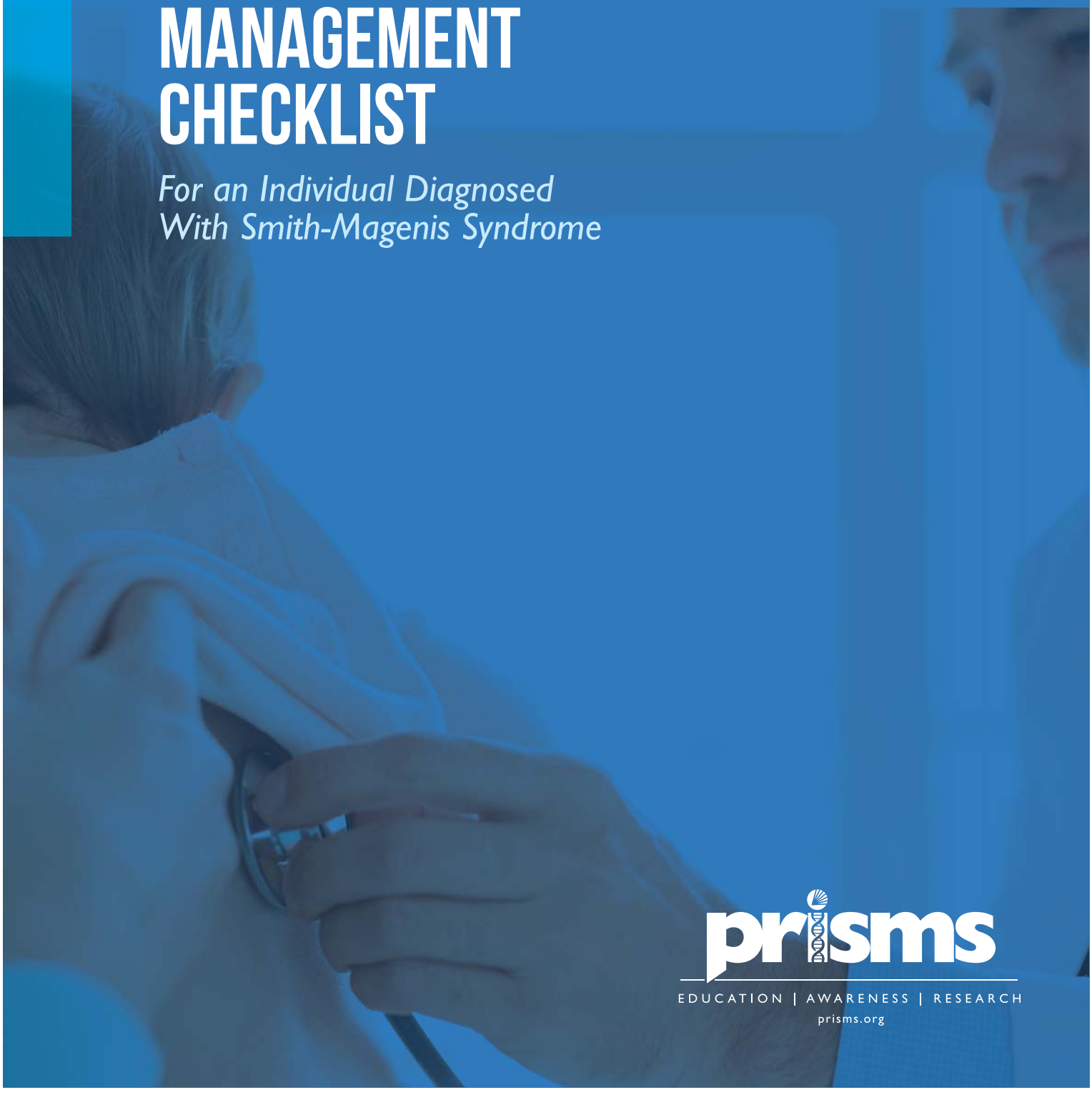
PRISMS PROFESSIONAL ADVISORY BOARD

SMS MANAGEMENT CHECKLIST

For an Individual Diagnosed With Smith-Magenis Syndrome



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Management involves evaluation for manifestations of Smith-Magenis Syndrome (SMS) and treatment to mitigate associated symptoms and conditions. Variability among individuals and developmental changes are important to recognize. These guidelines were developed and approved by PRISMS Professional Advisory Board. First published as part of the in-depth review of SMS that appears in GeneReviews (Last update June 2012), these guidelines were updated and approved by PRISMS Professional Advisory Board[1]. The terminology used here that is USA-focused may be adapted, as appropriate, for use in other countries.

Source: PRISMS Professional Advisory Board

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Parents and Researchers Interested in Smith-Magenis Syndrome

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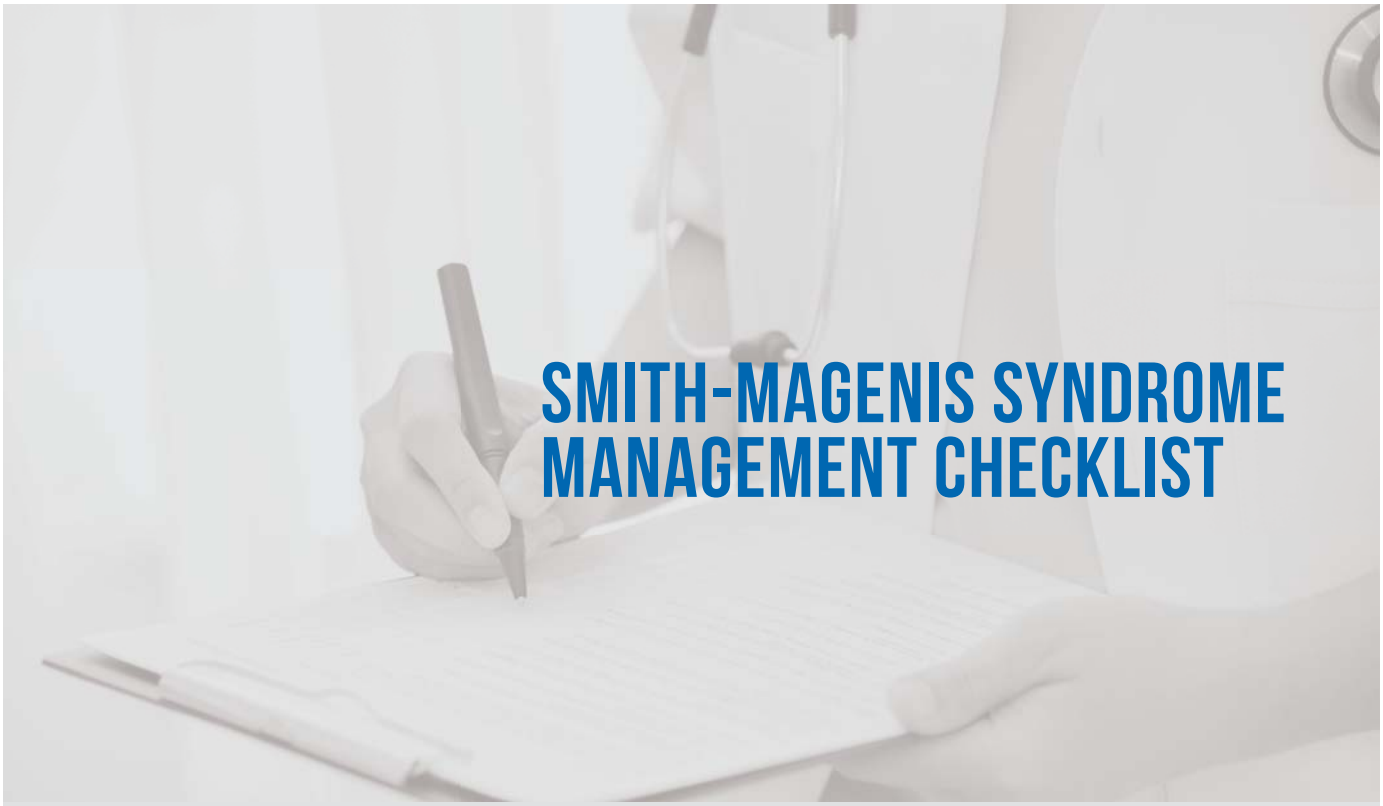
Source: Written by PRISMS' Management Guidelines Working Group (ACMS, KB, CB and JC) with review and final approval by PRISMS Professional Advisory Board 24 January 2018.



SMITH-MAGENIS SYNDROME MANAGEMENT CHECKLIST

	CHECKLIST This checklist is intended for use by physicians caring for a child with Smith-Magenis syndrome
1. GROWTH	
• Birth parameters usually in normal range. Failure to thrive (FTT)and short stature are often observed at early ages (17p11.2 deletion cases especially). • Obesity with increased BMI appreciated with age, especially for RAI1 mutation cases. • Hyperphagia, food foraging at night (especially. at older ages), psychotropic medication side effects (increase appetite; weight gain), and/or general sedentary lifestyle contribute to risk of obesity.	☐ Obesity: A “hands on” approach to stay active, have fun, and stay fit ideally should begin at a young age. Weight management requires dietary changes and food portioning in combination with increased movement and physical activity, limiting overall time spent in sedentary activity, and avoidance of nighttime eating. Encourage movement and exercises that are fun.

Source: PRISMS Management Guidelines Working Group (Ann CM Smith, Kerry Boyd, Jane Charles, Christine Brennan) with review and final approval by PRISMS Professional Advisory Board on January 24, 2018. Format adapted from the Health Watch Table from Surrey Place [www.surreyplace.on.ca/Clinical-Programs/Medical Services/Pages/PrimaryCare.aspx].

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2. HEENT (Head, Eyes, Ears, Nose, Throat)	
• Vision: ~ 85% have eye abnormalities, including strabismus, myopia, iris anomalies, and microcornea. • Retinal detachment, which may be related to high myopia and self-injurious/aggressive behaviors, occurs in ~20% (age 10 years - adult). • Hearing: Chronic ear infections & middle ear dysfunction is common (>50%), with hearing loss documented in >75%. Conductive loss is more common at younger ages and mixed and/or sensorineural loss at older ages. Hearing loss may fluctuate and worsen with age. Hyperacusis is recognized in ~75%. • Throat: Almost all have delayed speech, ~ 65% have palatal abnormalities such as velopharyngeal insufficiency (VPI) and cleft palate. A deep, hoarse voice is common. • Prone to recurrent sinus infections and/or upper respiratory infections (including pneumonia), which occur in 50-75%. • Speech/language – communication delays (~90%): diminished vocalization/sound production and feeding difficulties' in infancy; significant oromotor dysfunction; expressive language skills more delayed than receptive language.	☐ Refer to an ophthalmologist following initial diagnosis and annually thereafter ☐ Refer to an ENT surgeon regarding palatal abnormalities following initial diagnosis and annually thereafter. ☐ Routine and careful assessment of middle ear function; annual audiologic surveillance across the lifespan to facilitate early identification and intervention. ☐ Recognition of hyperacusis to permit implementation of helpful management strategies: explanations and warnings before anticipated sound exposure (e.g., fireworks); use of headphones or earplugs to dampen the sound; and/or complete avoidance of the upsetting sounds. ☐ Immunologic evaluation with infectious prophylaxis considered in accordance with standard practice. Quantitative serum immunoglobulins (IgG, IgA, IgM) and vaccine titers (pneumococcus especially) at initial diagnosis, with additional studies as clinically indicated. ☐ Refer to a speech and language pathologist in early childhood to address feeding difficulties, optimize functional communication and oral motor abilities; encourage use of sign language and total communication approach to reduce maladaptive behaviors by improving communication. ☐ Consider referring to an occupational therapist (OT) or physical therapist (PT) regarding oral sensorimotor development.
3. DENTAL	
• Children and Adults: ~ 75% have dental • anomalies including tooth agenesis (premolars), taurodontism and/or root dilacerations. • Poor dental hygiene may lead to cavities.	☐ Arrange early and regular dental assessments ☐ Review brushing and flossing techniques with each dental cleaning. Strategies to assist with oral hygiene and gingival care usually require parental supervision (e.g., rechargeable toothbrush with 2-minute timer)

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4. CARDIOVASCULAR	
• ~ 50% have congenital cardiovascular abnormalities (17p11.2 deletion cases); structural defects of heart have not been reported in RAI1 mutation cases. • Hypercholesterolemia in childhood is common (57%). • While the risk for premature atherosclerosis in adulthood is unknown, screening for premature atherosclerotic disease may be warranted given rare reports of cerebrovascular accidents.	☐ Obtain an echocardiogram at time of initial diagnosis. ☐ Refer to a cardiologist at initial diagnosis with follow up arrangements with congenital heart disease clinics, depending on the abnormalities detected. ☐ In adulthood, follow-up as clinically indicated. ☐ Monitoring of hypercholesterolemia by annual lipid profiles; treatment with diet or medication at older ages in accordance with standard practice.
5. GASTROINTESTINAL	
• Feeding problems and gastro-esophogeal reflux disease (GERD) are common. • Over 75% have history of constipation, which can greatly influence behavior, comfort level, mood, activity level & appetite.	☐ Undertake a clinical assessment in infancy with attention to feeding problems and evidence of GERD ☐ Monitor regularly for constipation and manage proactively.
6. GENITOURINARY	
• Congenital renal or urinary tract abnormalities occur in ~35% of 17p11.2 deletion cases but are not reported in RAI1 mutation cases. • Nocturnal enuresis is common (80%) in children and may remain an issue into school age.	☐ Obtain a renal ultrasound at initial diagnosis ☐ Screen for urinary tract infections with an annual urinalysis or as indicated.

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7. MUSCULOSKELETAL	
• Delayed gross and fine motor skills • ~ 75% of children develop scoliosis, which may become more severe with age. • Markedly flat or highly arched feet (pes planus or pes cavus) and unusual gait (foot flap), tight heel cords (equinus; decreased dorsiflexion), and/or persistent toe-walking (60%) are generally appreciated in childhood. Low tone (truncal hypotonia) persists into adulthood.	☐ Obtain spine X-rays at diagnosis to assess for vertebral anomalies then annually to assess for scoliosis. ☐ Assessment/fitting for orthotics may be helpful. ☐ Exercises/activities that focus on improving abdominal and truncal tone are recommended.
8. NEUROLOGY	
• Children: ~ motor delay with hypotonia (particularly in infancy); truncal hypotonia persists into adulthood (lordotic postural issues). • ~ 75% have peripheral neuropathy, often associated with decreased pain and temperature sensation. • Hereditary neuropathy with liability to pressure related palsies may occur in those with relatively large chromosomal deletions including the PMP22 gene. • ~ 10% - 30% have evident and subclinical epilepsy. Onset of seizures associated with menses (catamenial) at puberty have been seen in some females. • Mild intention tremor of hands may be noted in early childhood.	☐ Undertake a neurological assessment at diagnosis and annually thereafter as clinically indicated ☐ Provide periodic neurodevelopmental assessments during infancy and childhood. Assessments should be completed approximately every three years unless an acute change in clinical presentation or imaging results necessitates more frequent testing. ☐ Consider subclinical seizures if behavior change occurs ☐ To evaluate type and etiology of seizures, consider electroencephalography (EEG), and Computed Axial Tomography (CAT) scan and Magnetic Resonance Imaging (MRI) scan of head as indicated during infancy and childhood. Consider medication for seizures, taking into account side effects (wakefulness, weight gain).

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9. ENDOCRINE	
• ~ 25% are mildly hypothyroid. • Hypercholesterolemia is common (>50)%) • Hypoadrenalism (adrenal insufficiency), though rare, can occur, particularly in children.	☐ Undertake annual thyroid function and fasting lipid testing ☐ Start screening for hypercholesterolemia in childhood and consider dietary modification for hypercholesterolemia and the possible role of medication ☐ Assess for hypoadrenalism in the event of any serious illness
10. INFECTIOUS DISEASE / IMMUNIZATION	
• Lowered serum immunoglobulins profiles, observed >50%, may contribute to chronic otitis media, sinusitis and/or upper respiratory infections.	☐ Arrange qualitative immunoglobulin testing at diagnosis ☐ Immunization in accordance with AAP guidelines ☐ Undertake periodic review if recurrent infections ☐ Evaluation by immunologist with prophylactic strategies to prevent infections may benefit select patients

	CHECKLIST This checklist is intended for use by physicians caring for a child with Smith-Magenis syndrome
11. SLEEP	
• Virtually 100% have sleep disturbances. These are usually associated with an inverted circadian rhythm of melatonin release (daytime high, nighttime low). Inverted melatonin rhythm occurs in >90%. • Frequent nighttime awakenings, shortened sleep periods, absence of REM sleep, and daytime napping are common. • Wandering at night and/or food foraging is common and may present safety issues. • Chronic sleep debt impacts daytime functioning. Daytime sleepiness with sudden short naps are common.	☐ Undertake a sleep study with attention to sleep disturbance, short sleep cycle, early rising, frequent night awakenings, and daytime napping ☐ If there is evidence of snoring, symptoms of obstructive sleep apneaand/or other signs of sleep abnormalities, arrange a sleep study and multiple sleep latency testing. ☐ Consider evening melatonin (< 3 mg) and morning acebutolol (presumed to counter daytime melatonin release) ☐ Melatonin and acebutolol (beta-blocker) have been used with some success. Over-the-counter melatonin dosages may be inexact and acebutolol use has some contraindications ☐ Consider strategies to address nighttime safety issues (e.g., enclosed bed system) ☐ An accommodation for a scheduled nap or “quiet time” should be included in the educational plan during school years. Ideally this should occur late morning or after lunch, but not late afternoon (>3pm).

	CHECKLIST This checklist is intended for use by physicians caring for a child with Smith-Magenis syndrome
12. COMMUNICATION, MOTOR, AND SENSORY PROCESSING	
• Evaluations and services will be needed early (as soon as a diagnosis is confirmed) and will very likely be required through the school years.	☐ Arrange assessments by a speech-language pathologist (SLP), Physical Therapist (PT), and Occupational Therapist (OT) in infancy and periodically thereafter as appropriate. ☐ In the USA, SLP, PT, and OT services may be available free of charge in the US through early intervention programs for children under the age of 3. ☐ Use of sign language and total communication programs, including sign, computer assisted devices and tablets, augmentative communication, voice output systems, and/or picture exchange (PECS) may serve as additional forms of communication to traditional speech-language therapy that focuses solely on spoken communication. This will promote improved communication skills, which may have a positive impact on behavior. Note that using alternative forms of communication will not hinder the development of speech or spoken communication, but will promote development of language abilities. ☐ Need for PT, OT or SLP to be determined annually at school meetings.

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13. BEHAVIORAL/MENTAL HEALTH	
• Maladaptive behaviors prominent in the neurobehavioral phenotype of SMS include a unique constellation of repetitive (stereotypic) and self-injurious behaviors (SIB) (e.g., teeth grinding, self-hugging, head banging, self-hitting and/or biting, and inserting objects into body orifices). The pattern/range of maladaptive behaviors may change with age. For example, onset of ~~nail yanking~~ onychotillomania (i.e., pulling out finger- and toe-nails) often occurs in late childhood or adulthood rather than in infancy or preschool years. • Impaired behavioral regulation, cognitive inflexibility (i.e., difficulties tolerating change/transitions), and frustration intolerance, combined with intellectual and communication difficulties, likely contribute to challenging behaviors (i.e., impulsivity, aggression, tantrums, disobedience, hyperactivity, avoidance, elopement). • Clinical behavioral diagnoses include autism spectrum disorder (ASD), intellectual disability (ID), attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and obsessive-compulsive disorder (OCD). • Socialization skills, while deficient, emerge as relative strengths in adaptive functioning compared to delays in communication and daily living skills. • Relative strengths exist in visual processing (i.e., visual learners alert to environment and attentive to meaningful visual details); long-term memory for faces, places, and people; engaging personality; and good sense of humor. • Caregivers of individuals with SMS demonstrate high rate of anxiety and depression symptoms and report difficulties with caregiver well-being and self-care.	☐ In children, arrange early intervention with specific preventative behavioral strategies and special education techniques that emphasize individualized instruction. ☐ Behavior support plans can be implemented to help mitigate behavioral concerns at home and school. Psychologists, , teachers, and occupational therapists typically develop and implement such plans ☐ Use of computer-assisted technology may be helpful to promote adaptive communication skills, which in turn can lessen maladaptive behaviors. ☐ Sensory dysregulation is a factor contributing maladaptive behaviors. Providing compensatory positive sensory experiences may help reduce behavioral concerns. ☐ Psychotropic medications: There is limited research on the efficacy of psychotropic medications in the treatment of co-morbidities (cognitive impairment, learning disabilities, behavioral disorders, obsessive compulsive features, anxiety and mood symptoms) associated with SMS. Clinicians must rely on best practices of managing underlying reasons emotional and/or behavior disturbances (health, environment, life stressors) and engaging in medication trials specific to the presenting behavioral problems. Psychotropic medications should be initiated by an experienced physician (preferably in the context of a multidisciplinary team), one at a time, aiming for lowest effective doses. Regular medication reviews are required to monitor efficacy, side effects and to avoid long term use and polypharmacy. ☐ An annual interdisciplinary team assessment of socio-emotional needs and behavioral difficulties is warranted. These should include the use of well-validated parent, teacher (if available), and self-report (if cognitively able to complete) measures. ☐ Plan respite care, family psychological, and social supports. ☐ Facilitate contact with advocacy organizations, such as Parents and Researchers interested in Smith-Magenis Syndrome (PRISMS- www.prisms.org), to provide support and education.

	CHECKLIST This checklist is intended for use by physicians caring for a child with Smith-Magenis syndrome
14. SCHOOL/ACCOMMODATION & SERVICES[#]	
• Services – ongoing need (PT/OT/speech) beginning in early childhood through school years. • Transition planning should begin when children are in middle school. Transition planning will facilitate a student's move from school to post-school activities. [#]The terminology used here is USA focused and may be adapted, as appropriate, for use in other countries.	☐ Early Intervention (EI) for birth-3 years. EI is a system of services for infant/toddlers with developmental delays or disabilities focus on intervention to facilitate development of skills that typically develop during the first three years of life (can include the following skills: speech/communication, motor, cognitive, social/emotional, self-help). For infants and child prior to the third birthday, there will also be an individualized family service plan (IFSP). ☐ For school age, child should have an Individualized Education Plan (IEP) for learning and behavioral accommodations. "Otherwise health impaired" is often the category used to designate services. ☐ If the child is on medication, an Individualized Health Plan (IHP) should be in place by the School RN. ☐ If behaviors are disrupting the child's learning, the school is required to do a Functional Behavioral Assessment (FBA) and implement a Positive Behavior Intervention Plan (BIP) ☐ LINK: management/functional-behavior-assessment-and-behavior-intervention-plans. ☐ The IEP should be updated annually or when learning or behavior issues arise. Consider eligibility classification to be "Otherwise Health Impaired" to accommodate medical concerns and behavioral challenges. ☐ Needs for PT, OT or ST to be determined annually at IEP meeting. ☐ Transition planning, which begins in middle school (~ age 13-14y), is a process mandated in the US by the Individuals with Disabilities Education Act (IDEA) for all students who have an Individualized Education Program (IEP) in K-12 education. The purpose is to facilitate the student's move from school to post-school activities. The transition planning must start before the student turns 16, be individualized, be based on the student's strengths, preferences, and interests; and include opportunities to develop functional skills for work and community life.

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15. OTHER ISSUES	
• Transition to Adulthood • Transition Medicine (shift from pediatric to adult healthcare)	☐ Guardianship/medical decision maker ☐ Adulthood: The Individual Service Plan (ISP) is the written details of the supports, activities, and resources required for the adult individual to achieve personal goals. The general welfare and personal preferences of the individual are the key consideration in the development of all plans to articulate decisions and agreements made during a person-centered process of planning and information gathering. The ISP team, (the individual, medical specialists, specific provider staff, and guardians and caregivers), is focused on assessment of the individual's needs, including personal choices and preferences, significant health care, mental health or behavioral needs and related maintenance needs and safety and financial skills. ☐ Limited data and recommendations are currently available for adults (GUIDE) but more information is emerging as identified – LINK to PRISMS GUIDE ☐ Transition Medicine provides appropriate medical care and social support services to the growing population of adolescents/young adults with SMS as they move from pediatric to adult healthcare.

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Resources: www.prisms.org - The official website for Parents and Researchers Interested in Smith-Magenis Syndrome

REFERENCES

Brendal MA, KA, King1, Zalewski CK, Finucane BM, Introne W3, Smith ACM3, Carmen C Brewer CC. Auditory Phenotype of Smith-Magenis Syndrome. J. Speech, Language, and Hearing Research, 2016 (in press)

Darfour L, Verleyen P, Lesage K, Holvoet M, Devriendt K. Bilateral renal tumors in an adult man with Smith-Magenis syndrome: The role of the FLCN gene. European Journal of Medical Genetics. 59:499-501

De Leersnyder H, Bresson JL, de Blois MC, Souberbielle JC, Mogenet A, Delhotal-Landes B, Salefranque F, Munnich A. Beta 1-adrenergic antagonists and melatonin reset the clock and restore sleep in a circadian disorder, Smith-Magenis syndrome. J Med Genet. 2003; 40:74–8. [PMC free article] [PubMed]

Edelman EA, Girirajan S, Finucane B, Patel PI, Lupski JR, Smith AC, Elsea SH. Gender, genotype, and phenotype differences in Smith-Magenis syndrome: a meta-analysis of 105 cases. Clin Genet. 2007; 71:540–50. [PubMed]

Finucane B, Dirrigl KH, Simon EW. Characterization of self-injurious behaviors in children and adults with Smith-Magenis syndrome. Am J Ment Retard. 2001; 106:52–8. [PubMed]

Finucane ref for EYE findings;

Foster RH, Kozachek S, Stern M, Elsea SH. Caring for the caregivers: an investigation of factors related to well-being among parents caring for a child with Smith-Magenis syndrome. J Genet Couns. 2010;19:187–98. [PubMed]

Greenberg F, Lewis RA, Potocki L, Glaze D, Parke J, Killian J, Murphy MA, Williamson D, Brown F, Dutton R, McCluggage C, Friedman E, Sulek M, Lupski JR. Multi-disciplinary clinical study of Smith-Magenis syndrome (deletion 17p11.2) Am J Med Genet. 1996; 62:247–54. [PubMed]

Gropman AL, Duncan WC, Smith AC. Neurologic and developmental features of the Smith-Magenis syndrome (del 17p11.2). Pediatr Neurol. 2006; 34:337–50. [PubMed]

Gropman AL, Elsea S, Duncan WC Jr, Smith AC. New developments in Smith-Magenis syndrome (del 17p11.2). Curr Opin Neurol. 2007; 20:125–34. [PubMed]

Hildenbrand HL, Smith AC. Analysis of the sensory profile in children with smith-magenis syndrome. Phys Occup Ther Pediatr. 2012; 32:48–65. [PubMed]

Hildenbrand HL, Smith AC. Analysis of the sensory profile in children with smith-magenis syndrome. Phys Occup Ther Pediatr. 2012; 32:48–65.

Itoh M, Hayashi M, Hasegawa T, Shimohira M, Kohyama J. Systemic growth hormone corrects sleep disturbance in Smith-Magenis syndrome. Brain Dev 2001. 26:484–486.

Perkins T, Rosenberg JM, Le Coz C, Alaimo JT, Trofa M, Mullegama SV, Antaya RJ, Jyonouchi S, Elsea SH, Utz PJ, Meffre E, Romberg N. Smith-Magenis Syndrome Patients Often Display Antibody Deficiency but Not Other Immune Pathologies. J Allergy Clin Immunol Pract. 2017 Sep - Oct;5(5):1344-1350.

Smith ACM and Gropman A. Smith-Magenis syndrome (chapter) in Management of Genetic Syndromes, 3rd Edition. Suzanne B. Cassidy, Judith E. Allanson (Eds), (2010), John Wiley & Sons, Inc., Hoboken, NJ, USA. ISBN: 978-0-470-19141-5.

Smith ACM, Boyd KE, Elsea SH, et al. Smith-Magenis Syndrome. 2001 Oct 22 [Updated 2012 Jun 28]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1310/

Spadoni E1, Colapietro P, Bozzola M, Marseglia GL, Repossi L, Danesino C, Larizza L, Maraschio P. Smith-Magenis syndrome and growth hormone deficiency. Eur J Pediatr. 2004 Jul;163(7):353-8. Epub 2004 May 8.

Stamatakis L, Metwalli AR, Middelton LA, Marston Linehan W. Diagnosis and management of BHD-associated kidney cancer. Fam Cancer. 2013 Sep;12(3):397-402

Tomona N, Smith AC, Guadagnini JP, Hart TC. Craniofacial and dental phenotype of Smith-Magenis syndrome. Am J Med Genet A. 2006; 140:2556–61. [PubMed]

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