CME

Care of the Adult Patient with Down Syndrome

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Abstract: Individuals with Down syndrome have an increased risk for many conditions, including cardiovascular disease, cancer, infections, and osteoporosis, and endocrine, neurological, orthopedic, auditory, and ophthalmic disorders. They also are at increased risk for abuse and human rights violations and receive fewer screenings and interventions than the population without Down syndrome. In this literature review, the most common health conditions associated with Down syndrome are examined, along with the topics of sexual abuse, menstrual hygiene, contraception, and human rights. Clinical guidelines for this population are summarized in an effort to assist practicing physicians in improving their provision of health care to the adult patient with Down syndrome.

Key Words: adult, Down syndrome, medical care

Down syndrome, also known as trisomy 21, occurs in 1 of every 691 live births in the United States.[1] It is by far the most common birth defect and chromosomal disorder in live-born infants.[2] Despite its prevalence, there is minimal literature on the comprehensive care of adult patients with Down syndrome. Guidelines for the care of pediatric and adolescent patients with Down syndrome have been discussed more thoroughly elsewhere.[3–6] Patients with Down syndrome are at risk for the same conditions as the population without Down syndrome, in addition to the health problems associated with trisomy 21.[7] The most common causes of death in people with Down syndrome include Alzheimer disease–related conditions, respiratory infections, leukemia, ischemic heart disease, cerebrovascular accidents, diabetes, and seizures.[8–11]

We examine the most common health conditions associated with Down syndrome, along with sexual abuse, menstrual hygiene, contraception, and human rights. We discuss clinical guidelines for this population in an effort to assist practicing physicians in improving their provision of health care to the adult patient with Down syndrome (see also the online-only table that summarizes the recommendations, http://links.lww.com/SMJ/A29).

Cardiovascular Disease

Because life expectancy has increased to almost 60 years in people with Down syndrome,[12,13] atherosclerotic cardiovascular disease is a rapidly growing problem.[8,10] Patients with Down syndrome are at increased risk for cardiovascular risk factors, including diabetes mellitus, centripetal obesity, and hypothyroidism.[8,14,15] They also have a less favorable lipid profile, with higher total cholesterol and triglycerides and lower high-density lipoprotein compared with their siblings.[15] Adult studies show increased mortality in the Down syndrome population from ischemic heart disease, cardiovascular disease, and cerebrovascular disease.[8,10] Table 1 outlines suggested screening guidelines.

Congenital heart disease is the most frequent systemic malformation in children with Down syndrome and is present in 40% to 50% of the population.[14,16,17] Adults with Down syndrome who have congenital heart disease have higher all-cause mortality rates[10]; however, one study has shown that at an experienced center, these patients could undergo cardiac surgery with a low risk of morbidity and mortality.[18]

Key Points

- Individuals with Down syndrome have a continually lengthening life expectancy, leading to expanded healthcare needs in adult patients.
- Individuals with Down syndrome have a higher risk of many conditions, including atherosclerosis, cardiovascular disease, endocrine disorders, some cancers, Alzheimer dementia, osteopenia, ophthalmic disorders, dysmenorrhea, and abuse; however, they do not, in general, receive the quality of care provided to the population without Down syndrome.
- The health needs of adults with Down syndrome should be viewed from the perspective of current standards of care and management while making adjustments to match individual needs and medical conditions.

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Table 1. CVD screening for individuals with Down syndrome

Population	Intervention	Caveats
Individuals 2–20 y	Fasting lipid panel every 3–5 y[a] (as long as results remain within normal limits)	If any of following CVD risk factors are present: overweight (BMI ≥85th percentile), obesity (BMI ≥95th percentile), hypertension (BP ≥95th percentile or ≥140/90), cigarette smoking, diabetes mellitus OR positive family history of dyslipidemia or premature CVD
All individuals ≥20 y	Fasting lipid panel every 5 y[b]	None
All individuals ≥18 y	BP measurement every 1–2 y[c]	Screen every year in people with BP 120–139/80–89, screen every 2 y in people with BP <120/80

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease.
[a]*American Academy of Pediatrics recommendation.*
[b]*US Preventive Services Task Force 2008 recommendation.*
[c]*US Preventive Services Task Force 2007 recommendation.*

Endocrine Disorders

Thyroid Disease

Although Down syndrome is well known to be associated with thyroid dysfunction,[14,19–23] more recent literature suggests that this association has been overstated.[24,25] Much debate exists as to optimal screening frequency and benefit of treating subclinical hypothyroidism. Several studies showed that transient hypothyroidism in this population is common, self-resolving, and not necessarily a precursor to definite hypothyroidism.[22,25,26] Subclinical hypothyroidism is the most common type of thyroid dysfunction, and there is no benefit to using thyroid replacement therapy to treat it[22,24,27] unless the patient is symptomatic or has thyroid peroxidase antibodies.[24,28] A screening interval of 5 years is recommended in asymptomatic adults.[24,28,29] In patients with subclinical hypothyroidism, we recommend obtaining a thyroid antibody assay (thyroid microsomal and thyroid autoantibodies); if results are normal, patients with subclinical hypothyroidism should continue to be screened every 5 years.[26,28] If autoantibodies are positive, then more frequent screening should be pursued.

Diabetes Mellitus

Data on the prevalence of diabetes mellitus in patients with Down syndrome are conflicting. Several studies show individuals with Down syndrome have a 3- to 10-fold increased risk of diabetes mellitus and a 10-fold increase in mortality[9,30,31]; however, other studies do not confirm this.[12,32] Given the lack of data on diabetes mellitus in adults with Down syndrome, it is appropriate to test blood glucose and hemoglobin A1c in symptomatic patients and to follow the American Diabetes Association screening recommendations (Table 2).

Early Menopause

Consensus exists that menopause occurs early in women with Down syndrome, but clinical management has not been determined.[33,34] In 2001, the general population median age of menopause was 51.2 years, whereas the median age for women with Down syndrome ranged from 44.7 to 47.1.[19,34,35] In women ages 13 to 27, there is no difference between the percentage with Down syndrome who are ovulating (76%) and that in the control group (73%).[19] Menopausal symptoms may

Table 2. American Diabetes Association screening recommendations

Population (age)	Intervention	Caveats
Individuals 10–21 y (or beginning at puberty if occurs before age 10)	Fasting plasma glucose every 2 y	If any of following CVD risk factors are present: overweight (BMI ≥85th percentile or weight >120% ideal for height) PLUS any 2 of the following risk factors: family history of type 2 diabetes mellitus in first- or second-degree relative, nonwhite race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander), signs or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, or PCOS)
Individuals 21–45 y	Consider fasting plasma glucose	If overweight (BMI ≥25) and if additional risk factors are present: habitually physically inactive, first-degree relative with diabetes mellitus, member of high-risk ethnicity (same as for children), have delivered a baby weighing >9 lb or have been diagnosed as having GDM, hypertensive (≥140/90), have dyslipidemia or PCOS, have signs associated with insulin resistance, history of vascular disease
All individuals ≥45 y	Fasting plasma glucose every 3 y	None

BMI, body mass index; CVD, cardiovascular disease; GDM, gestational diabetes mellitus; PCOS, polycystic ovary syndrome.
Adapted from Diabetes Care *2013;36(Suppl 1):S11–S66.*

be difficult to identify in patients with decreased verbal skills, but they should be treated just as they are in people without Down syndrome, with hormone therapy for hot flushes, irritability, and sleep disturbances. Hormone therapy should not be used in women with an increased risk of thrombosis.

Neurological Disorders

Investigators have noted anatomic and physiologic differences in the brains of individuals with Down syndrome. Two neurologic pathologies that occur with increased prevalence in Down syndrome are Alzheimer disease and seizure disorder.[36–38] Both conditions increase in prevalence with advancing age.[39] Seizures occur in a trimodal distribution: 40% occurring in those less than 1 year of age and 40% in those 20 to 30 years of age.[36] The third peak of seizure onset is believed to correlate with the onset of Alzheimer dementia later in life. The histopathology consistent with this dementia is present with near uniformity by age 35; however, prevalence studies indicate that not everyone develops the accompanying clinical symptoms.[40,41] Diagnosing Alzheimer dementia in patients with Down syndrome can be challenging because personality and behavioral changes present as the first symptoms.[38,40,42] This differs from the general population, in whom deficits of short-term memory, language, and orientation prevail.

Most mental status examinations do not take into account intellectual disability; Down syndrome–specific screening examinations are required. The Dementia Scale for Down's Syndrome, the Dementia Questionnaire for Persons with Mental Retardation, and the Cambridge Examination for Mental Disorders of Older People with Down's Syndrome and Others with Intellectual Disabilities have been tested in this population.[43,44] A baseline battery of dementia testing should be performed for all patients with Down syndrome at least once before age 35, with repeat testing every 1 to 5 years thereafter.[40,44]

Cancers

Leukemia occurs with high frequency in the Down syndrome population.[30,45] The most common types are acute lymphocytic leukemia and myeloid leukemia of Down syndrome. With acute lymphocytic leukemia, the presentation and course of disease are similar to that of the general population; however, with myeloid leukemia of Down syndrome, the counterparts of which are myeloid dysplastic syndrome and acute myeloid leukemia, the course and response to treatment differ. Intensive treatment leads to better survival rates than in patients without Down syndrome.[45]

Patients with Down syndrome also have increased risks of retinoblastoma, germ cell tumors (especially testicular carcinoma), and lymphomas.[8,45] Conversely, solid tumors, most notably breast and lung cancers, and secondary malignancies are significantly decreased.[45] Although no screening examinations show improved leukemia outcomes in the general population, because of the increased risk in Down syndrome, signs and symptoms of leukemia and lymphoma such as refractory anemia, lethargy, fever, painful joints and extremities, pallor, lymphadenopathy, hepatosplenomegaly, bleeding, or easy bruising should be evaluated with a complete blood count.[3] Diligent yearly testicular and ophthalmic examinations may help in the detection of these cancers. It is recommended that women with intellectual disabilities follow the same mammography screening as that in the population without intellectual disabilities,[46] but there is insufficient evidence to reach a definitive conclusion regarding women with Down syndrome.[47]

Infectious Diseases

Infectious diseases account for one-fifth of all Down syndrome deaths.[8] Respiratory illnesses account for the largest proportion of infections and are the leading cause of infectious death.[11,12,48] The increased susceptibility to respiratory infections is thought to be multifactorial and includes immune system deficiency,[6,49] anatomical defects of the respiratory tract, obstructive sleep apnea, gastroesophageal reflux, and chronic silent aspiration. Because of this high mortality, yearly influenza vaccinations should be encouraged and individuals with Down syndrome considered candidates for serial boosters of Pneumovax.[4]

Digestive System Disorders

Of the autoimmune digestive diseases, only celiac disease has been extensively studied in individuals with Down syndrome. Celiac disease usually is diagnosed in childhood[50]; however, it can present at any age and is most commonly silent or latent.[4] The prevalence is 5% in the Down syndrome population.[30,50] There are no screening guidelines for adults with Down syndrome, but because of the increased risk, chronic abdominal symptoms (including vague symptoms such as dyspepsia, diffuse abdominal pain, and flatulence), mouth sores, and skin rashes should be addressed and evaluated with serologic antibody testing; a combination of immunoglobulin A tissue transglutaminase and total immunoglobulin A is recommended.[51]

Decreased gut motility leading to chronic constipation is a common problem in people with Down syndrome. Referral to an occupational therapist or dietitian to assist with strategies to improve fiber and fluid intake and to increase physical activity should be considered. Fiber supplements and safer laxatives, such as polyethylene glycol, can be used to treat chronic constipation.[4,6] Severe constipation should trigger screening for celiac disease and hypothyroidism. Gastroesophageal reflux disease also occurs with increased frequency in Down syndrome and should be managed in the same manner as in the non–Down syndrome population.

Orthopedic Disorders

Atlantoaxial instability occurs in 15% of individuals with Down syndrome and should be assessed during the adult patient's childhood.[4] Concerning symptoms that should prompt immediate medical evaluation are neck pain, decreased range of motion,

torticollis, changes in gait, changes in bowel or bladder control, paresthesias, weakness, or paralysis.[3,4]

Individuals with intellectual disabilities are at increased risk of low bone mineral density (BMD),[52–55] and Down syndrome is an independent risk factor for low BMD and fractures.[56] Despite the increased risk and greater frequency of fractures, individuals with intellectual disabilities have a much lower screening rate than the general population.[52,57,58] The International Society for Clinical Densitometry lists among its target populations for BMD testing "adults with a disease or conditions associated with low bone mass or bone loss," a category that includes adults with Down syndrome (Table 3).[59] No baseline age at which to begin screening has been established.[55,59] Screening at age 40 for individuals living in institutions and age 45 for those living in the community has been suggested.[60] Treatment of low BMD and osteoporosis should be approached in the same way as in the general population.

Individuals with Down syndrome tend to have ligamentous laxity, which can lead to acquired hip dislocation, chronic patellar dislocation, pes planus, and ankle pronation.[4] Other common orthopedic problems are scoliosis, osteoarthritis, and degenerative joint disease.

Ophthalmic and Auditory Disorders

In adults with Down syndrome, cataracts are the most frequent ophthalmic disorder, followed by refractive errors, strabismus, and presbyopia.[7] Ophthalmic disorders increase with age[7] and contribute to a reduced quality of life and decreased ability to perform instrumental activities of daily living.[61] Yearly vision screening and an ophthalmic examination should be performed at least every other year, with increased frequency as a person ages.[62] It is important to investigate the possibility of impaired vision whenever declines in functional abilities occur in older adults with Down syndrome.

Common auditory conditions found in this population are large amounts of cerumen causing auditory canal blockage, abnormal tympanic membrane structure, and increased adenoid tissue in the hypopharynx, all of which can lead to profound hearing loss. It is recommended that adults with Down syndrome undergo an annual clinical hearing assessment and audiology assessment every 2 years.[62,63]

Gynecological Concerns

Menstrual problems are common and frequently disruptive to both patients and caregivers, yet provider involvement in this area is suboptimal.[64,65] Intellectual disabilities make menstrual hygiene especially challenging and can lead to absenteeism from school and have a negative impact on the patient with Down syndrome and her family.[66] It is important, therefore, to use a consistent approach and have a positive and supportive outlook on menstruation.[67] Many girls and women with intellectual disabilities can manage menstruation themselves or with assistance if given support. Preparation and education beginning at approximately age 9 using visual aids (eg, anatomically correct dolls, personalized books) are helpful.[67,68] Practical considerations to address are the types of products to use, whether reusable or disposable, the girl's or woman's comfort, ease of use, and cost per year.[67] Other topics to address are increasing the frequency of bathing routines during menstruation, ensuring the patient wears feminine hygiene products (eg, tampons, sanitary napkins) for no longer than 4 hours before changing, and encouraging the use of firm-fitting cotton or cotton-blend underpants to avoid vaginal infections and rashes.[67]

Many women with Down syndrome may be unable to sufficiently express their experience. A menstrual chart can help correlate changes in behavior with menstrual discomfort.[67] Changes in position, massage, or placing a hot pad or cold pack on the abdomen may help. Treatment with nonsteroidal anti-inflammatory drugs throughout the menstrual cycle is a first-line treatment for dysmenorrhea. If after 3 months adequate pain management has not been achieved, then a second-line treatment with a hormonal agent should be considered.[68]

Papanicolaou (Pap) tests and pelvic examinations may be difficult to perform because of poor comprehension and cooperation, and for many women with intellectual disabilities it is painful, frightening, and may call to mind past episodes of abuse.[46]

Table 3. International Society for Clinical Densitometry bone mineral density screening recommendations[a]

Population	Recommendation
Adults with Down syndrome age ≥40 y living in institutions[b]	Test every 2 y with DEXA scan of hip and lumbar spine
Adults with Down syndrome age ≥45 y living in the community[a]	Test every 2 y with DEXA scan of hip and lumbar spine
Women ≥65 y, men ≥70 y	Test every 2 y with DEXA scan of hip and lumbar spine
Postmenopausal women <65 y, men <70 y	Testing indicated if risk factors present: low body weight, prior fracture, use of high-risk medications, or presence of disease or condition associated with bone loss
Adult of any age	Testing indicated if any of the following present: fragility fracture, disease condition associated with low bone mass or bone loss, taking medications associated with low bone mass or loss, or being considered for pharmacologic therapy

[a] *Adapted from International Society for Clinical Densitometry official positions—adult.*[60]
[b] *Adapted from* J Am Board Fam Med *2007;20:399–407.*[61]

Studies and changes in cervical screening guidelines show that it is safe to reduce the frequency of Pap testing. The risk for women with Down syndrome developing cervical cancer is variable because its occurrence in women who have never been sexually active is rare. It should not be assumed, however, that individuals with Down syndrome are sexually inactive, and screening should be offered to all women older than 21 years. Screening intervals should be individualized to each woman's risk profile.[46] Education and an explanation of the examination using terms the patient understands and visual teaching aids are an important parts of the process. The use of a long, narrow Huffman speculum is preferable because a pediatric speculum is too short for the adult vagina.[69] If the speculum examination is not tolerated, then a blind swab used in human papillomavirus testing can be attempted. Although the blind swab only has a 44% yield of endocervical cells, it is a reasonable alternative for obtaining Pap tests in women who otherwise may not be screened.[69] If screening for sexually transmitted infections (other than human papillomavirus) is required, the less invasive urine test should be performed.[46]

Hormonal contraceptive agents frequently decrease menstrual flow and duration. The options for the types of contraception (with risks and benefits of each) should be addressed with the patient and her caregivers. Low-dose combined contraceptives are useful for obtaining menstrual regularity or decrease in flow. Chewable oral contraceptives or a transdermal patch should be considered in cases of swallowing difficulty. Depot medroxyprogesterone acetate (DMPA) given intramuscularly every 12 weeks has been used successfully, with amenorrhea rates approaching 70% over time.[68] DMPA carries the Food and Drug Administration "black box" warning of potentially irreversible osteopenia, which may be more detrimental in Down syndrome because of the higher risk of osteoporosis.[69a] The vaginal ring is generally not recommended because of placement difficulties. Implanon has not been studied in this population, but the common adverse effect of unscheduled bleeding makes it less desirable. Intrauterine devices have been shown to decrease menstrual flow and are useful as an alternative treatment for women with heavy cycles and normal uterine cavities if they are candidates for insertion.[69b]

In addition to the risks seen in the general population, women with intellectual disabilities may be at increased risk for deep vein thrombosis as a result of their more sedentary lifestyle and increased repercussions of weight gain (most problematic with DMPA) secondary to impeded mobility.[68] Patients with Down syndrome who are at increased risk for thromboembolic events may benefit from nonestrogen contraception such as Depo-Provera injections and intrauterine devices, just as women without Down syndrome.

Abuse in Patients with Intellectual Disabilities

The prevalence of physical, psychological, and sexual abuse is greater in people with intellectual disabilities.[70–72] The US Department of Justice reports that 68% to 83% of women with developmental disabilities will be sexually assaulted in their lifetime and fewer than half will seek assistance from legal or treatment services.[73] In studies around the world, female learners (younger than age 22) with intellectual disabilities were more likely to experience sexual violence than the rest of the population and girls and women were more likely to be sexually abused than their male counterparts.[74] Research suggests that an abuser is most likely to be a male family member or caregiver who is well known to the woman, and much less commonly a boy or man with intellectual disabilities.[2,67] Because of the inability of some patients with intellectual disabilities to verbalize abuse, sexual abuse may be diagnosed only via physical or behavioral symptoms (eg, random inappropriate sexual behavior [grabbing or hitting genitals, self-caressing, excessive masturbating]; alterations in bowel- or bladder-emptying patterns; alterations in appetite, sleep, or mood; changes in participation in community), sexually transmitted infections, or pregnancy. All patients with Down syndrome should be screened for physical and sexual abuse. This is the moral and professional duty of the provider and is required by many legal jurisdictions.[71]

Human Rights

Healthcare providers can support the rights of individuals with intellectual disabilities and act as their advocate. An important role is helping families seek sound advice regarding estate planning, application for medical disability, independent living facilities, and transition care plans after they graduate from school-based support systems.[4] Decisions about guardianship should be determined early. When guardianship is not appropriate, the question of advanced directives, especially medical and financial powers of attorney, should be addressed.[63]

Article 16 of the United Nations Universal Declaration of Human Rights states "men and women of full age, without any limitation due to race, nationality or religion, have the right to marry and to found a family. They are entitled to equal rights as to marriage, during marriage and at its dissolution." These universal human rights are breached when people with intellectual disabilities lacking the capacity to consent are sterilized.[75] Although forced sterilization is no longer used for eugenic purposes, hysterectomies continue to be performed for menstrual management in several countries, including the United States.[75] Hormone treatment usually is adequate to address menstrual issues in women with intellectual disabilities, but in some instances, the family may request surgical measures, such as endometrial ablation or hysterectomy. Both of these procedures render the patient sterile, which has ethical and legal implications. The decision to end a woman's fertility is a difficult decision, and the clinician and patient's family should strongly consider all other options before proceeding with this course of action.[67,76] Providers should consult ethics committees and educate themselves about state laws,[68] keeping in mind that an adult with Down syndrome is considered competent to make medical decisions unless he or she has a court-appointed guardian.[63]

Conclusions

This review advocates for excellence in the care of adult patients with Down syndrome. The complexity of care required by patients with Down syndrome can be challenging, but their families and those who care for them find it rewarding.[6] To provide individuals with Down syndrome the high quality of care they deserve, scheduling for more frequent appointments or longer appointment blocks may be required. In all aspects of care, it is essential to follow this basic principle: the health needs of individuals with intellectual disabilities should be viewed from the perspective of current standards of care and management, while making adjustments to match their individual needs and medical conditions.[76]

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