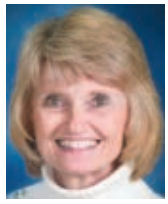
An Overview of Moebius Syndrome: Diagnosis, Supportive Treatment, and Valuable Community Resources

Bryn D. Webb, MD, and Vicki McCarrell

Moebius syndrome was first described by German ophthalmologist Alfred Graefe in 1880, but is named for German neurologist Paul Julius Moebius, who reported cases of this condition in 1888 and 1892.[1-3] Varying descriptions of Moebius syndrome have since been reported in the medical literature, and there have been major differences in opinion regarding the necessary key features for a diagnosis of this condition.

Diagnostic Criteria Plus Associated Findings

To improve consistency in diagnosis, minimum diagnostic criteria for a diagnosis of Moebius syndrome were established by an international group of experts at a Moebius Syndrome Foundation research conference in 2007. Minimum diagnostic criteria are the following:

- congenital, nonprogressive facial weakness
- inability to abduct (move the eye away from the nose) one or both eyes.

Both criteria must be present to make a diagnosis of Moebius syndrome (Figure 1.).[4, 5]

Keep in mind that congenital facial weakness can occur secondary to a defect in the facial nucleus or cranial nerve 7, and therefore might be a neurogenic problem. The term *congenital facial paresis* refers to decreased facial nerve function; *congenital facial paralysis* refers to absent facial nerve function.

Clinical characteristics of facial weakness can include facial droop; absence of forehead, nasolabial, or periorbital folds; lagophthalmos (incomplete eyelid closure), open-mouthed posture or U-shaped upper lip; drooling; and inability to make facial expressions (such as smiling), wrinkle the forehead, or whistle. A defect in the abducens nucleus or cranial nerve 6 can result in failure to abduct the eye, due to impaired ability to contract the lateral rectus extraocular muscle.

In addition to the 2 above-mentioned minimum diagnostic criteria, other signs or symptoms might be present, but are not necessary, in persons with Moebius syndrome (Table 1).

FIGURE 1: Congenital facial weakness

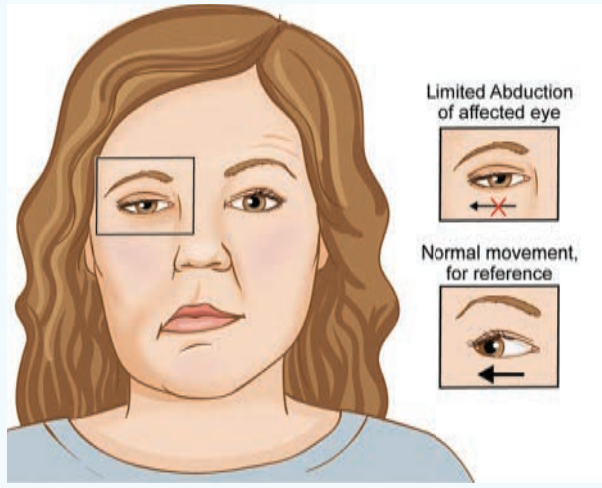


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TABLE 1. Moebius syndrome: Diagnostic criteria, other signs and symptoms

Minimum required diagnostic criteria
Congenital, nonprogressive facial weakness
Inability to abduct (move the eye away from the nose) either or both eyes
Additional signs and symptoms*
Autism
Congenital heart disease
Developmental delay or intellectual disability
Hearing loss
Limb-reduction defects
Muscular hypotonia
Poland anomaly (underdevelopment of the pectoralis major chest muscle, often with ipsilateral syndactyly)
Strabismus (misalignment of the eyes)
Talipes equinovarus (clubfoot)
Other cranial-nerve involvement
Other limb anomalies.

*Not required for diagnosis; not found in every patient. Not an exhaustive list.

The incidence of Moebius syndrome is roughly 2 to 20 cases in every 1 million births. The condition occurs in all ethnicities. There is no gender bias: males and females are affected equally.

The etiology of Moebius syndrome is poorly understood; the syndrome might be caused by genetic or environmental factors, or both. Prenatal exposure to misoprostol or cocaine has been associated with a Moebius syndrome phenotype, suggesting that vasoconstriction in the developing hindbrain or diminished or interrupted blood flow might be a cause.[6,7] In very rare cases, in patients affected with congenital facial weakness and a variety of additional findings, de novo heterozygous mutations in *PLXND1* or *REV3L* have been identified.[8]

In addition, there are several other separate conditions with similarities to Moebius syndrome that have identified genetic causes. These include hereditary congenital facial paresis, *TUBB3* syndrome, Carey-Fineman-Ziter syndrome, and CHARGE syndrome (coloboma of the eye; heart defects; atresia of the nasal choanae; retardation of growth or development, or both; genital and/or urinary abnormalities; and ear abnormalities and deafness).

Multidisciplinary Supportive Care Is Needed

There is no specific cure or treatment for Moebius syndrome. Treatment is supportive and aimed at treating symptoms of the condition individually. Comprehensive care and a multidisciplinary approach are needed to optimize patient health and clinical outcomes. Patients are often treated by a primary care physician, neurologist, ophthalmologist, otolaryngologist, medical geneticist, plastic surgeon, speech therapist, dentist, psychologist, or other specialists.

Infants with Moebius syndrome often have feeding difficulties; they might benefit from the use of special bottles, such as the Haberman feeder, and may require a feeding tube for additional nutritional support. Respiratory support is sometimes also needed. Speech and physical therapies are often recommended from an early age, with the aim of improving swallowing and feeding, speaking, and motor skills and coordination. School-aged children and adults might benefit from specialized oral-motor exercises to improve awareness and sensation of particular facial muscles, and might aid in strengthening facial movement.

Facial reanimation surgery (so-called smile surgery) is often an option to improve facial movement. Aims of this surgery include enabling the patient to smile, achieving symmetry, reducing pronunciation difficulties or swallowing problems, and improving dental health. Techniques vary, and include gracilis muscle transfer with use of the masseteric nerve or a cross-facial nerve graft, temporalis tendon transfer, and lengthening temporalis myoplasty. Eye surgeries, such as tarsorraphy or gold weights, may be recommended to prevent corneal exposure.

Additional surgeries might be recommended, based on the individual patient's symptoms, including for strabismus, limb anomalies, and scoliosis.

Foundation Support Has Been Essential and Effective

In 1994, the Moebius Syndrome Foundation (MSF) was launched as the first national patient advocacy organization for patients and families affected by Moebius syndrome. The organization was formed after 2 women, Vicki McCarrell and Lori Thomas, whose children were affected with Moebius syndrome, met and noted that few resources were available for those with Moebius syndrome. The first MSF conference was held in 1994 in Los Angeles.

Over the years, the foundation has grown tremendously and now has more than 2,800 members. Detailed information about the foundation can be found at www.moebiussyndrome.org. The mission of the MSF is to provide information and support to people with Moebius syndrome and their families, promote greater awareness and understanding of Moebius syndrome, and advocate for scientific research to advance the diagnosis and treatment of Moebius syndrome and associated conditions.

To fulfill this mission, the MSF hosts a large, 4-day family and scientific conference every other year in the United States. The conference has an international presence; at the last conference, held in the summer of 2018 in St. Petersburg, Florida, there were 410 attendees for the family conference and 50 investigators in attendance for the scientific conference. Sessions at the

family conference covered such topics as smile surgery, hand surgery techniques, speech and feeding therapies, treatment for sleep disorders, psychological issues, and an overview of Moebius syndrome research. Social events at the conference included a highly attended talent show and dance party.

The 2020 Moebius Syndrome Foundation Conference will be held in Minneapolis, Minnesota, July 17-19, 2020.

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New Resources in 2019

The MSF is also initiating a mini-conference series to enable additional networking within the Moebius syndrome community. Mini-conferences will include a full-day schedule of events and will be held twice yearly in the United States.

Additionally, the MSF hosts a closed Facebook group, "The Home for the Moebius Community," to enable additional networking within the Moebius syndrome community. This active group has 534 members.

The MSF also has supported scientific research on Moebius syndrome since 2005. Funding priorities include the following:

- projects that advance the diagnosis, treatment, or quality of life of people with Moebius syndrome and associated conditions
- projects that promote sustainable and comprehensive programs of research focused on Moebius syndrome by providing seed funds for larger research programs and grant submissions to larger funding organizations.

The MSF research grant program encourages early-career and established investigators to apply for funding. Researchers can learn more about these opportunities at www.moebiussyndrome.org. To date, the MSF has provided nearly $900,000 in research support.

The MSF also interacts with other global Moebius syndrome foundations to increase awareness of Moebius syndrome as well as share information and resources with physicians and individuals and families affected by Moebius syndrome. The MSF is also proud to be one of the initial members of Face Equality International, headquartered in England, and founded in 2018. This alliance of nongovernmental organizations works to "improve the life prospects of any person anywhere in the world who has a facial difference or disfigurement, an unusual-looking, scarred or asymmetrical face."

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