



Search

Advanced Search


[for Patients and Families](#) ▼
 [for Patient Organizations](#) ▼
 [for Clinicians and Researchers](#) ▼

[NORD Rare Disease Advocacy](#) ▼
 [Get Involved](#) ▼

[Home](#) / [For Patients and Families](#) / [Rare Disease Information](#) / [Thyroid Eye Disease](#)

Rare Disease Database

[0-9](#) • [A](#) • [B](#) • [C](#) • [D](#) • [E](#) • [F](#) • [G](#) • [H](#) • [I](#) • [J](#) • [K](#) • [L](#) • [M](#) • [N](#) • [O](#) • [P](#) • [Q](#) • [R](#) • [S](#) • [T](#) • [U](#) • [V](#) • [W](#) • [X](#) • [Y](#) • [Z](#)
[Print](#)

Thyroid Eye Disease

NORD gratefully acknowledges Raymond Douglas, MD, PhD, International Aesthetic Orbit & Oculoplastic Surgeon, for assistance in the preparation of this report.

Synonyms of Thyroid Eye Disease

- Graves' eye disease
- Graves' ophthalmopathy
- Graves' orbitopathy
- TED

General Discussion

Summary

Thyroid eye disease is a rare disease characterized by progressive inflammation and damage to tissues around the eyes, especially extraocular muscle, connective, and fatty tissue. Thyroid eye disease is characterized by an active disease phase in which progressive inflammation, swelling, and tissue changes occur. This phase is associated with a variety of symptoms including pain, a gritty feeling in the eyes, swelling or abnormal positioning of

the eyelids, watery eyes, bulging eyes (proptosis) and double vision (diplopia). The active phase can last anywhere from approximately 6 months to 2 years. This is followed by an inactive phase in which the disease progression has stopped. However, some symptoms such as double vision and bulging eyes can remain. In some people, cosmetic changes and significant disability can develop. Although uncommon, in severe instances, vision loss can occur. Thyroid eye disease is an autoimmune disorder. An autoimmune disorder is one in which the body's adaptive immune system, which protects the body from infectious or other foreign substances, mistakenly attacks healthy tissue instead.

Introduction

Thyroid eye disease most commonly occurs as part of Graves' disease, which is an autoimmune disease that affects the thyroid and often the skin and eyes. The thyroid is a butterfly-shaped gland located at the base of the neck. The thyroid is part of the endocrine system, the network of glands that secrete hormones that regulate the chemical processes (metabolism) that influence the body's activities as well as regulating the heart rate, body temperature, and blood pressure. Graves' disease is characterized by abnormal enlargement of the thyroid (goiter) and increased secretion of thyroid hormone (hyperthyroidism). Some people with Graves' disease eventually develop thyroid eye disease. Less often, thyroid eye disease can occur in people who have or have had an overactive thyroid (hyperthyroidism) or in individuals with an underactive thyroid (hypothyroidism) such as people who have a disorder called Hashimoto thyroiditis.

Signs & Symptoms

The signs and symptoms can vary greatly from one person to another. Eye symptoms can range from mild to severe. For some individuals, the symptoms can lead to pain, disfigurement of the eye socket, and, eventually, potentially threaten eyesight. The disorder can vary greatly in expression as well. For some people, the disorder remains little changed for many years, while for others it will worsen or slightly improve. Occasionally people experience repeated episodes of worsening (exacerbations) of the disease, and improvement of the disease (remission).

Initial symptoms include redness, irritation, and discomfort of the eyes and eyelids. Dry eyes and pain when moving the eyes may also occur. Eyelid retraction is also common which is when the upper eyelid is positioned too high and/or the lower eyelid too low thus exposing the eye. The most noticeable symptom can be exophthalmos or proptosis, which means that the eyes bulge or protrude outward out of the eye socket. Bulging of the eyes can cause a person to appear as if they are constantly 'staring'.

Additional symptoms and signs can include blurred vision, double vision (diplopia), misalignment of the eyes (strabismus), chronic bloody eyes, white area of eye inflamed, constant, watery eyes due to the excess formation of tears, swelling near the upper and lower eyelids, an intolerance of bright lights and difficulty moving the eyeballs.

Progressive swelling can cause increased pressure within the eye socket and pain or headaches. In severe cases, additional symptoms can develop including corneal erosion, in which there is an eroded area on the clear (transparent) outer layer of the eye (cornea). In some, enlarged eye muscles can compress and cause damage to the optic nerve (optic neuropathy), which is the main nerve of the eye and carries nerve impulses to the brain. Corneal ulceration and optic neuropathy can, sometimes, progress to cause vision loss.

Thyroid eye disease is a progressive disorder in which progressive damage to various tissues around the eyes can lead to scarring (fibrosis) and tissue remodeling. The extent of scarring and tissue remodeling tends to become apparent during the inactive phase, after inflammation and swelling has subsided. This can change the appearance of the eyes and lead to affected individuals looking tired all the time, or to appear different from people without such changes. These cosmetic issues can have a significant impact on emotional well-being and quality of life.

Causes

Thyroid eye disease is an autoimmune disorder, which means that a problem with the body's adaptive immune system, which protects the body from infectious or other foreign substances, mistakenly attacks health tissue instead. The immune system normally produces specialized proteins called antibodies. Antibodies react against foreign materials (e.g. bacteria, viruses, toxins) in the body bringing about their destruction. Antibodies can directly kill microorganisms or coat them so they are more easily destroyed by white blood cells. Specific antibodies are created in response to specific materials or substances. A substance that stimulates an antibody to be produced is called an antigen.

The exact underlying process by which thyroid eye disease occurs is not fully understood. In individuals with Graves' disease, the immune system creates an abnormal antibody called thyroid-stimulating immunoglobulin. This antibody mimics the function of thyroid-stimulating hormone, which is normally produced by the pituitary gland. These abnormal antibodies also affect the cells surrounding the eyes causing the symptoms associated with the disorder. Researchers think that the affected eye tissue contains proteins that appear similar to proteins of the thyroid gland and the antibodies mistakenly target these proteins. Patients often also have overexpression of a protein called insulin-like growth factor 1 receptor (IGF-1R), and this is thought to play a significant role in the development of the disorder. However, not everyone with thyroid eye disease has these immune system abnormalities suggesting that other abnormal antibodies or other factors can cause thyroid eye disease in some people. Researchers are still investigating the underlying cause of the disorder.

Individuals with thyroid eye disease may carry genes for, or have a genetic susceptibility to, thyroid eye disease. A person who is genetically predisposed to a disorder carries a gene (or genes) for the disease, but it may not be expressed unless it is triggered or "activated"

under certain circumstances, such as due to particular environmental factors (multifactorial inheritance).

Individuals who smoke are at a greater risk of developing thyroid eye disease. Individuals who have undergone radioactive iodine therapy as a prior treatment (e.g. for treatment of hyperthyroidism) are at a greater risk of developing thyroid eye disease. Individuals who have other disorders caused by malfunction of the immune system such as diabetes type 1 or rheumatoid arthritis may be at a greater risk of developing thyroid eye disease.

Affected Populations

Thyroid eye disease affects more women than men, although men are more likely to have a severe form of the disease. There is a genetic component to the disorder and people who have a family member with the disease or a family member with an autoimmune disease are at a greater risk of developing the disorder. The disorder is more likely to occur during middle age. The exact prevalence (i.e. the number of people who have a disorder in a specific population at a specific time) of thyroid eye disease is not known, but is estimated to be 16 per 100,000 women in the general population, and 2.9 per 100,000 men in the general population.

Related Disorders

Symptoms of the following disorders can be similar to those of thyroid eye disease. Comparisons may be useful for a differential diagnosis.

A variety of different disorders can be associated with symptoms similar to those seen in thyroid eye disease. These disorders include severe obesity, a painful, bacterial skin infection affecting the eye socket (orbital cellulitis), inflammation of the muscles of the eye socket (orbital myositis), and orbital tumors. Hay fever, allergies, and inflammation of the conjunctiva (conjunctivitis) can also cause symptoms similar to those seen in mild thyroid eye disease.

Myasthenia gravis is a neuromuscular disorder primarily characterized by muscle weakness and muscle fatigue. Although the disorder usually becomes apparent during adulthood, symptom onset may occur at any age. The condition may be restricted to certain muscle groups, particularly those of the eyes (ocular myasthenia gravis), or may become more generalized (generalized myasthenia gravis), involving multiple muscle groups. Most individuals with myasthenia gravis develop weakness and drooping of the eyelids (ptosis); weakness of eye muscles, resulting in double vision (diplopia); and excessive muscle fatigue following activity. Additional features commonly include weakness of facial muscles; impaired speech (dysarthria); difficulties chewing and swallowing (dysphagia); and weakness of the upper arms and legs (proximal limb weakness). In addition, about 10% of affected individuals may develop potentially life-threatening complications due to severe involvement of muscles used during breathing (myasthenic crisis). Myasthenia gravis results from an abnormal immune reaction in which

the body's natural immune defenses (i.e., antibodies) inappropriately attack and gradually destroy certain receptors in muscles that receive nerve impulses (antibody-mediated autoimmune response). (For more information on this disorder, choose "myasthenia gravis" as your search term in the Rare Disease Database.)

Cushing syndrome is a rare endocrine disorder characterized by a variety of symptoms and physical abnormalities that occur due to excessive amounts of the hormone cortisol, a vital glucocorticoid. Glucocorticoids are a class of steroid hormones that are important in the regulation of the metabolism of glucose, and also modulate the response to stress. Although it may occur in children, Cushing syndrome most commonly affects adults between the ages of 25 to 40. It can be caused by prolonged exposure to elevated levels of glucocorticoids produced within the body (endogenous) or introduced from outside the body (exogenous). Symptoms can include weight gain, obesity, a rounded face, thin purple streaks (purple striae) which occur on the skin, increased fat around the neck, and slender arms and legs. Children with Cushing syndrome are typically obese and have delay in growth. (For more information on this disorder, choose "Cushing" as your search term in the Rare Disease Database.)

Diagnosis

A diagnosis of thyroid eye disease is based upon identification of characteristic symptoms, a detailed patient history, a thorough clinical evaluation and a variety of specialized tests. Certain symptoms that occur in thyroid eye disease are often obvious and can lead to a diagnosis upon a physical examination. Some affected individuals have reported that their eyes "didn't feel right" before symptoms of the disease began.

Individuals suspected of having thyroid eye disease will undergo a complete eye examination. This may include measuring the degree of proptosis (eye bulging) using a device called an exophthalmometer. This small device enables an eye doctor to measure how far forward the eyes have moved (displacement).

Clinical Testing and Workup

In moderate to severe disease, a specialized imaging technique called computerized tomography (CT) scanning may be used to assess whether the optic nerve is compressed by inflamed, enlarged muscles in the eye. During CT scanning, a computer and x-rays are used to create a film showing cross-sectional images of certain tissue structures. Regular eye tests may be given to assess a person's clarity of vision (visual acuity).

Affected individuals may undergo thyroid function tests to detect an underlying cause of thyroid eye disease such as Graves' disease or hypothyroidism. These tests can detect elevated levels of thyroid hormones or antibodies in the blood.

Standard Therapies

Treatment

Treatment may require the coordinated efforts of a team of specialists, general internists, physicians who specialize in diagnosing and treating eye disorders (ophthalmologists) including eye doctors with experience treating thyroid eye disease, physicians who specialize in diagnosing and treating disorders of the hormone system (endocrinologists), psychologists, and other healthcare professionals may need to systematically and comprehensively plan treatment. Psychosocial support is essential as well.

In January, 2020 the U.S. Food and Drug Administration (FDA) approved teprotumumab trbw (Tepezza®), the first approved drug indicated to treat thyroid eye disease.

Teprotumumab inhibits (or blocks) the activity of the protein insulin-like growth factor-1, which is believed to play a significant role in the development of the disorder.

Affected individuals have shown significant improvement in proptosis, double vision, and overall quality of life when taking teprotumumab.

In affected individuals who have underlying Graves' disease, treatment includes reversing hyperthyroidism. Treating hyperthyroidism of Graves' disease is important, but will not improve symptoms of thyroid eye disease.

Some individuals with mild thyroid eye disease may be treated with supportive measures such as dark sunglasses to treat sensitivity to light, ointments, artificial tears, and/or prisms that are attached to glasses. Prisms can help correct double vision. Some people may wear an eyepatch to manage double vision.

Individuals with moderate-to-severe disease may receive corticosteroids, which are drugs that reduce inflammation and swelling, but do not affect diplopia and proptosis.

Prednisone is a common corticosteroid that is used to treat individuals with thyroid eye disease.

Some individuals with moderate-to-severe disease may eventually require surgery.

Surgery is also used to treat individuals with severe disease. Generally, it is recommended to avoid surgery until after the active phase of the disease has ended. Doctors will treat the symptoms to the best of their ability and then perform surgery once the inflammation and swelling has reduced. Surgery may be necessary during the active phase if doctors feel that a person's vision is at risk by the disease progression.

Surgical options include orbital decompression, motility, and lid surgery. During orbital decompression surgery, a surgeon takes out the bone between the eye socket (orbit) and the sinuses. This allows the eye to fall back into its natural position within the eye socket. This surgery is generally reserved for individuals who are at risk of vision loss due to pressure on the optic nerve or in whom other treatment options have not worked.

Surgical options can also help to improve bulging eyes (proptosis) and the position of the eyelids. Motility surgery involves repositioning certain muscles around the eyes to reduce or eliminate double vision.

Thyroid eye disease can cause noticeable changes in a person's facial appearance that cannot be treated completely. Depression is common in individuals with the disorder and cosmetic changes can cause significant emotional distress and affect emotional well-being. A psychologist is recommended to be part of a treatment plan for individuals with thyroid eye disease to work with affected individuals during and after treatment.

Investigational Therapies

Some individuals with mild forms of the disease have benefited from selenium, which is an over-the-counter supplement. It is a mineral commonly found in the soil, and found in tiny amounts in many foods. In limited studies, selenium was most effective in individuals living in areas where selenium was not common in the soil, and it is not known whether affected individuals living in selenium-rich areas would see the same benefits.

Several medications are being studied for thyroid eye disease including tocilizumab, rituximab, and mycophenolate mofetil. Some of these medications are in clinical trials. More research is necessary to determine the long-term safety and effectiveness of these medications as potential treatments for thyroid eye disease.

For decades, orbital radiation therapy has been used to treat some people with thyroid eye disease. Radiation therapy uses x-rays or similar forms of radiation to directly destroy damaged tissue. In thyroid eye disease, radiation therapy is directed toward the eye socket (orbital radiotherapy). Orbital radiotherapy can be given alone or in conjunction with corticosteroids or decompression surgery. However, most research into orbital radiotherapy has returned conflicting results as to its effectiveness as a therapy for thyroid eye disease.

Information on current clinical trials is posted on the Internet at <https://clinicaltrials.gov/>. All studies receiving U.S. Government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

Toll-free: (800) 411-1222

TTY: (866) 411-1010

Email: prpl@cc.nih.gov

Some current clinical trials also are posted on the following page on the NORD website: <https://rarediseases.org/for-patients-and-families/information-resources/info-clinical-trials-and-research-studies/>

For information about clinical trials sponsored by private sources, contact: <http://www.centerwatch.com/>

For information about clinical trials conducted in Europe, contact: <https://www.clinicaltrialsregister.eu/>

Supporting Organizations

Autoimmune Association

19176 Hall Road, Suite 130
Clinton Township, MI 48038 USA
Phone: (586) 776-3900
Toll-free: (888) 852-3456
Email: hello@autoimmune.org
Website: <https://autoimmune.org>

Genetic and Rare Diseases (GARD) Information Center

PO Box 8126
Gaithersburg, MD 20898-8126
Phone: (301) 251-4925
Toll-free: (888) 205-2311
Website: <http://rarediseases.info.nih.gov/GARD/>

Graves' Disease & Thyroid Foundation

P. O. Box 2793
Rancho Santa Fe, CA 92067
Phone: (877) 643-3123
Toll-free: (877) 643-3123
Email: info@gdatf.org
Website: <http://www.gdatf.org/>

Thyroid Foundation of Canada

P.O. Box 298
Bath ON K0H 1G0, Canada
Toll-free: (800) 267-8822
Website: <http://www.thyroid.ca>

References

JOURNAL ARTICLES

Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med*. 2020;382:341-352.

<https://www.nejm.org/doi/full/10.1056/NEJMoa1910434>

Douglas R. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: a focus on proptosis. *Eye (Lord)*. 2019;33:183-190. <https://www.ncbi.nlm.nih.gov/pubmed/30575804>

Roos JCP, Murthy R. Update on the clinical assessment and management of thyroid eye disease. *Curr Opin Ophthalmol*. 2019;30:401-406.

<https://www.ncbi.nlm.nih.gov/pubmed/31313753>

Wang Y, Patel A, Douglas RS. Thyroid eye disease: how a novel therapy may change the treatment paradigm. *Ther Clin Risk Manag*. 2019;15:1305-1318.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6858302/>

Li Z, Cestari DM, Fortin E. Thyroid eye disease: what is new to know? *Curr Opin Ophthalmol.* 2018;29:529-534. <https://www.ncbi.nlm.nih.gov/pubmed/30124533>

Strianese D. Update on Graves disease: advances in treatment of mild, moderate and severe thyroid eye disease. *Curr Opin Ophthalmol.* 2017;28:505-513. <https://www.ncbi.nlm.nih.gov/pubmed/28700384>

Rao R, Macintosh PW, Yoon MK, Lefebvre DR. Current trends in management of thyroid eye disease. *Curr Opin Ophthalmol.* 2015;26:484-490. <https://www.ncbi.nlm.nih.gov/pubmed/26397888>

McAlinden C. An overview of thyroid eye disease. *Eye Vis (Lond).* 2014;1:9. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4655452/>

Dolman PJ, Rath S. Orbital radiotherapy for thyroid eye disease. *Curr Opin Ophthalmol.* 2012;23:427-432. <https://www.ncbi.nlm.nih.gov/pubmed/22729183>

INTERNET

British Thyroid Foundation. Your Guide to Thyroid Eye Disease. Updated: 2019. Available at: <https://www.btf-thyroid.org/thyroid-eye-disease-leaflet> Accessed February 13, 2020.

Douglas RS. Kellogg Eye Center. Thyroid Eye Disease (TED or Graves Eye Disease). Available at: <https://www.umkelloggeye.org/conditions-treatments/thyroid-eye-disease> Accessed February 13, 2020.

Davies TF, Burch HB. Clinical features and diagnosis of Graves' orbitopathy (ophthalmopathy). UpToDate, Inc. 2019 Jun 26. Available at: <https://www.uptodate.com/contents/clinical-features-and-diagnosis-of-graves-orbitopathy-ophthalmopathy> Accessed February 13, 2020.

Davies TF, Burch HB. Treatment of Graves' orbitopathy (ophthalmopathy). UpToDate, Inc. 2018 Sep 27. Available at: <https://www.uptodate.com/contents/treatment-of-graves-orbitopathy-ophthalmopathy> Accessed February 13, 2020.

Years Published

2020

The information in NORD's Rare Disease Database is for educational purposes only and is not intended to replace the advice of a physician or other qualified medical professional.

The content of the website and databases of the National Organization for Rare Disorders (NORD) is copyrighted and may not be reproduced, copied, downloaded or disseminated, in any way, for any commercial or public purpose, without prior written authorization and approval from NORD. Individuals may print one hard copy of an individual disease for personal use, provided that content is unmodified and includes NORD's copyright.

National Organization for Rare Disorders (NORD)
55 Kenosia Ave., Danbury CT 06810 • (203)744-0100

Report Index

Synonyms

General Discussion

Signs & Symptoms

Causes

Affected Populations

Related Disorders

Standard Therapies

Investigational Therapies

Supporting Organizations

References

Related Content

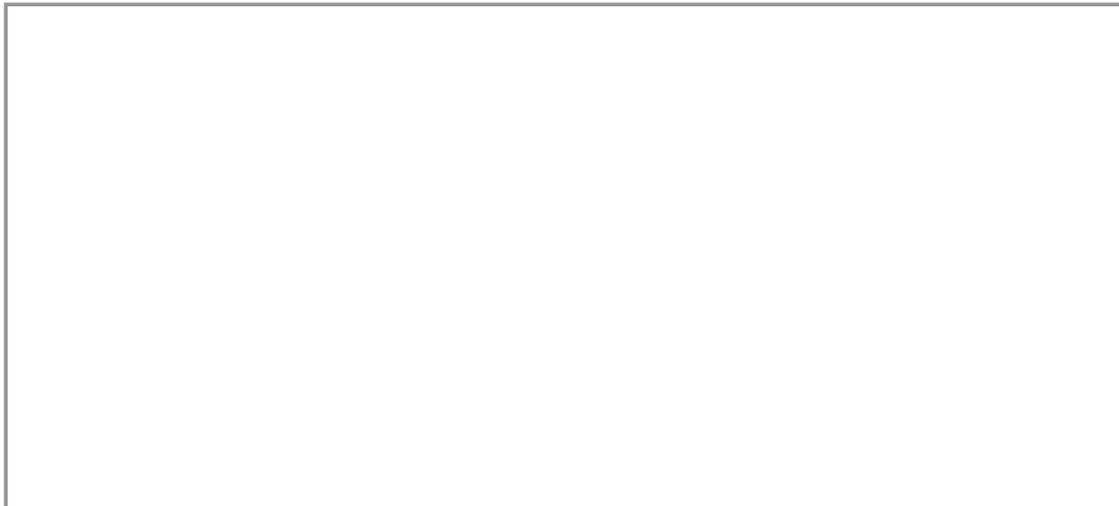
NORD Patient Assistance

**Are you a patient or
caregiver of someone
with Thyroid Eye
Disease?**

Check out our current
patient assistance
programs

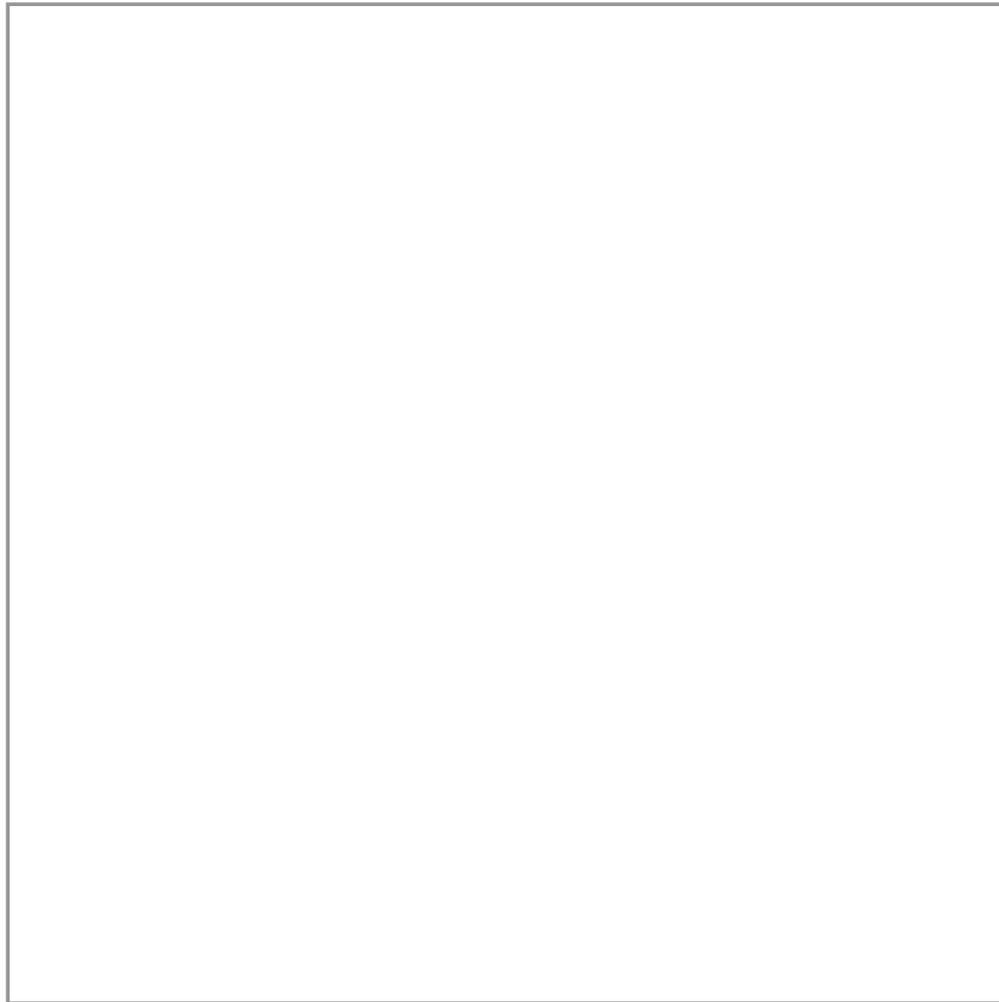
[Learn More >](#)

NORD Video: Rare Disease Facts





NORD Program



Alone we are rare. Together we are strong.®

For Patients and Families

For Clinicians and Researchers

For Patient Organizations

Advocate

Get Involved

Home

About

News

Events

Contact

Careers

Brand Usage Guidelines

Sign Up for NORD News!

Follow NORD



[SITE MAP](#) | [WEBSITE CREDITS](#) | [PRIVACY](#)

Copyright ©2021 NORD - National Organization for Rare Disorders, Inc. All rights reserved. NORD is a registered 501(c)(3) charity organization. Please note that NORD provides this information for the benefit of the rare disease community. NORD is not a medical provider or health care facility and thus can neither diagnose any disease or disorder nor endorse or recommend any specific medical treatments. Patients must rely on the personal and individualized medical advice of their qualified health care professionals before seeking any information related to their particular diagnosis, cure or treatment of a condition or disorder.