is now 1 month old. He has been following with you every week since discharge, and has now re-gained his birthweight. He has seen Genetics, Cardiology, and Endocrinology.
What other recommendations do you have for this patient (hint – think long-term planning)
Enrollment into EFMP
Recommendation for Down Syndrome Support Group for parents
Enrollment into Infants and Toddlers – don't need to wait to be delayed – should be enrolled based on diagnosis alone

Brent Lee is now 12 months old.
According to the AAP Health Supervision of Children with Down Syndrome, what recommendations do you have for his care?

Hearing screen/ENT referral if frequent OM
Ophthalmology
Hg or full CBC (needs anyway to assess for iron-defiency anemia – along with lead)
Thyroid studies
Routine 12 month vaccinations

His mother is worried because he doesn't have any teeth yet. **Are you worried?**
No
Children with Trisomy 21 have delayed dental eruption, and unusual pattern of tooth eruption. After tooth eruption, he should have regular and routine dental care

Case 2
Greg is a 5yo male who presents to the office for a well child visit. He has Trisomy 21 diagnosed at birth. You skim his AHLTA records and see that his last well-visit was at 24 months. According to mother, he is followed by multiple subspecialty doctors, but the family has been very busy over the past 2years. **What additional information do you want to know?**
Faculty: provide this additional information to the residents:

- PMHx: hypothyroidism, VSD, AOM x 8, anemia
- Medication: synthroid 25mcg PO daily, multivitamin with iron
- Fam Hx: Donnie is child # 4 of 4, all other kids are healthy and developmentally normal
- Immunizations: UTD through 24mo; has not received annual flu since that visit

Greg is a picky eater, and prefers chips and cookies, which mother usually indulges to avoid a battle. His weight is 22kg and height is 102cm, **what growth chart would you use to plot these values? What nutrition guidance would you review with mother?**

- Use Down-syndrome specific growth chart – newly available since 2015 – available on Share Drive and "additional resources" section of this module.
- Patient is at 90% for weight, and 10% for height
- Children with T21 are at **risk for obesity**. PCMs should promote healthy, well-balanced diets and regular safe exercise and activity (*see below for discussion of myelopathy risk*).

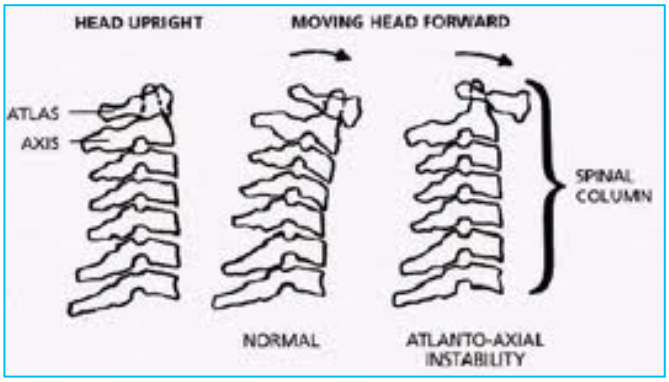
On ROS, mother reports that Greg has not been listening as well over the past year. His special education teacher also notes that she repeats things to him more than the other children. **What further studies do you recommend? What significant PMHx may be contributing?**

- Greg has had multiple episodes of OM, so he is at risk of hearing loss associated with **chronic serous otitis media**. He should be seen ASAP by Pediatric ENT. Serous otitis media risk in children ages 3-5y with DS is 50-70%.
- Initial hearing studies should be performed in nursery (**BAER or OAE**). If initial study passed, **rescreen at 6 mos** for confirmation. If any of the studies failed, refer to Peds ENT to determine if middle-ear anomaly is present (e.g. stenotic canals). A **behavioral audiogram** may be attempted at 1yr of age, but many children will not be able to complete the study and may need additional testing by BAER. Repeat screening **q6mo until normal b/l ear-specific hearing** is established, usually by age 4. Then, do **annual behavioral audiograms.** Children who demonstrate hearing loss should be referred.

Would you perform any labs today in clinic? Any other screening test?

- Annual **CBC ± ferritin** (at risk for iron-deficiency anemia, leukemia, and transient myeloproliferative disorder or TMD)
- Annual **TSH ± T4** (*Donnie already has diagnosis of hypothyroidism;* annual testing recommended regardless as risk increases with age in DS patients).
- Annual **vision screening** (refer to pediatric ophthalmologist—DS patients ages 3-5 have a 50% risk of refractive errors, which may lead to amblyopia)

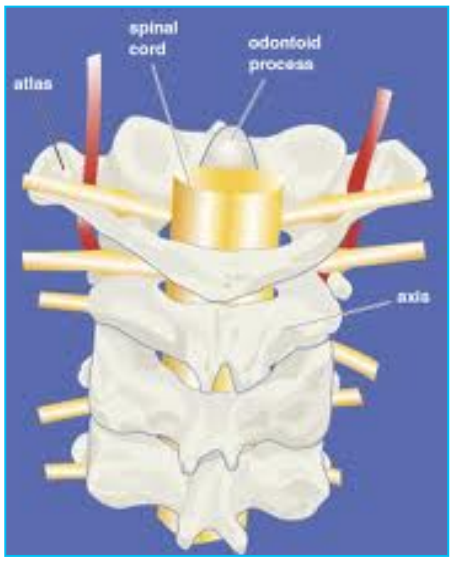
Greg's friend Lori got a trampoline for her 6th birthday. His mother wants to make sure he can play with Lori on her new trampoline. She also asks whether he can join the neighborhood soccer team. **What sports-specific guidance would you give Greg's mother? About which specific signs/symptoms would you caution Greg's mother?**



Atlanto-axial instability is found in 1-15% of children with DS. The vertebral joint space between the atlas (C1) and axis (C2) are at risk for instability with backward movement of the odontoid process of the axis. This can lead to frank dislocation and compression of the spinal cord. On **radiograph,** atlanto-axial instability

appears as a space larger than 5mm btwn the posterior aspect of the anterior arch of C1 and the ondontoid process of C2.

- Previous **AAP recommendation** was to screen *all* children with DS with lateral neck films prior to participation in sports. No evidence has proven that screening films prevent symptomatic alanto-axial instability. Therefore, the current recommendation is careful neurological evaluation for s/s consistent with spinal cord injury with annual sports physical, and reviewing these with parents. **Emergent signs of myelopathy** include neck pain, abnormal gait, change in tone, hyperreflexia, increasing clumsiness, changes in bowel or bladder control, and sensory changes.



- *N.B.* **Special Olympics** still requires XR screening of all children with DS. If alantoaxial instability is found, avoid activities that extend the neck or place pressure on head/neck muscles that cause the neck to be in extension (e.g. diving, butterfly stroke, high jump, soccer).

What other psychosocial issues would you want to address with mother today?

- Greg's last well-check was at 24mo. You should use this delay in care to inquire about **how the entire family is coping** with having a special-needs child. How are parents handling his medical needs? Are they aware of local DS support groups?
- At least 1 well child visit should involve educating parents about **increased risk of sexual exploitation**. Remind them that perpetrators are more often people their child knows and trusts, not strangers.

Down Syndrome Board Review

1. A couple comes to you with questions following the diagnosis of trisomy 21 in their now 18-week fetus. They ask what medical problems may be anticipated for the child who has Down Syndrome. **Of the following, the medical problem that is encountered MOST frequently in infants who have trisomy 21 is:**
   A. Cardiac Defec
   B. Duodenal atresia
   C. Hypotonia
   D. Polycythemia
   E. Strabismus

A syndrome is a recognizable pattern of features owing to a specific cause. Down syndrome is caused by trisomy for all, or a critical portion of, chromosome 21. Almost 99% of affected individuals have extra chromosome 21 material in every cell in their bodies; approximately 1% have a mosaic chromosome complement (46,XX/47,XX+21 or 46,XY/47,XY+21). Chromosome 21 is composed of about 400 genes. An extra copy of some or all of these genes causes a variety of potential medical problems, which should be discussed with the parents who are expecting an affected baby. It is important to note that each child who has DS is unique, and there is a spectrum of potential outcomes. Of note, individuals who have mosaic DS are anticipated to have similar features/cognitive ability to those who have full trisomy 21 because it is not possible to know which tissues contain the abnormal chromosome complement. If these individuals are affected more mildly than the typical person who has DS, this fact becomes evident over time.

Hypotonia is one of the most common abnormalities in babies who have DS, occurring in up to 90%. The degree of hypotonia varies from child to child, but usually it is not so severe as to interfere with feeding in the newborn period, and most babies who have DS are able to breastfeed effectively (assuming there is not a cardiac abnormality that precludes this). Early intervention programs should address hypotonia by offering appropriate therapies. The natural history of low muscle tone in DS is that it improves over time.

Approximately 12% of children who have DS are born with anomalies of the gastrointestinal tract, including Hirschsprung disease, esophageal atresia, tracheoesophageal fistula, and pyloric stenosis. Duodenal atresia occurs in approximately 4%.

Cardiac abnormalities are present in approximately 45% of newborns who have DS. Most are atrioventricular canal defects (almost 50%), followed by ventricular septal defects (~33%), but a variety of anomalies can occur. All newborns who have DS should undergo echocardiography, regardless of their physical examination findings.

Polycythemia is a complication during the newborn period in approximately 18% of individuals who have DS. Polycythemia can interfere with oxygenation, and sometimes partial exchange transfusion is recommended for treatment. Otherwise, this problem typically is self-limiting.

Problems affecting the eye occur in approximately 60% of children who have DS and include cataracts, lacrimal duct stenosis, nystagmus, and refractive errors. Strabismus occurs in up to 50%. Direct ophthalmoscopic examination should be performed regularly during pediatric visits, with referral to a pediatric ophthalmologist for baseline evaluation between 6 and 12 months of age. Ophthalmology follow-up should take place at least every 2 years.

2. You are called to exam a newborn girl who has multiple congenital anomalies. On physical exam you notice several "punched-out" scalp ulcers, bilateral cleft lip and palate, postaxial polydactyly of hands, and a small omphalocele. **Of the follow the infant's karyotype MOST likely is:**
   A. 45, X
   B. 45, X/47, XXX
   C. 47, XX +13
   D. 47, XX +18
   E. 47, XX +21

The newborn described in the vignette has a 47,XX+13 karyotype consistent with trisomy 13. Her unusual features of "punched-out" scalp lesions (also known as "aplasia cutis"), bilateral cleft lip and palate, and polydactyly are present in at least 50% of newborns who have this diagnosis. Other common anomalies in affected individuals include holoprosencephaly (incomplete septation of the frontal lobes), microcephaly, and cardiac defects (80%). Trisomy 13 has a poor prognosis, with approximately 50% of affected individuals dying by 2 weeks of age and 90% dying by 1 year.

Approximately 50% of individuals who have Turner syndrome have a 45,X karyotype; the remainder have a mosaic karyotype that includes a cell line consistent with Turner syndrome, such as 45,X/47,XXX, or a karyotype with 46 chromosomes wherein one of the X chromosomes is aberrant (eg, ring X, isochromosome Xq). Affected newborns may exhibit dysmorphisms or may appear completely normal. Unusual features include webbed neck with low posterior hairline, broad chest with widely spaced nipples, narrow and hyperconvex nails, and cardiac defects, most commonly bicuspid aortic valve.

Individuals who have trisomy 18 usually have a 47,XX(or XY)+18 chromosome complement. Characteristic features include intrauterine growth restriction, prominent occiput, small facial features, clenched hands with overlapping of the second finger over the third and the fifth finger over the fourth, and hypertonia. Trisomy 18 has a poor prognosis; approximately 50% of affected individuals die by 2 weeks of age and 90% die by 1 year.

47,XX(or XY)+21 is the most common karyotype seen in individuals who have Down syndrome. Affected newborns typically exhibit midface hypoplasia with epicanthal folds, upslanting palpebral fissures, small ears with overfolded pinnae, redundant nuchal skin, and hypotonia. Many affected individuals have fifth finger clinodactyly (in-curving), and almost 50% have a single transverse palmar crease. Approximately 45% of affected individuals have congenital heart defects.

3. You are attending a delivery at term for a woman who received limited prenatal care. Upon reviewing the chart while awaiting the delivery, you find that she first presented for prenatal care at the beginning of the second trimester. Limited screening was done, but you note that the maternal serum alpha-fetoprotein concentration measured at 16 weeks' gestation was described as "low." Ultrasonography was scheduled, but the mother did not show up for the appointment. She was lost to follow-up after that time, and no further was performed. **Of the following, the MOST likely potential diagnosis for the infant is:**
   A. Anencephaly
   B. Omphalocele
   C. Spina bifida
   D. Tracheoesophageal fistula
   E. Trisomy 21

Maternal serum alpha-fetoprotein (msAFP) first emerged as a screening tool for open neural tube defects in the fetus in the early 1970s. Alpha-fetoprotein (AFP) is produced by the fetal yolk sac, gastrointestinal tract, and liver, with concentrations in the fetus and amniotic fluid significantly higher than those in the maternal serum. AFP normally enters the amniotic fluid through fetal urine, with transplacental and transamniotic diffusion leading to the maternal serum concentrations. In conditions such as neural tube (eg, anencephaly, spina bifida) and ventral abdominal wall (eg gastoschisis, omphalocele) defects, where the AFP can enter the amniotic fluid as a transudate across the exposed membranes and blood vessels, the increased AFP in amniotic fluid translates to elevated maternal serum values. For unclear reason, fetuses that have tracheoesophageal fistulas may also have increased AFP concentrations. Low msAFP levels, as reported for the woman in the vignette, may be associated with fetuses affected by trisomy 18 and 21 and are felt to be related to decreased hepatic production.

Maternal screening in pregnancy has grown in complexity since the development of msAFP testing. Many centers offer a first-trimester screen between the 11^{th} and 13^{th} weeks of pregnancy. It including 3 parts: maternal serum blood testing for pregnancy associated plasma protein (PAPP-A) and human chorionic gonadotropin (hCG) as well as ultrasound measurement of the fetal nuchal translucency. This testing permits the potential identification of fetuses at risk for certain conditions including trisomy 21 and trisomy 18, but it does not detect neural tube defects.

4. You are evaluating a newborn 6 hours after his birth. Labor and delivery were uncomplicated, but amniocentesis performed during the pregnancy revealed trisomy 21. Fetal echocardiography at 20 weeks' gestation showed normal findings. The infant currently is sleeping and is well-perfused, with a heart rate of 140 beats/min and no audible murmurs. His physical features are consistent with Down syndrome. **Of the following, the MOST appropriate diagnostic study to perform is**
   A. barium swallow
   B. cervical spine radiography
   C. echocardiography
   D. head ultrasonography
   E. radiography of the abdomen

Congenital heart defects (CHDs) are the most common of the congenital anomalies, occurring with an incidence of approximately 5 to 8 per 1,000 live births (0.5% to 0.8%). The incidence of CHD is greater in stillbirths and there is an increased incidence of CHD in those who have aneuploidy. It is believed by some that the abnormal chromosomal composition rather than the cardiac abnormality is responsible for the fetal demise of those who have CHDs. The strong association between chromosomal abnormality and CHD has been shown in a number of studies that focus on identification of fetal cardiac abnormality. A number of well-defined chromosomal anomalies are associated with CHD.

Early and accurate diagnosis of CHD is important in counseling parents of children in whom a chromosomal abnormality or syndrome is suspected. Such diagnoses may have significant effects on the health and well-being of the newborns because some CHDs may require ductal patency for perfusion of either the systemic or pulmonary circulation. Therefore, echo now is considered an important component of the routine health supervision of infants who have Down syndrome and other syndromes predisposing to structural heart defects.

Although results of fetal echocardiography for the infant in the vignette were interpreted as normal, not all CHDs can be diagnosed routinely with fetal echocardiography because of the shunting pathways of the fetal circulation. For example, persistent patency of the ductus arteriosus and secundum atrial septal defects are diagnosed postnatally. Small ventricular septal defects frequently are not seen during fetal echocardiography because the pressure in the right and left ventricles are equal due to the ductus arteriosus, resulting in minimal flow across the defect prenatally.

Given the strong association between Down syndrome and CHD, echocardiography should be performed in the newborn described in the vignette. Although children born with Down syndrome have an increased incidence of duodenal atresia and other types of gastrointestinal obstruction, a barium swallow is not an appropriate initial test for an asymptomatic newborn. Cervical radiography, beginning at age 3, is important because of the risk of atlantoaxial (C1-C2) subluxation ***(PREP-2009—note new rec)***. There is no indication for routine head U/S or abdominal radiography in an otherwise asymptomatic newborn who has Down syndrome.

5. A 7-year-old patient who has Down syndrome is brought to the clinic by her mother, who is worried that the child has an increasingly abnormal gait and worsening clumsiness. At age 3 years, she was screened for cervical instability with flexion and extension cervical spine films, which showed normal results. On physical examination today, you note that she has an unsteady gait, and she has brisk deep tendon reflexes diffusely. These findings represent a significant change from 9 months ago when your neurologic examination showed only slightly diminished tone. **Of the following, the MOST likely cause of these symptoms and signs in a child who has Down syndrome is:**
   A. cerebellar medulloblastoma
   B. Chiari I malformation
   C. leukemia involving the central nervous system
   D. subluxation of the atlantoaxial joint
   E. transverse myelitis of the cervical cord

Atlantoaxial instability (AAI) is present in an estimated 15% of children (<21 years of age) who have Down syndrome (DS). Most affected individuals are asymptomatic, but an estimated 10% (1.5% of all who have DS) have symptoms relating to spinal cord compression.

The American Academy of Pediatrics (AAP) Committee on Genetics and the Down Syndrome Medical Interest Group recommend routine screening of all children who have DS between 3 and 5 years of age with lateral cervical radiographs in the neutral, flexed, and extended positions. Both groups note that screening may be a requirement for participation in the Special Olympics. The space between the posterior arch of C1 and the anterior segment of the odontoid process of C2 should be measured. Measurements of less than 5 mm are normal, 5 to 7 mm indicate instability, and more than 7 mm are markedly abnormal. However, this recommendation for routine screening for AAI remains controversial for a number of reasons.

In 1995, the Committee on Sports Medicine and Fitness of the AAP published a review of AAI in DS, highlighting several concerns regarding routine radiographic screening for AAI in children between 3 and 5 years of age. First, individuals who have DS and normal findings on screening may have abnormal radiographic results later in childhood. Conversely, some individuals whose study results initially are abnormal eventually have normalized results. Symptomatic AAI in DS is rare, raising the question of whether routine screening is necessary. Reproducibility of radiologic test results for AAI is poor in some studies. Asymptomatic AAI has not been shown to be a major risk factor for symptomatic AAI, and it is not clear that sports trauma is likely to precipitate symptomatic AAI. Finally, several publications report that individuals who have DS and AAI and symptoms or signs of cervical cord compression rarely present with rapid decompensation. ***(*PREP-2008; note NEW 2011 Recs*)***

Physical examination findings suggestive of spinal cord compression may be more predictive of significant spinal cord injury than plain radiographs, and it is wise for all individuals who have DS to undergo a careful neurologic examination prior to sports participation. At present, however, the recommendation for screening cervical spine radiographs stands, and further study is necessary before this recommendation is changed.

The child described in the vignette has symptoms and signs suggestive of subluxation of the atlantoaxial joint with compression of the cervical spinal cord. Individuals who have symptomatic AAI may present with easy fatigability, difficulty walking, unusual gait, abnormal positioning of the neck, clumsiness, sensory deficits, and hyperreflexia or spasticity. Magnetic resonance imaging of the spinal cord is warranted in such instances.

Cardiac health is the other major concern affecting participation in sports for individuals who have DS. Parents of children who have congenital heart disease should discuss this topic with their child's cardiologist. The most likely presenting symptom of central nervous system leukemia is headache. Cerebellar medulloblastoma, Chiari malformation, and transverse myelitis are no more common in those who have DS than in the general population.