Parents and Researchers Interested in Smith-Magenis Syndrome

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MISSION STATEMENT:

"PRISMS is dedicated to providing information and support to families of persons with Smith-Magenis Syndrome (SMS), sponsoring research and fostering partnerships with professionals to increase awareness and understanding of SMS."

History and programs:

PRISMS was founded in 1993 by Margaret and Scott Miller, parents of a child with Smith-Magenis Syndrome, and Ann C.M. Smith, M.A., D.Sc., (hon.), co-discoverer of "SMS," and Brenda Finucane, M.S., CGC. PRISMS is a registered 501c(3) non-profit organization.

PRISMS serves as a central clearinghouse for information about SMS, providing a range of educational and support services, including:

- Telephone and email support, (including e-blasts with updated news and events)
- Database of registered families
- Official newsletter – Spectrum
- SMS brochure, bookmarks, wristbands, (awareness items)
- Website – www.prisms.org
- Facebook Page - http://www.facebook.com/prisms.smithmagenis
- PRISMS online store, (see the link on our homepage)
- Parent to Parent Program
- International Conferences every 2-3 years, (next conference July 28-31, 2016, St. Louis, MO)
- Professional Advisory Board that oversees all medical and research data that is available on the PRISMS website and in PRISMS publications. The PAB also provides support and help to individual families.

For more information about PRISMS, please contact us at info@prisms.org or by telephone at 972-231-0035.

Overview:

Smith–Magenis syndrome is a rare (1/25,000) neurodevelopmental disorder characterized by a well-defined pattern of craniofacial and skeletal anomalies, expressive speech/language delay, middle ear dysfunction, sleep-wake abnormalities, elevated daytime melatonin and cognitive impairment with behavioral and psychiatric symptoms. All individuals have some degree of cognitive delay/intellectual disability. The majority of SMS cases are due to a common 3.7 Mb interstitial deletion of chromosome 17p11.2 that includes the retinoic acid induced 1 (RAI1) gene. However, about 10% of cases without deletion result from a heterozygous de novo mutation within the RAI1 gene.

Behavioral problems, some unique to SMS, represent the major management problem for both parents and professionals working with children/adults with SMS. The neurobehavioral phenotype that characterizes SMS includes hyperactivity and attention problems, impulsivity, mood lability, explosive outbursts/tantrums (often due to changes in routine), anxiety, aggression, and other maladaptive, autistic-like and self-injurious behaviors. These behaviors are influenced by a chronic sleep disorder that is worsened by daytime melatonin secretion that distinguishes SMS from other developmental disabilities. Diminished nocturnal sleep, virtually universal in SMS, reflects an advanced sleep phase with early sleep onset/offset, frequent nocturnal awakenings that lead to chronic and significant daytime sleepiness. One of the likely contributing factors to these sleep disturbances is an inverse circadian pattern of the sleep-promoting hormone, melatonin. In SMS, plasma melatonin is high during the day and low at night, which is opposite the expected normal pattern of elevated nighttime levels. The unusual daytime melatonin pattern is distinctive to persons with SMS.

Self-injurious behaviors, seen in over 90% of individuals with SMS, include head banging, wrist biting, hitting self or objects, skin picking (especially sores/open wounds), and two behaviors unique to SMS, onychotillomania (i.e., pulling out finger and/or toenails or nail yanking), and polyembolokoilamania (the insertion of foreign bodies in their body orifices). They exhibit a relative insensitivity to pain and consequently, may cause self-injury from persistent picking, biting and/or hitting themselves. In a few cases, parents have been reported to social services for suspicion of child abuse due to the child's self-inflicted injuries.

Individuals with SMS are adult-oriented, demanding an unusual amount of individualized attention from the teacher, parent and other adults (rather than their peers); when this is denied, aggression toward others, tantrums, and self-injurious behavior frequently result. All individuals with SMS exhibit development delay and some degree of cognitive impairment ranging from mild to moderate/severe intellectual disability. Generally they have difficulties with tasks requiring sequential processing skills and using short-term memory to place information in order; however, long-term memory and visual reasoning skills are general strengths. Their socially engaging personality and ability to converse (often perseverate) on topics of interest to them, often suggests a higher level of functional abilities; however, executive function is impaired. Among older individuals with SMS, deficits are found in all domains of adaptive behavior, with daily living skills and communication significantly more impaired than socialization skills. Increased anxiety and/or perseveration about pending events intensify with age, and reports of fright-or-flight response, disrobing, and aggressive outbursts

occur with increased frequency. The chronic sleep deprivation that occurs in SMS only serves to intensify the intrinsic behavior problems that impact daytime function, as the individuals with SMS struggles to stay awake, "fighting" the urge to sleep. The daytime secretion of melatonin (inverted pattern) is a bit like taking a sleeping pill in the middle of the day when one is already tired. In effect, persons with SMS have a "night shift" body that is constantly trying to adjust to living in a day shift world.

Several positive attributes of behavior in SMS should also be emphasized. They have engaging and endearing personalities (impish smile; self-hugging; good eye contact) are very appreciative of attention and often exhibit a great sense of humor. They enjoy (and actively seek!) interaction with adults rather than peers, are eager to please, and are visual learners with excellent long-term memory for names, places and faces. Most exhibit early speech delays, yet with appropriate early intervention including sign language, they are very communicative (gestural, signing and verbally) developing full verbal speech by school age; parents often report that they won't stop talking/asking repetitive questions.

Diagnostic confirmation of SMS:

The vast majority of SMS cases are confirmed by molecular cytogenetic study documenting interstitial deletion of 17p11.2. However, in 2003, a group of individuals with suspected SMS but without detectable deletions were shown to have SMS due to a de novo mutation in RAI1 gene. Thus, deletion or mutation of RAI1 gene is now recognized as the genetic cause of SMS.

There is no cure for SMS; however, diagnostic confirmation has significant implications for treatment and intervention strategies, including potential pharmacologic approaches, to guide behavioral management. Moreover, recognition and understanding the biologic basis of the chronic sleep disorder that occurs in SMS has major relevance for management and optimizing the sleep cycle. The behaviors that occur in SMS are not malicious in nature and do not reflect a "bad kid", but are symptoms of the medical "illness"/disorder; i.e., most of the negative behaviors have their origins in internally driven impulses (impulsivity, hyperactivity aggression, fight-or-flight response, sensory seeking with decreased pain sensation; self-injury) that are coupled with a biologically based circadian sleep disorder. Drastic changes in the educational or living environment may result in severe behavioral destabilization. Unfortunately, once destabilized, it is often very difficult for individuals with SMS to get back on track without intensive and costly interventions.

Family Support:

PRISMS provides the building blocks for families to receive accurate medical and educational information via the website, brochure, newsletters, New Member Packets and other publications and awareness items. We also have a Parent-to-Parent program that matches families to other families to initiate support and fellowship. PRISMS organizes international conferences that are held about every two years. Families and professionals attend from all over the world and the conference generates support and dialogue between parents and professionals. The PRISMS Board of Director's are all parents of a child with Smith-Magenis Syndrome who have volunteered their time to help run this organization. PRISMS is a member of NORD, (National Organization of Rare Diseases), and Genetic Alliance.