Medical Issues in Patients With Down Syndrome

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In 1866, when Down Syndrome was first described by John Langdon Down, most of the individuals affected would die early, usually in their teens or twenties. As recently as the 1970’s individuals who lived longer than 45 were rare. However, today a patient with Down Syndrome does not necessarily die young. A report by Baird and Sadovnick3 in 1989 indicated that over half of individuals born with Down syndrome live into their 50’s, 40% into their 60’s and 13% to the age of 68. Today’s physician will find the care of individuals with Down Syndrome extending into their 60’s and 70’s. What may be unique about caring for these patients, however, is the kind of care they require. The medical management of Down syndrome spans the lifetime, from childhood to geriatrics. Patients with Down syndrome require the same preventative care as any other patient: vaccinations, dental care and medical care. They also require a few specialized screenings and appropriate follow up care. Not only are there issues specific to age of the patient, but also specific to systems of the body. This article will describe some of the standard and specialized care that may be required for a patient with Down syndrome.

Keywords: Alzheimer’s Disease, depression, Down syndrome, hypothyroidism, medical, mental retardation, pseudodementia, psychiatric

Down syndrome is the partial or complete trisomy of chromosome 21. This presents in 95% of cases as true trisomy 21. Mosaicism (some cells having a trisomy, some having normal diploid chromosomes) makes up 2% and Robertsonian translocation of part of chromosome 21 onto another chromosome accounts for about 3% of the diagnoses. Prevalence is estimated at 0.9 per 1,000 live births. Incidence rises relative to the mother’s age and, when maternal age is over 35 years, it is recommended that all pregnancies be screened for prospective Down syndrome defects.

Life expectancy for an infant born with Down syndrome has always been lower than that of the general population, however with advanced care now available and increased social interaction, life expectancy is approaching normal for many. Other factors that are thought to contribute to the etiology of Down syndrome include abnormal folate metabolism and a mutation in the methylenetetrahydrofolate reductase (MTHFR) gene in some mothers, indicating a potential for prevention by folic acid supplementation. For parents with increased risk, it is recommended that the mother be offered amniocentesis or CVS for chromosome studies. Explanation of the attendant risks and sensitivity/specificity profiles should be carefully made to allow the parents the freedom to make the best decision for their own peace of mind.

**INFANCY AND EARLY CHILDHOOD**

Following birth, all infants undergo routine testing, including Apgar score, thyroid screening and physical exams. An infant scoring poorly on the Apgar score due to decreased muscle tone may be suspected of having Down syndrome. Other indications that a newborn may have Down syndrome include: a flat facial profile with depressed nasal bridge and small nose, upward slant to the eyes or small skin folds on the inner corner of the eye (epicanthal folds), abnormally shaped ears, a single palmar crease, increased flexibility, fifth finger with one flexion crease instead of two, excessive space between the first and second toes, widened inter-nipple space or an overly large tongue. These infants usually undergo further testing, including a chromosomal analysis. (see Tables 1 and 2)

A congenital cataract should be suspected in an infant without a red reflex on ocular exam and should be referred immediately to an ophthalmologist for evaluation of congenital cataracts. These occur in approximately 0.3% of all infants and have a tenfold increased incidence in infants with Down syndrome.

<table>
<thead>
<tr>
<th>TABLE 1. SIGNS OF DOWN SYNDROME IN INFANTS</th>
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<tr>
<td>• Hypotonia</td>
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<td>• Flat facial profile</td>
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<td>• Overly large tongue</td>
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### Table 2. Medical Issues for Age Groups

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<td>Congenital Cataracts</td>
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<td>Congenital Cardiac anomalies:</td>
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<td>• Atrioventricular Septal Defect</td>
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<td></td>
<td>• Ventricular Septal Defect</td>
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<td></td>
<td>• Atrial Septal Defect</td>
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<td>• Tetralogy of Fallot</td>
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<td>• Patent Ductus Arteriosus</td>
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<td>Feeding problems</td>
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<td>• Failure to thrive</td>
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<td>• Muscular hypotonia</td>
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<td>• Gastroesophageal Reflux</td>
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<td>Duodenal Atresia</td>
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<td>Hirschsprung Disease</td>
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<td>Congenital Hypothyroidism</td>
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<td>Childhood &amp; Adolescence</td>
<td>Dental problems</td>
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<td>Ear infections</td>
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<td>Deafness or Hearing loss</td>
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<td>Visual deficits</td>
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<td>Acquired Cataracts</td>
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<td>Pneumonia/Bronchitis</td>
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<td>Acquired Cardiac problems</td>
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<td>Food Allergies:</td>
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<td>Sexuality and Reproduction</td>
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<td>Gastroesophageal Reflux</td>
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<td>Acquired Thyroid Disease</td>
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<td>Urinary Tract Infections</td>
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<td>Osteoarthritis</td>
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<td>Germ Cell Cancers</td>
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<td>Seizures</td>
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<td>Pseudodementia (Depression)</td>
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<td>Alzheimer’s Dementia</td>
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Fifty to sixty percent of infants with Down syndrome are born with some sort of cardiac anomaly and early detection is necessary. The most common abnormalities associated with Down syndrome are:
atrioventricular Septal Defect, Atrial or Ventricular Septal Defect alone (ASD or VSD), Persistent Ductus Arteriosus (PDA) and Tetralogy of Fallot. Atrioventricular Septal Defect is the most common, occurring in 60% of children with Downs and coexistent cardiac anomalies.\textsuperscript{31}

Infants with Down syndrome should be monitored for feeding and digestive problems. Muscular hypotonia and a protuberant tongue may make the feeding difficult. The infant may tire easily, have difficulty attaching to the breast or have trouble swallowing.

The two most serious gastrointestinal problems in this age group are duodenal atresia and Hirschsprung disease. Both are correctable surgically and produce few problems later in life.\textsuperscript{9} Congenital hypothyroidism occurs in 0.7% of infants with Down syndrome, a rate of about 30 times that of the general population.\textsuperscript{40} It is virtually undetectable at birth without the routine screening, which has become mandated in most states. Without appropriate treatment, hypothyroidism produces increased developmental delay. In fact, prior to the use of routine screening, it represented the most common preventable form of mental retardation.\textsuperscript{66}

\textbf{CHILDHOOD/ADOLESCENCE}

In 1999 a cohort study of school-aged children in Western Australia identified the most common medical needs in this population. In the results, Leonard et al.\textsuperscript{34} reported that one third of school-aged children had been hospitalized during the previous 12-month period, more than three times the 9% of the general population. Nearly half of these admissions were due to the need for general anesthesia for dental or other simple procedures. In cost of care, cardiac and ear disease were the largest financial burdens to the health care system.

Celiac disease was a problem for 0.95% of the group compared with 0.03% of the general population. The most problematic gastrointestinal complaint was constipation, a chronic concern for these children due in part to smooth muscle hypotonia of the bowels.

Auditory problems were reported 2.5 times more commonly than in the general population. Additionally, as stated above, otolaryngological procedures were the most common reason for hospitalization. Nearly 50% of children with Down syndrome reportedly had “glue ear,” a condition in which the mucus-secreting lining of the middle ear is overactive with a concomitant blockage of the eustachian tube. This seemingly innocent problem can lead to permanent hearing loss in the affected ear unless a drainage tube is inserted into the tympanic membrane. This may also be called simply a middle ear infection.

Cardiac problems were usually diagnosed in infancy. They will not be addressed here.

Sexuality is an issue often overlooked in this population. Keep in mind that adolescents and adults with Down syndrome have sexual desires paralleling those of the general population. Masturbation should be expected and is a healthy part of self-discovery. Incidence of masturbation has been estimated at 42% in males and 52% in females (compared to 100% in males and 25% in females in the general population). Sexual activity may also occur, both willingly and unwillingly.

Contraception and personal safety should be addressed before these issues surface.\textsuperscript{64}

\textbf{ADULTHOOD}

In an article similar to Leonard’s, Van Allen et al.\textsuperscript{63} examined the health care concerns of adults with Down Syndrome in 1999. The group in their study was a population of institutionalized patients in British Columbia. Health concerns for adults are also widespread. Eye disorders were the norm and chief concerns were cataracts, refractive errors, strabismus and amblyopia. Other problems, such as keratoconus were reported and were more common in the elderly. By the time these patients had
reached adulthood, half had hearing loss, usually secondary to otitis media. In at least a quarter of them, the hearing loss was significant.

Of the chronic respiratory problems, pulmonary hypertension due to congenital cardiac anomalies was the most serious. Other problems included recurrent pneumonia with incomplete recovery and chronic interstitial changes of the lungs due to recurrent aspiration. Gastroesophageal reflux is a problem common in this group. It is increased in any population when the patient has neurogenic dysphagia (neurological problems swallowing), obesity and a sedentary lifestyle. Obesity occurs in 70% of male and 95% of female adults with Down syndrome. This condition responds to dietary restriction when utilized.

Urinary problems documented in this group included recurrent urinary tract infections (25%), which, if severe, may progress to pyelonephritis and potential renal failure.

Musculoskeletal disorders include degenerative osteoarthritis with osteoarthritis of the spine affecting nearly a quarter of the population. The incidence predictably increases with age. Spinal degeneration is a problem with this group too and has an insidious presentation. It may go unnoticed in less communicative adults. Carpal tunnel disease may present similarly to spinal degeneration and is much easier to correct. Fractures and trauma are common, increasing with age. Atlantoaxial instability is a serious but infrequent complication of Down syndrome and should be screened for in childhood.

Zipursky et al. reported in 1992 that the overall rate of leukemia in the Down syndrome population is twenty times the rate of the general population. Testicular germ cell tumors have been reported in a series of case reports by Dieckmann. Solid tumors most common to this population include lymphomas, extragonadal germ cell tumors, testicular germ cell tumors. Cancers related to lifestyle risks are lower, including lung and cervical cancers.

Neurological concerns in this population include seizures and Alzheimer disease. Seizures occur in 5-10% of children with Down syndrome, up to 50% of middle-aged and up to 55% of elderly. Seizure incidence increases with the onset of Alzheimer disease. Estimates of Alzheimer’s disease in the Down syndrome population indicate that approximately 25% of adults over 35 years old have symptoms of Alzheimer’s. It occurs approximately 3-5 times more often than in the general population and at 20 or more years earlier in the life of the patient. Individuals with suspected dementia need to be evaluated carefully, as a pseudodementia caused by depression may be present.

Specific Systems

Ophthalmology

1. **Congenital cataract**: if present at birth and uncorrected, may lead to permanent visual loss due to atrophy of the optic tract. Cataracts may occur at any time during a patient’s life. Approximately 33% of middle-aged adults and 65% of elderly adults with Down syndrome have cataracts. It is recommended that infants see a pediatric ophthalmologist within the first six months of life and then annually thereafter.69

2. **Glaucoma** is a serious eye problem which may appear in infancy or later in life. If left untreated may lead to increased intraocular pressure and visual loss.

3. **Myopia, strabismus and amblyopia**, which require corrective lenses, are the rule rather than the exception. It is estimated that 60% of children with Down syndrome have strabismus and 50% have refractive errors.74
Dental

1. In her 1998 article, Pilcher described the dental care of children with Down syndrome very thoroughly. Children with Down syndrome should be monitored frequently by a dental specialist who is familiar with problems common in this group. Communication between dental and medical professionals is important. Oral lesions, for example may be serious; leukemia may present initially as an oral lesion or gingival hemorrhage. Due to hypotonia of the oral musculature, the angle of the mouth is frequently down-turned and drooling may lead to oral cheilitis at the lateral lips.

2. Tongue: may become scalloped or crenated due to tongue thrusting and the pressure of the teeth on the tongue. It may also become fissured, plicated or “scrotal” due to mouth breathing. Care must be taken to keep these fissures from becoming impacted by food.

3. Microdontia: 35-50% of Down syndrome individuals have microdontia in primary and secondary teeth. This may lead to odd shaped teeth or wide spacing where food can become trapped and decay. Partial anodontia, or congenitally missing teeth, is present in approximately 50%.

4. Hypoplasia and hypocalcification: Surface bonding is recommended for all children with Down syndrome (as with those without Down syndrome) and fluoride in the water is optimal.

5. Teeth: Mal-alignment, malocclusion and poor resorption of primary teeth may lead to the need to adjust and may require orthodontic work.

6. Bruxism: This grinding of teeth or clenching of the jaw is a common finding in individuals with Down syndrome. It can lead to overloading the teeth and subsequent breakdown. Dental appliances are available to displace the pressure.

Auditory

Sixty to 80% of children with Down syndrome have hearing loss. Hearing loss may be sensorineural or a conductive loss or both. Ear infections in individuals with Down syndrome are common. Contributing causes include a smaller than normal ear canal, frequent obstruction of the eustachian tube (a tube that goes from the ear to the throat to normalize pressure within the ear) or the increased production of fluid by the inner ear mucosa, leading to retraction ear infections, sometimes called “glue ear.” Individuals who are less communicative, frequently ear infections will go unnoticed until they progress to mastoiditis and hearing loss. This occurs in approximately one fifth of some populations. Recommended testing of hearing includes Brainstem Auditory Evoked Response (BAER) by the age of two months, evaluation by otolaryngologist (ENT specialist) if the patient has recurrent ear infections, annual auditory testing from ages 3-13 and every other year after that. All patients with DS should be tested with otoscopy at every visit.

Immune System, Hematology, Oncology

1. In a study by Miller and Pothos, abnormalities were described in the following components of the immune system: IgA, IgM, IgG2 and IgG4. Additionally, pre-B cells and natural killer cells were low in a subset of their study population. The abnormalities in IgM and IgG2 may predispose individuals with Down syndrome to common bacterial infections. The lack of pre-B and natural killer cells may predispose to viral infections.

2. Hepatitis B is common in institutionalized patients with and without Down syndrome. Given the lack of pre-B and natural killer cells, institutionalized individuals with Down syndrome are more likely to develop Hepatitis B than other patients in the same institution. Of those who contract Hepatitis B and develop a carrier state, there is a higher risk of acute thyroiditis. A series of three Hepatitis B vaccinations are recommended at some point early in the life of these patients, however, especially prior to institutionalization. Individuals with abnormalities in IgA may still receive vaccinations. Children with chronic cardiac and respiratory disease are candidates for use of pneumococcal, respiratory syncytial virus, and influenza vaccines.
3. **Disorders of Red Blood Cells**: Frequently, infants are born with erythrocytosis. This usually resolves in 2-3 weeks and is not a problem. Another condition involving RBC’s is macrocytosis. This is due to a disorder in the metabolism of folate. Unless anemia accompanies the macrocytosis, no treatment is needed.\(^{35}\)

4. **Platelet Disorders**: Thrombocytopenia may require transfusion. Thrombocytopenia needs to be monitored closely as it may indicate a transient leukemia. Thrombocytosis, or elevated platelet counts, can be seen in approximately 20% of newborns. This does not cause a problem and usually resolves in approximately one month.\(^{35}\)

5. **Disorder of White Blood Cells (WBC)**: Up to 10% of newborns with Down syndrome may have an elevated WBC.\(^{14}\) This is a condition called “transient leukemia” because it usually disappears within weeks to months. Approximately 30% of these infants will later develop acute non-lymphoid leukemia (ANLL), also called acute myeloid leukemia (AML). If this happens, it is most likely before the age of four years.\(^{54}\)

   a. **Acute Non-Lymphoid Leukemia (ANLL)** is a very rare kind of leukemia in children without Down syndrome. Recent studies have shown that the gene AML-1 is located on Chromosome 21.\(^{23}\) The extra copy of AML-1 increases the risk by 50% of cells with this gene progressing to leukemia. While ANLL is quickly fatal if left untreated, it responds remarkably well to current therapy and one study reported a 100% four-year survival after treatment.

   b. The development of another kind of leukemia, **Acute Lymphoblastic Lymphoma (ALL)** is also frequent in children with Down syndrome. The prognosis of ALL in children with Down syndrome is similar to that of other children. It is thought that the presence of the third chromosome 21 causes a genetic disruption and leads to cytogenetic changes. This is supported by data showing that in mosaic Down syndrome, the cells which go on to develop leukemia are those with the trisomy present. Overall, leukemia affects approximately 1 in 150-200 children with Down syndrome. It is 10 to 30 times more prevalent in the Down syndrome population than the general population. According to Zipursky,\(^{65}\) about half of leukemia in the Downs population is ANLL, half ALL. In patients with Down syndrome and ALL, the leukemia is less likely to go into the lymphatic system, however it is more likely to have specific chromosomal changes called translocations which are associated with poorer prognosis. Treatment is the same as in the General population. Methotrexate is the mainstay of chemotherapy. Even if the child can tolerate the effects of the chemotherapy, prognosis for patients with ALL has been poor. In one study of British patients, survival at 5 years after ALL diagnosis was only 28% in patients with Down syndrome; survival was 59% in patients without Down syndrome. Most deaths occurred during the induction phase of treatment.\(^{39}\) Despite this grim history, however, intense treatment has improved survival in these patients. The studies now show a survival equal to that of children without Down syndrome. Additionally, for those with acute megakaryoblastic leukemia (a subtype of ALL), event free survival at four years was reported as nearly 100% in one study.\(^{55}\)

**GASTROINTESTINAL**

1. **Hirschsprung disease**: Hirschsprung disease is the congenital absence of neural development in all or part of the colon. This condition makes it impossible to pass stool through the bowel. It is usually diagnosed in the first 48 hours of life, however milder cases may not present seriously until later in life. Hirschsprung disease occurs in 0.3-2.7% of children with Down syndrome.\(^{8,11,20,32}\) Diagnosis is made by barium enema followed by rectal biopsy if needed. Treatment is partial colectomy with reanastomosis at a later date.

2. **Gastroesophageal reflux**: is also a common problem, seen as early as infancy. It is thought to be due to muscular hypotonicity producing decreased pressure at the gastroesophageal sphincter. In infants, 85% of the cases are evident by seven days old and another 10% by the sixth week. The problems associated with GER in all ages are heartburn, indigestion or chest pain. In the very young or non-communicative adult population, this may simply present as increased fussiness, irritability or food avoidance. Several studies may be used to investigate this
including barium swallowing studies, an upper GI study, gastric-emptying test, endoscopy or an esophageal pH probe. Treatment of GER in infants is positioning the infant in a semi-upright position while feeding and either on the side or stomach while sleeping and possibly dietary changes such as either thickening the formula or changing to a soy-based formula. In infants where these changes are not effective, acid reducing agents such as H2 blockers (nizatidine, famotidine, cimetidine, or ranitidine) or proton pump inhibitors / PPI’s ( pantoprazole, omeprazole, lansoprazole, or esomeprazole) may be helpful. In adults with GER, dietary changes may include thickened or bland food, not eating for more than one hour prior to retiring, sleeping with the head of the bed elevated, and, of course, H2 blockers or PPIs. If all the above is not successful, both infants and adults may need to resort to surgical correction. Gastric fundoplication is a folding of the gastric fundus at the point of esophageal entry to apply an artificial pressure at the lower esophageal sphincter. It is effective in about 90% of cases.

3. **Hernias**: are seen in one fifth of patients with DS. These include hiatal, ventral, post-operative incisional and inguinal hernias. Predisposing factors include to muscular hypotonicity, non-compliance with post-operative instructions and obesity.

4. **Constipation**: can cause discomfort, is predisposed in this population by decreased motor activity and hypotonia. Recommendations for treatment are primarily dietary: fiber, stool softeners, lactulose. Recently, some literature has indicated that low serotonin activity in the bowels may be responsible. A trial of an SSRI at very low doses may be useful to rule out this condition.

5. **Celiac disease**: is caused by an autoimmune response in the small bowel to foods with gluten. These foods include wheat, barley, rye and oats. Celiac disease is thought to be fairly uncommon in the general population but some studies have shown a higher incidence in patients with Down syndrome. In a cohort study of children in Sweden, Carlsson reported the incidence of celiac disease in approximately 2% in the general population compared to 19% in the children with Down syndrome. Please note that incidence does show racial diversity. Symptoms include diarrhea and/or vomiting, “failure to thrive,” and later, rashes and arthralgias. Serum screening is done with antigliadin antibody (AGA), antiendomysium antibodies (EMA) and IgA antibodies to transglutaminase. The latter two tests are felt to be a good screening and are recommended by some gastroenterologists for all children with Down syndrome, even if no gastrointestinal symptoms are present. This is still expensive and yield may be low. Gastroenterologists may want to treat if these are positive. The gold standard, however, remains small bowel biopsy. Treatment is withdrawal of gluten from the diet. Dietary restrictions are difficult to enforce so after symptoms are controlled, a trial of adding the grains one at a time back into the diet may be helpful as an individual may not react to all of them. Symptoms of celiac disease, as listed above, may also be caused by annular pancreas.

**CARDIOPULMONARY**

1. **Inborn anomalies**: Cardiovascular anomalies are present 50-60% of all infants born with Down syndrome. The most common defect in these patients is atrioventricular septal defect, or AV canal defect. It makes up 60% of all cardiovascular anomalies in the Down population. In contrast, the atrioventricular septal defect makes up only 2.9% of cardiac anomalies in the general population. Atrial or ventricular septal defects may occur independently as well and they, along with patent ductus arteriosus and Tetralogy of Fallot make up another 20% of cardiac anomalies in this population. Pulmonary hypertension frequently accompanies cardiac anomalies. Since children with Down syndrome have more immature lung development at birth than the general population, this is a special concern. In infants with left-to-right shunt, as occurs in atrioventricular, ventricular septal defects or Tetralogy of Fallot, excessive pressure is placed on the blood vessels of the lungs. This pressure can quickly cause irreversible changes to both the blood vessels and the lung parenchyma (tissue). Surgical correction of cardiac anomalies that produce pulmonary hypertension is vital to the infant’s survival and is advocated between six and 12 months of age. Mortality in infants with Down syndrome who
have uncorrected cardiac anomalies is high. Of those who have appropriate surgical correction and survive past 5 years, however, 50% will likely survive into their sixties.\(^{69}\)

2. **Mitral valve prolapse**: MVP occurs at a frequency 5-15% more often in children with Down syndrome than in the general population. Mitral valve prolapse and other cardiac anomalies are not always detectable by physical examination. Echocardiography with review by a pediatric cardiologist is strongly recommended for all infants with Down syndrome by their third month of life. Antibiotic prophylaxis treatment protocols should be followed when MVP is detected. In a study of asymptomatic adults with Down syndrome, Hamada et al.\(^{22}\) found that 27% had echocardiographic evidence of MVP, 20% showed mitral calcification, 16% had mitral valve regurgitation and 12% had aortic valve regurgitation.

3. **Acquired valvular problems**: Adults may develop cardiac problems such as aortic insufficiency, congestive heart failure, valvular problems and myocardial infarction (heart attack). Less vocal patients may not tell anyone about shortness of breath or chest pain, therefore, annual chest x-ray and echocardiogram as well as lipid profiles are recommended in all adults with Down syndrome. Cardiology consultation should be requested when warranted.

4. **Sleep apnea** is a common problem in Down syndrome. The enlarged tongue, uvula and soft palate predispose toward obstruction. Hypotonia and tracheomalacia both complicate the picture as well. An individual with heavy snoring or daytime somnolence or irritability (often mistaken for Attention Deficit Hyperactivity Disorder) should be carefully evaluated for this condition. Sleep studies are the gold standard in the diagnosis. Treatment with Continuous Positive Airway Pressure (CPAP) machines or surgical correction may be warranted.

**RENAL, SEXUAL/GENITOURINARY**

1. **Congenital Renal Anomalies**: Infants with Down syndrome may be born with renal problems. These can often be seen on screening ultrasound before the baby is born. The most common problem with the kidneys is obstruction of the ureteropelvic pelvic junction, which may cause hydronephrosis. There are also sometimes alterations in the structure or maturation of the kidney tissue.\(^{75}\)

2. **Genitalia**: Other physical anomalies associated with the genitourinary system include hypospadias in 25-50% of males, undescended testes in 5% of males and small penis and scrotum (incidence unreported). The first two need to be corrected surgically.\(^{75}\)

3. **UTI’s**: Urinary tract infections can go undetected in individuals with Down syndrome due to decreased reporting. Symptoms may include new onset or increased frequency of urinary incontinence or foul odor. Renal disease may also be present in these individuals and a careful evaluation should be done annually of the renal system.

4. **Sexuality**: Sexuality in patients with Down syndrome is a complex and often ignored issue. Individuals with Down syndrome are sexual beings as much as any other patients.\(^{64}\) They have similar issues to deal with, including sexual identification as a child and maturation as an adolescent. Social issues regarding sexuality will not be addressed in this article.

5. **Reproduction**: Reproduction is possible in this population, although it is less common. Fertility is impaired in both genders. Males were long assumed to be sterile but there is one case report in 1980 of a male infant fathered by a man with Down syndrome. Women with Down syndrome may conceive and carry to term infants with and without Down syndrome. A report by Bovicelli et al.\(^{7}\) in 1982 documented that of 26 pregnancies in women with Down syndrome, 10 were normal, 10 had Down syndrome, 2 mentally retarded. Three were malformed, 1 had microcephaly, 2 were aborted and the remainder were born stillborn. Contraception and gynecologic treatment is similar to that in the general population.\(^{7}\)
ENDOCRINE

1. **Congenital hypothyroidism:** Congenital hypothyroidism is the most common cause of preventable mental retardation in the world. This statement applies to infants with and without Down syndrome. Infants develop a complete working hypothalamic-pituitary-adrenal axis system by the third trimester and hypothyroidism may develop in utero. The fetus is thought to be protected by maternal thyroid hormone until delivery. Following delivery, every newborn is tested for hypothyroidism to allow for early correction if necessary. For infants with Down syndrome, this is even more important.

2. **Acquired Thyroid Disorders:** While different researchers' reports vary, it is estimated that between 10% and 30% of patients with Down syndrome have thyroid disease. Hypothyroidism is the most common thyroid disease. It is important to keep in mind that symptoms of Down syndrome itself may mimic those of hypothyroidism: decreased growth, hypotonia, slowed development, dry skin and hair, constipation and tongue enlargement. Causes of thyroid disease include autoimmunity and thyroiditis. It is recommended that all individuals with Down syndrome be screened for thyroid malfunction at birth, six months, one year and annually. This involves only a TSH level initially with T4 and possibly T3 if the TSH is abnormal. Additionally, testing anti-thyroglobulin and anti-microsomal antibodies may be predictive of future thyroid problems. Hyperthyroidism is much less common than hypothyroidism, but is estimated to occur in approximately 1-5% of patients with Down syndrome. It is usually caused by the autoimmune disease Graves disease. Hyperthyroidism is usually symptomatic with tachycardia, anxiety, sweating, flushed skin and hot flashes, occasionally hair loss and decreased attention span. Treatment is identical to that in the general population. It involves a choice between: 1) suppression with antithyroid drugs, 2) surgical resection of the thyroid, and 3) radioactive iodine ablation treatment. Both resection and ablation require lifetime hormone replacement.

MUSCULOSKELETAL

1. **Atlanto-Axial Instability (AAI)** is estimated to occur in 85% of individuals with Down syndrome, however only 12-20% of these cases are found on radiographic screening. Further, only 1-2% require treatment. The American Academy of Pediatrics recommends screening radiographs for all individuals who wish to participate in Special Olympics or any other sports event. Regardless of sports participation, screening is recommended by the start of school or if the patient has symptoms of instability. The screening consists of lateral radiographs of the spine. Symptomatic AAI may present in a variety of ways. Some symptoms include gait changes, fatigue, neck pain or limitation, torticollis (twisting the neck), clumsiness, sensory deficits, spasticity, hyperreflexia, clonus, extensor-plantar reflex, and other upper motor neuron and posterior column signs and symptoms. AAI is something that other professionals need to keep in mind too, as manipulation of the neck can occur under anesthesia, during dental procedures or spinal manipulation by chiropractors.

2. **Hip dysplasia** is also a common finding among individuals with Down syndrome. Hip dysplasia appears to occur in phases, starting as early as childhood and progressing throughout life. In children it has been reported to occur in 1.3% – 4.5% and by the age of 70, up to 18% may be affected.

NEUROLOGIC

1. **Development:** Caregivers should be informed that development of motor function may be delayed as compared to the general population. Physical and occupational therapy may facilitate both the development of the motor function and the caregiver's understanding of the process.

2. **Alzheimer's dementia:** This progressive dementia occurs with greater frequency in individuals with Down syndrome. The gene for Familial Alzheimer's Dementia (FAD) has been identified on chromosome 21. The gene encodes a protein which produces amyloid A, the protein in the
amyloid plaques which are believed to be the cause of Alzheimer’s dementia. Individuals with trisomy 21 are thought to produce even more of the amyloid A and develop Alzheimer’s dementia at a younger age than individuals with the normal chromosomal complement. Lott states that approximately 25% of individuals with Down syndrome will develop Alzheimer’s dementia by the time they are 35. This contrasts to the general population where only 5-10% of those in their 60’s develop Alzheimer’s. Cognitive screening, therefore, is recommended for all individuals with Down syndrome by the age of 30.

3. **Pseudodementia**: It was previously thought that Alzheimer’s was unavoidable and any mental deterioration was diagnosed as Alzheimer’s dementia. However, increased treatment for depressive illness with subsequent positive response, indicates that many previously diagnosed dementia cases were likely pseudodementia due to depression.

4. **Seizures**: Seizures can occur at any time. It is estimated that 5 to 10% of individuals with Down syndrome have seizures. There appear to be two peaks in incidence. “Infantile spasms” occur in the first two years of life. An infantile spasm may be a generalized or complex partial seizure. A second peak occurs in the second or third decade of life. This usually represents generalized seizures. Seizures may be associated with a variety of problems: infection, tumor, Alzheimer’s dementia or may be idiopathic. Evaluation may require EEG (electroencephalogram), magnetic resonance imaging (MRI) of the brain or lumbar puncture and cerebrospinal fluid analysis. Treatment with anticonvulsants is usually effective although, if the cause is Alzheimer’s disease, seizures may become harder to control with advanced disease.

**SUMMARY**

In summary, Down syndrome is not a simple disease. The triplication of the smallest chromosome in the body produces consequences that are manifest in every area of development and every system. A thorough examination and close follow-up using the guidelines above should serve as a foundation of medical care for these individuals.

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