Myhre Syndrome
Patient and Family Handbook

Contents

Introduction

When faced with a diagnosis as rare and complex as Myhre syndrome, managing it can seem like a daunting task. Little information is available and much of it is in a language that is difficult to understand.

While the Myhre Syndrome Foundation would never create a document that takes the place of evidence-based guidelines or medical advice, we hope to translate some of the information into a more user-friendly format by creating this *Myhre Syndrome Patient and Family Handbook*.

It in no way replaces the advice of a medical professional or substitutes for getting medical care. Our hope is to provide information for you, or your child, as a starting point for care as well as give you the tools to understand that care. Please know this handbook is not all-encompassing. Myhre syndrome is a complex disorder with many different levels of needs. We cannot possibly address them all. We are trying to provide a baseline to begin your journey.

About Myhre Syndrome Foundation

The Myhre Syndrome Foundation (MSF) was established in 2019 as a patient advocacy organization dedicated to providing hope and improving the lives of those impacted by Myhre syndrome.

We do this by bringing together all the relevant stakeholders to build a strong, global community in order to advance research, as well as support, educate and advocate for those impacted by Myhre syndrome.

Simply put, we are here for you.

1. What is Myhre Syndrome?

Myhre syndrome is an extremely rare genetic disorder, caused by a mutation* (or pathogenic variant)* in the *SMAD4** gene*.

The mutation in Myhre syndrome is referred to as a *de novo* mutation because in most cases, it occurs by chance, and occurs at the time of egg or sperm formation. This means that it is not caused by anything a parent did or didn't do.

Myhre syndrome is unique because the mutation causes the *SMAD4* gene to work more or increase its function (called gain-of-function), rather than slow it down (called loss-of-function).

This is important, as there are other genetic conditions caused by loss of function *SMAD4* mutations. When a person is born with a gain-of-function *SMAD4* mutation, they develop Myhre syndrome.

Myhre syndrome can be viewed as a connective tissue* disorder. Of the many body systems which are affected, the skin is usually firm or thick, and scars can become thick or heal abnormally.

There is also a risk in some people to have scar tissue (fibrosis*) with surgery. Joints are stiff and can progress to contractures* or arthritis. The rib cage is stiff (restrictive). Affected individuals often have problems with the cardiovascular and respiratory systems and stenosis* can sometimes develop. Currently there is no cure.

Every person who has Myhre syndrome is slightly different. Some common characteristics include:

- Short stature
- Characteristic facial features, such as small eyes, small mouth or prominent chin
- Intellectual/social disability and/or autism
- Hearing loss
- Limited joint mobility
- Problems with lungs and airways
- Problems with heart and blood vessels
- Thickened skin

Every case of Myhre syndrome is unique and individuals may not have all of the symptoms listed above. The treatment of Myhre syndrome is directed toward the specific symptoms that are present in each individual.

Treatment requires comprehensive, coordinated efforts of a team of specialists that could include primary care physicians, cardiologists, pulmonologists, geneticists, orthopedists, otolaryngologists, ophthalmologists, endocrinologists, gastroenterologists, nephrologists, neurologists, physiotherapists and other healthcare professionals.

Each of these specialists are explained in **Section 3 on page 9.**

When diagnosed with Myhre it is important to talk to your medical team about your, or your child's, specific case, associated

symptoms and overall prognosis. Early diagnosis and intervention and regular follow up are essential to ensuring children and adults with Myhre syndrome are able to live their fullest lives.

While the true number of individuals with Myhre syndrome is currently unknown, it is however a very rare syndrome. If you, your child, or another family member is believed to have Myhre syndrome, it is recommended to seek genetic counseling.

> *"Myhre syndrome occurs when the instructions from our DNA have been altered."*

Definitions

Mutation: A mutation occurs when a DNA gene is damaged or changed. In some cases, such as in Myhre syndrome, it alters the genetic message carried by that gene. As a result, the gene behaves differently.

Pathogenic variant: This is a term that scientists and clinicians often use as an alternative word for mutation.

SMAD4: The gene in which the mutation occurs in individuals with Myhre syndrome. *SMAD4,* also called SMAD Family Member 4, is a Protein Coding gene, which means that it plays an important role in helping our bodies carry out their necessary functions.

Gene: Small molecules within our bodies that provide instructions that allow us to grow and live; DNA is needed in order to create genes.

Connective tissues: Support and connect different tissues and organs of the body. They are widely distributed in every part of the body.

Fibrosis: Fibrosis means thickening or scarring of the tissue.

Contractures: shortening and hardening of muscles, tendons, or other tissue.

Stenosis: Narrowing.

2. How Is It Diagnosed & What Do The Genetics Mean?

Myhre is usually diagnosed via a genetic test that confirms the mutation on the *SMAD4* gene. The test is usually a whole exome sequence or whole genome sequencing.

However, some individuals with Myhre syndrome have single-gene testing done for *SMAD4* or other multigene panels instead.

Genetic tests take a sample (often blood or saliva) from the patient, and it is then analyzed to look out for any changes in DNA* sequence. Because Myhre syndrome is rare and sometimes symptoms can be subtle, reaching a diagnosis can be a long process.

If you believe that you or your child may have this syndrome, please encourage your doctor to explore the sequence based genetic or genomic testing to confirm your diagnosis as it is the only accurate way to currently diagnose this syndrome.

Chromosome testing, often referred to as a karyotype, will not detect Myhre syndrome.

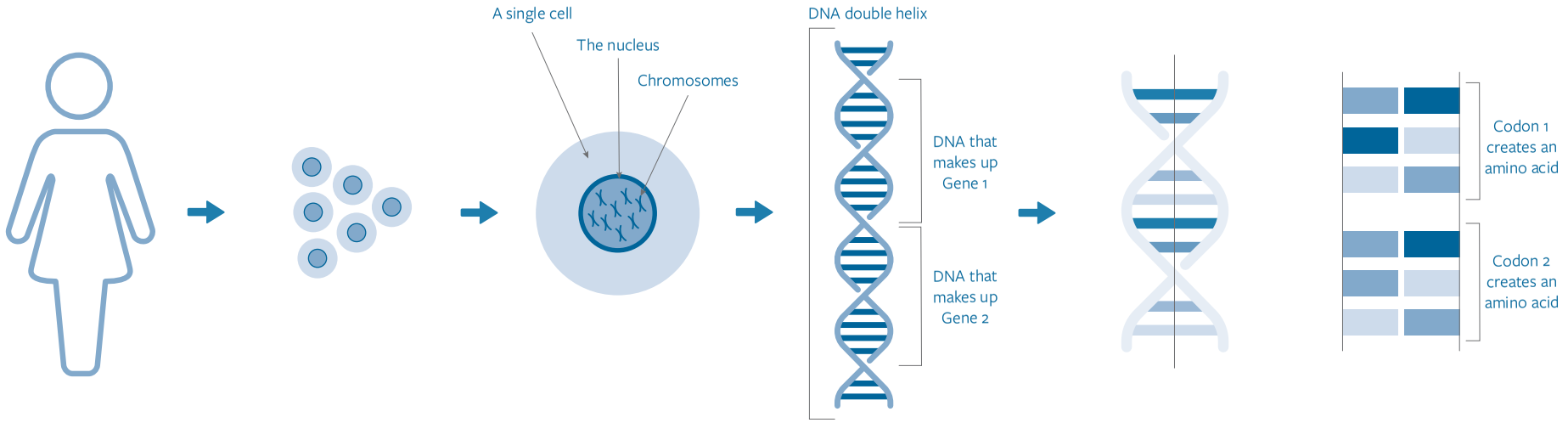
Myhre syndrome is caused by variants at only two positions in the *SMAD4* gene; this is part of what makes this condition unique.

A variant is a permanent change in the DNA sequence present in every cell of the body.

In Myhre syndrome, the two positions that these changes occur are at 496 and 500 (these numbers represent different codons* of the gene).

Our DNA contains instructions to make each gene. These instructions tell the body what amino acids are needed at each position to ensure proper functioning within the body. Amino acids are small biological molecules that link together to create genes. At a molecular level, each amino acid has its own unique structure. Myhre syndrome occurs when the instructions from our DNA have been altered.

Understanding DNA



Our bodies are made up of many tiny cells.

The picture above represents a cluster of cells from the body (each light blue circle is a cell).

The dark blue circles inside of each cell represents the **nucleus,** an important part of most cells.

The nucleus contains our genetic information.

The nucleus stores our genetic information as **chromosomes**, which are very long pieces of DNA.

Chromosomes are made up of tightly arranged strands of **DNA,** shown above.

This DNA is sometimes referred to as a double helix.

Different groups of the double helix create different **genes.**

The picture on the right shows a straightened out version of the double helix.

Each colored square represents a very small piece of DNA called a **base.**

Three bases in a row can create a **codon.** Certain codons make up specific **amino acids** within our body.

A **missense** mutation occurs when one of the three bases in a codon is atypical compared to the bases found in an individual without Myhre.

The location and identity of this atypical base is what creates the different **variants** of Myhre syndrome.

For Myhre the instructions have been altered at codon 496 or 500 depending on the mutation, instead of having the typical amino acid at codon 496 or 500 on the gene, a different amino acid has been chosen.

Arg496Cys	Arginine was substituted by the amino acid Cysteine
Ile500Val	Isoleucine was substituted by the amino acid Valine
Ile500Thr	Isoleucine was substituted by the amino acid Threonine
Ile500Met	Isoleucine was substituted by the amino acid Methionine
Ile500Leu	Isoleucine was substituted by the amino acid Leucine

The letters before and after this position number indicate the amino acid change at that exact place within the gene. There are a number of different amino acid changes with Myhre syndrome.

At position 496, there is only one type of amino acid change. This change is Arg496Cys. This means that at position 496, the amino acid called Arginine was substituted by the amino acid called Cysteine.

At position 500, there are several amino acid changes (Ile500Val, Ile500Thr, Ile500Met and Ile500Leu). This means that at position 500, the amino acid called Isoleucine was substituted by the amino acid called Valine, Threonine, Methionine or Leucine respectively.

To clarify, the type of mutation an individual with Myhre syndrome has will impact the amino acid change. Therefore, an individual with Ile500Val, will only have the Valine substitution and not the Threonine, Methionine or Leucine substitution.

As of right now, there is no substantial evidence of a difference between individuals with Myhre syndrome who have mutations at the 496 or 500 positions. However, Myhre syndrome researchers are continuing to investigate this topic.

Definitions

DNA: Deoxyribonucleic acid (abbreviated DNA) is the molecule that carries genetic information for the development and functioning of an organism. DNA is made up of four building blocks. DNA is translated into the 20-letter code of amino acids, which are the building blocks of proteins.

Codon: DNA is arranged in a 'triplet code'. Every three DNA bases codes for a specific protein building block called an amino acid. This is important for understanding how a variant in DNA leads to an abnormal *SMAD4* protein.

3. Diagnosis & Beyond

Responding to a diagnosis is deeply personal. For some it can feel overwhelming, for others a relief to finally have something confirmed.

We know from the experiences in the Myhre community that the emotions vary from one day to the next but at the Myhre Syndrome Foundation, we are by your side.

Here are some ideas and resources that can help you in the early days and beyond.

Build A Team (and Identify A Manager)

Within the global Myhre community, the experiences at the point of diagnosis can vary greatly. Some are already connected to a geneticist, or a diagnosis could come from your family doctor or pediatrician. Some patients get help with establishing all the initial appointments with the specialists, others are left with little to no support.

It has been recognized by Myhre experts that early diagnosis and intervention, with regular follow-ups are essential. Building a partnership with a doctor or specialist can enhance the care you receive, so our first recommendation is to **Build A Team.**

- Do you have a doctor who is coordinating the care?
- If you don't, is there someone who can take on this role for you? For instance, you may decide to talk to a trusted medical provider, such as your primary care physician or general practitioner, and ask if they will support you.
- The goal is to build a team of specialists but have a **manager** – a medical professional who knows the history and who is willing to learn about Myhre with you.
- Alert your Myhre manager to the research and data about Myhre (see **Myhre Clinical Updates** in **Section 5 on page 12)** and encourage them to view the videos.
- Discuss with them who you should contact in an emergency situation, if it is them, understand what the 'on-call' options are for you. Share these emergency contacts with your next of kin.

On our website you will find a Myhre Doctor Directory – if your area is not represented, please get in touch with us at **myhre@myhresyndrome.org** and we will try to help connect you.

A video that talks you through how to create a team and tips on how to get the most out of your team, can be found on our website and is called *PCP's Perspective: How To Create Your Home Team* by Dr Matt Thompson.

A Myhre Care Team

The list below is a guide on who might become part of a care team for Myhre syndrome. We encourage everyone with Myhre to be proactive in asking questions about what physical examinations should be completed. You may use this list as a guide to discuss with your main point of contact in your medical team.

In addition to the list below, reach out to your local authorities and bureaus to understand the support available. This could include assistance with paying bills, equipment for your home, technology support, and educational resources that are now available.

Genetics	study of genes, genetic variation, and heredity in organisms
Cardiology	heart
Pulmonology	lungs
Gastrointestinal	digestive system
Dermatologist	skin
Gynecology	female reproductive organs
Urology	includes the kidneys, adrenal glands, ureters, urinary bladder, urethra, and the male reproductive organs
Endocrinology	hormones and endocrine glands and organs
Ophthalmology	eye disorders
ENT	ear, nose and throat
Sleep Medicine	sleep studies and medication
Rheumatology	musculoskeletal diseases and autoimmune conditions (rheumatic disease)
Nephrology & Hypertension	diseases of the kidney and blood pressure
Neuropsychology	cognition and behavior related to the brain and the nervous system
Physical Medicine & Rehab	restore health through exercise and rehabilitation, can help with wheelchair fitting, and other adaptive equipment
Dentist	oral health
Physical Therapy	promote and maintain mobility
Occupational Therapy	assists physical, sensory, or cognitive problems
Speech Therapy	language pathologist or a speech and language therapist
ABA Therapy	Applied Behavior Analysis (ABA) applies understanding of how behavior works to real situations. The goal is to increase behaviors that are helpful and decrease behaviors that are harmful or affect learning

Appointments & Scheduling

The list of specialists and appointments that you need to make might be overwhelming. We recommend you approach the list in the following way.

- Discuss the priorities with your care team/ Myhre manager.
- A recommendation from the Myhre Clinic **(see Section 6 on page 15)** is to see a cardiologist at an early stage to check on heart function.
- Next look at the symptoms (if any) and discuss 'what needs attention right now?'
- Work through the list of specialists with your doctor and create a plan. After an initial consultation, the specialist will then let you know how often they want to see you.

In the Resources section of this document, you will find helpful templates for keeping track of the specialists and the frequency of the appointments.

Hints and Tips from the Myhre Community

1. Prioritize your care. Appointments can be overwhelming and frequent. Make sure you are utilizing your time on the most important issues and if nothing is pressing, take a break. Make sure you take time to enjoy life and breathe.

2. Before each appointment, review the notes from the previous visit. Has everything been followed up? Are there any outstanding tests?

3. Print out a list of the medication you/your loved one takes. Include dosage details and keep a copy in your bag or wallet. This is useful to produce at a visit but also important in an emergency situation where stress can affect us.

4. When you see a new doctor, let them know about the videos and expert guidance from the Myhre doctors and keep reminding them! They have many patients, so be proactive in educating your team.

5. Let your family and friends know what help you need. This could be practical, or emotional. Bring them into your journey and tell them what works for you. For some that might mean asking people to just listen, not find solutions. For others that might be a cooked meal or help in the house.

4. Thinking Ahead

Feedback from our community has indicated that planning for the future is so important. Below you'll find areas to consider. This is not a complete list or advice but based on experiences the Myhre community have shared with us. We will include further details on our website.

Protecting your interests or the interests of your loved one

There could be instances where you or your loved one are not able to express wishes directly. Having conversations about what is important, or preferences you or they have, is an important part of a care plan. Rather than wait until a situation arises, discussing these ahead of time can make a big difference.

Permissions for Personal, Health and Benefits

Depending on the country you live in, there will be different rules and guidance on this topic but areas to consider looking into include:

Access to benefits and welfare support:

What is available, and are there age considerations you need to be aware of as your child moves into adulthood?

Access to medical records:

Plan ahead for accessing your child's medical records, as the ages at which they gain independent medical records varies for each country.

Planning for the future

Financial assistance, housing and guardianships are areas the Myhre community parents have been discussing with us. This type of planning can take time so a first step could be discussing the options with your support network or a professional.

5. Myhre Syndrome Foundation Support

At MSF, we are here to support you. Below you'll find information on Myhre clinic updates, research funding and ways we can work together to achieve the goal of finding treatments and one day a cure.

Myhre Clinical Updates

MSF is supported by a team of Myhre doctors from around the world who meet regularly to discuss research, new findings and share knowledge.

Video Presentations from Myhre Experts

In 2021, we held our first virtual conference, two days of speakers covering many of the body systems that Myhre affects. These videos and updated content from our Summer Seminars event in 2022 have produced 37 video presentations.

Every video is available in over 100 languages via the Closed Caption feature on YouTube. If you are not sure how to use this there are many tutorials available.

Here are some suggested videos to get you started:

- *Your Child (or You) Have Myhre Syndrome - Now What?* by Dr Angela Lin
- *Cardiology: The Heart of Myhre Syndrome* by Dr Mark Lindsay
- *Myhre Clinic Update* – Dr Angela Lin
- *Ear, Nose & Throat* – Dr Michael Cohen

Grant Funding from MSF

In 2022, MSF awarded $150,000 in research grants that will advance knowledge of Myhre syndrome.

The first awardee was Dr Bert Callewaert, Ghent University, Belgium. His team will establish a zebrafish model to test potential treatment options.

The second awardees were Dr Angela Lin and Dr Mark Lindsay, Massachusetts General Hospital, Boston. Their team will use a mouse model to examine what happens to the heart with Myhre syndrome and then explore ways to improve treatment and prevent progression of any symptoms.

Look out for research progress updates on our website and sign-up to our monthly newsletter to get news delivered straight to your inbox.

Patient Registry

Enrolling in the Myhre Syndrome Patient Registry at CoRDS (Coordination of Rare Diseases at Sanford) is one of the most effective ways to help research and clinical treatment for those living with Myhre syndrome.

The Myhre Syndrome Patient Registry is an online, confidential database of standardized information about individuals with Myhre syndrome.

By sharing your diagnostic and treatment history, you can help provide researchers with data necessary to perform research.

If you also allow us at MSF to view your anonymous data (a simple checkbox), we can then provide the community with useful updates on symptoms. You can view the data in the Resources section.

Supporting Each Other

Our number one goal is to support the Myhre community and ensure everyone has a voice and feels heard. You might be one of a handful of people within your country affected by Myhre, and this can sometimes feel isolating. We are here to help you feel supported, and to help you navigate this journey, together.

Being part of an ultra-rare community means it is hard to get noticed by the medical and research community, but together our voice is strong. Together we can make such a difference to everyone living with Myhre syndrome. You can get involved in a number of ways...

Myhre Virtual Coffee Hour

Look out for details on virtual meetups where members of the international Myhre community come together to chat and say hello. These informal sessions are an opportunity to ask questions about each other's experiences and build deeper connections.

Myhre Community

A number of communities exist on social media that are independent from MSF but offer a place to share updates and experiences with a group who know what you are going through, and who are there for support.

Fundraising

We are rare. That means we need to fund our own research to get answers and to support our community. Generous donations have funded the first research grants, but we need to do more, and we need to do it today. Myhre is a progressive condition so we must act now. Here are some suggestions on how to help.

- Hold a fundraiser to explain what Myhre is and why we need to act now.
- Ask your friends and family to hold a fundraiser – they have a network of many more people who could help. Don't be afraid to ask.
- Make a donation if you are able. We encourage monthly donations so we can plan effectively.
- Planned Giving – could Myhre be part of your estate and will planning?

Research

Look out for ways you can get involved with Myhre research. You don't always need to be seen in person by the research institution. Sharing medical records and lab results are very helpful to research teams. Keep a lookout on our website and email at **myhre@myhresyndrome.org** if you're interested in finding out more.

Keep In Touch

Newsletters

Each month we send out a newsletter with updates and news. Sign up at the bottom of our homepage at: **www.myhresyndrome.org**

Social Media

Support us by liking, sharing and commenting on our posts, so that we get noticed.
The more you support MSF, the bigger our audience becomes.


facebook.com/myhresyndromefoundation


instagram.com/myhresyndromefoundation


myhre syndrome foundation


@myhresyndrome

Say Hello

We love to hear from the Myhre community. Drop us an email and say hello or let us know how we can help. We're here for you: **myhre@myhresyndrome.org**

6. The Myhre Syndrome Clinic

The Massachusetts General Hospital (MGH) in Boston is home to the Myhre Syndrome Clinic. MSF is not directly affiliated with this clinic, but we remain a proud partner of this team who shares the common goal of helping Myhre individuals live their fullest lives.

The Myhre Clinic, co-directed by Dr Angela Lin and Dr Mark Lindsay, is a multi-specialty clinic that has seen over 40 patients. The team shares findings on Myhre progression and symptoms in nearly every organ system. You can find video presentations about the Myhre Clinic on our website.

We recognize that visiting the Myhre Clinic in-person isn't always an option. However, once you have received a diagnosis, we would encourage you to reach out to the team at MGH so they are aware of your diagnosis and can make contact with your care team if necessary.

An alternative option to an in-person visit, is an Online Second Opinion where you provide specific questions for consultation. The process is supported by your local physician who will provide medical information and records. After the records are reviewed, there is a full report that is completed within two weeks from the specialist you have selected for your Second Opinion. This can be particularly useful if consideration is being given to a specific care plan or procedure.

You can find further details here: **www.massgeneral.org/children/myhre-syndrome** and **https://www.massgeneral.org/second-opinions**

Myhre Syndrome Foundation Patient Registry at CoRDS

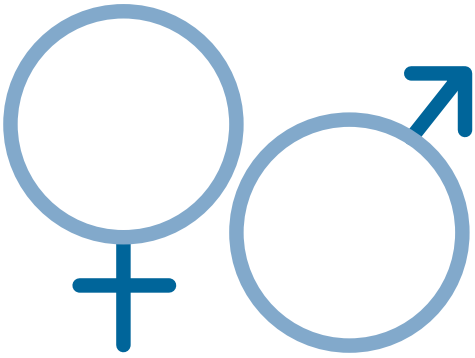
March 2022 update

Participants from:

13 countries across **5** continents

Including Argentina, Australia, Canada, France, Germany, Israel, Italy, Netherlands, Norway, Spain, United Kingdom and United States.

Sample size: 67



Of the registry participants:

61% Female

39% Male

Sample size: 62

Sample size: 51

Age of diagnosis:

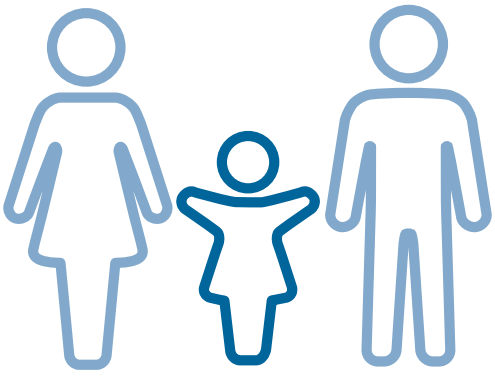
0-5: **45.1%**

6-10: **29.4%**

11-20: **19.6%**

21-30: **2.0%**

31+: **3.9%**



Thank you to all registry participants! **To learn more, go to: www.myhresyndrome.org/patient-registry**

Myhre Syndrome Foundation Patient Registry at CoRDS

March 2022 update

Myhre syndrome is caused by a change in the ***SMAD4*** gene. There are four gene changes or variants that have been reported.

Of the respondents that knew their variant:

51.4% had Ile500Val

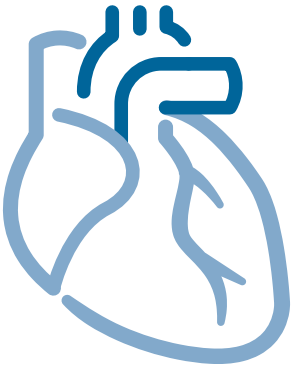
31.4% had Arg496Cys

11.4% had Ile500Thr

5.7% had Ile500Met

Sample size: 35

55% of registry participants reported having a cardiovascular condition.



Of those reporting cardiovascular conditions:

56% have 'arterial stenosis' (nonspecific term)

50% have hypertension

47% have a congenital heart defect

6% have cardiomyopathy

3% have pericardial disease

Sample size: 58

Thank you to all registry participants! **To learn more, go to: www.myhresyndrome.org/patient-registry**

Myhre Syndrome Foundation Patient Registry at CoRDS

March 2022 update

People with Myhre Syndrome reported the following skeletal features/abnormalities:

88% short stature

10% scoliosis

82% limited range of motion

39% shortened long bones

57% brachydactyly

14% thick calvarium

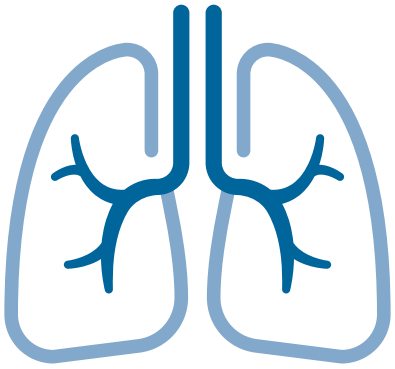
6% hemivertebrae

10% fused vertebrae

25% webbing of hands and/or feet

71% small hands and feet

Sample size: 51



57% of registry participants reported respiratory conditions including:

- Asthma
- Larynx and/or tracheal stenosis
- Obstructive sleep apnea
- 'Restrictive pulmonary disease' (nonspecific term)
- Subglottic stenosis

Sample size: 56

Almost **2/3rds** of registry participants reported hearing loss. Sensorineural, conductive and mixed hearing loss have all been reported.

Sample size: 55

Thank you to all registry participants! **To learn more, go to: www.myhresyndrome.org/patient-registry**

Patient and Family Interpretation of **GeneReviews 2022**

Patient and Family Interpretation of GeneReviews 2022

In this section of The Myhre Syndrome Patient and Family Handbook, we give a more detailed look at each body system and use the information from GeneReviews to describe how each system is affected.

The GeneReviews about Myhre syndrome is a compilation of what is known based on clinical experience and research. GeneReviews refers to a series of articles which provide clinically relevant and medically actionable information for inherited conditions in a standardized journal-style format. It covers diagnosis, management, and genetic counseling for patients and their families. Each chapter in GeneReviews is written by one or more experts on the specific condition or disease and goes through a rigorous editing and peer review process before being published online.

The Myhre Syndrome GeneReviews, first published in 2017, is widely read by physicians, other medical professionals, and consumers (patients and families) for diagnostic and management guidance. This is not a substitution for medical advice. Please see your physician for any questions.

The sections of the original GeneReviews 2022 document that we will review are as follows:

- Summary
- Diagnostic Testing of Myhre Syndrome
- Clinical Characteristics/Treatment/Management of Symptoms
- Prevention of Secondary Complications

GeneReviews has kindly given us permission to create this family friendly version of the updated 2022 version of the Myhre syndrome review. They will not be involved in any subsequent translation of the information. This is not intended to be a literal (word-for-word) interpretation. We took the liberty to omit some areas of repetition. We sincerely hope this information provides guidance and support on your journey with Myhre syndrome.

Please remember that not all people affected by Myhre will have all these clinical issues. Seek medical advice to discuss any concerns with your primary provider or appropriate specialist.

If you would like to review the journal article in its entirety, here is the link:
https://www.ncbi.nlm.nih.gov/books/NBK425723/

Summary

Myhre syndrome is a connective tissue disorder. **Connective tissue supports, protects, and gives structure to other tissues and organs in the body, such as joints and skin.**

Examples of connective tissue include bone, blood, cartilage, and skin. Because these tissues are a part of every organ system in the body, many specialists can be involved in the care of a Myhre patient.

For a person with Myhre syndrome, characteristic facial features are common and sometimes present in infancy. These features can often be more difficult to recognize in a younger child and become easier to notice as an individual ages. Short stature and hearing loss can develop over time as well as the highly distinctive (and often severe) findings of Myhre syndrome including joint stiffness, restrictive lung, cardiovascular disease, progressive and proliferative fibrosis, and thickening of the skin.

Proliferation (overgrowth) of connective tissue can occur spontaneously or may follow injury or surgery. For example, scar tissue can continue to thicken after the injury has healed or the surgery is complete.

Each person with Myhre syndrome is unique. Not all people have every feature. However, most individuals have many of the characteristic features by the time they are adults as this is a progressive condition.

The areas which are commonly involved in Myhre syndrome can include:

- **Cardiovascular** (heart and blood vessels)
- **Respiratory System** (network of organs and tissues that help you breathe)
- **Gastrointestinal System** (passageway of the digestive system that leads from the mouth to the anus)
- **Cutaneous** (skin)
- **Neuropsychological** (mental, emotional, and behavioral health as well as cognition which includes thinking, reasoning, and memory related to the brain)
- **Musculoskeletal System** (bones, muscles, and joints)
- **Immune System** (protects against bacteria, viruses, and fungi)
- **Ophthalmologic System** (eye and vision)
- **Hearing**
- **Endocrine System** (hormones and the related glands)
- **Neoplasia** (uncontrolled, abnormal growth of cells or tissues in the body)

Although at this time there is no special genetic treatment/medicine for Myhre syndrome (such as gene therapy), we typically can treat the symptoms with medications used for people without Myhre syndrome, such as high blood pressure.

If the evaluation of symptoms or if a medical problem requires a procedure, the specialist should be careful to prevent and limit any injury to the tissue (in particular blood vessels and airways). Medical management includes monitoring a larger number of features including (but not limited to) growth, breathing, sleeping, movement and exercise ability, urination, stooling, hearing, speech and language development, intellectual progress, education, and behavioral problems.

Communicate to everyone in your care team that limiting tissue injury is the single most important preventative step for most people with Myhre syndrome. However, many forms of fibrosis (thickening or scarring of the tissue) are not under the person with Myhre syndrome's control. When they develop, the person or parent should not feel responsible.

Diagnostic Testing of Myhre Syndrome

The diagnosis of Myhre syndrome is made after a clinical concern prompts a specialized DNA-based sequencing test that identifies a pathogenic variant (a change also known as a mutation) in the *SMAD4* gene.

The pathogenic variant usually happens by chance and is new in the family (often referred to as 'de novo'). However a few individuals with the variant (p.Arg496Cys) have passed this pathogenic variant to their children. In these instances, a parent with Myhre syndrome had a child with Myhre syndrome. Please see the initial part of this handbook for more information on genetics.

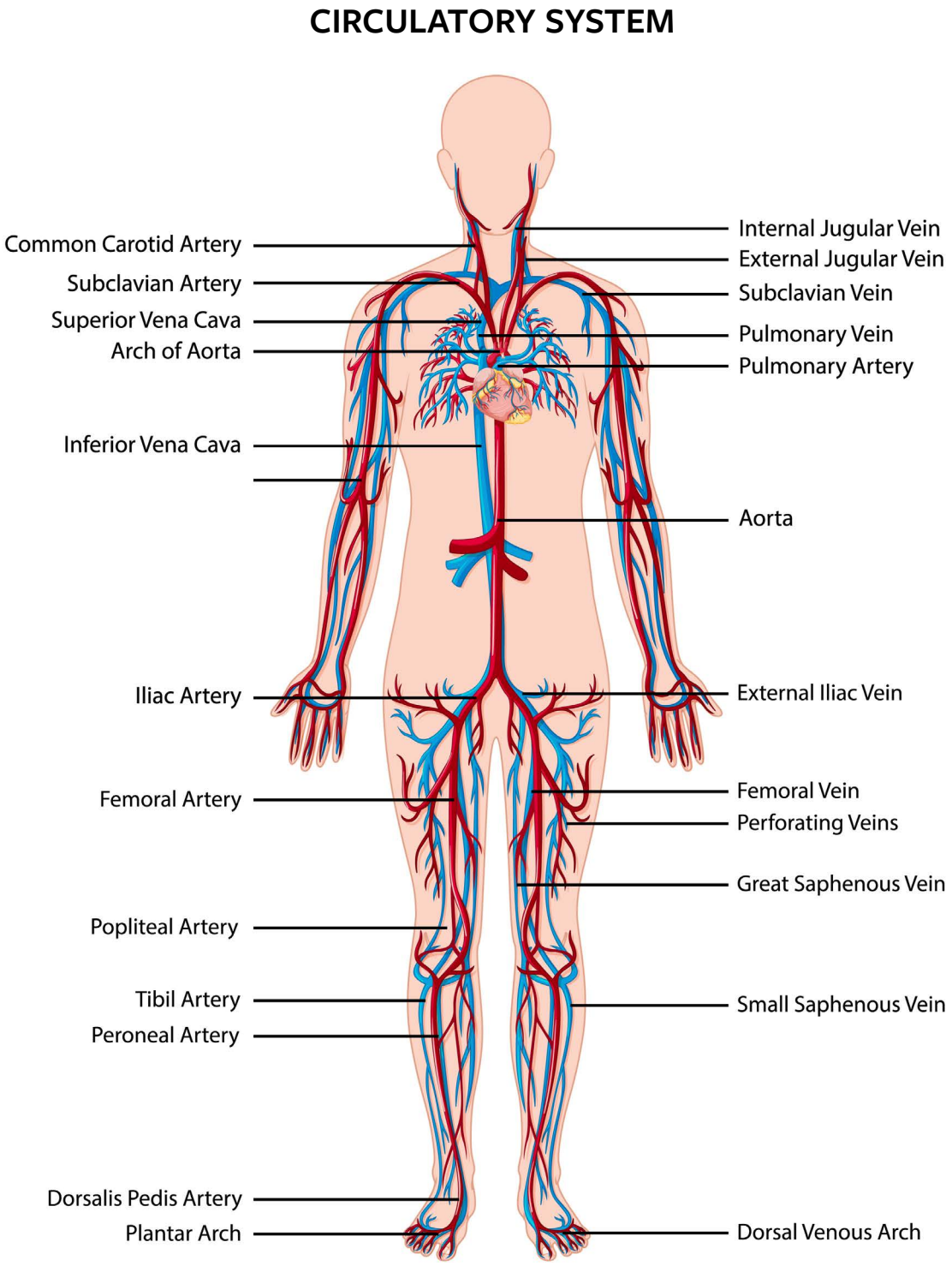
Clinicians who may be involved both before and after genetic testing are:

Clinical geneticists: This is a physician who specializes in genetic diagnosis and care for patients of all ages. After the diagnosis of Myhre syndrome is made, they also provide guidance and make medical recommendations for the families and primary care providers to follow.

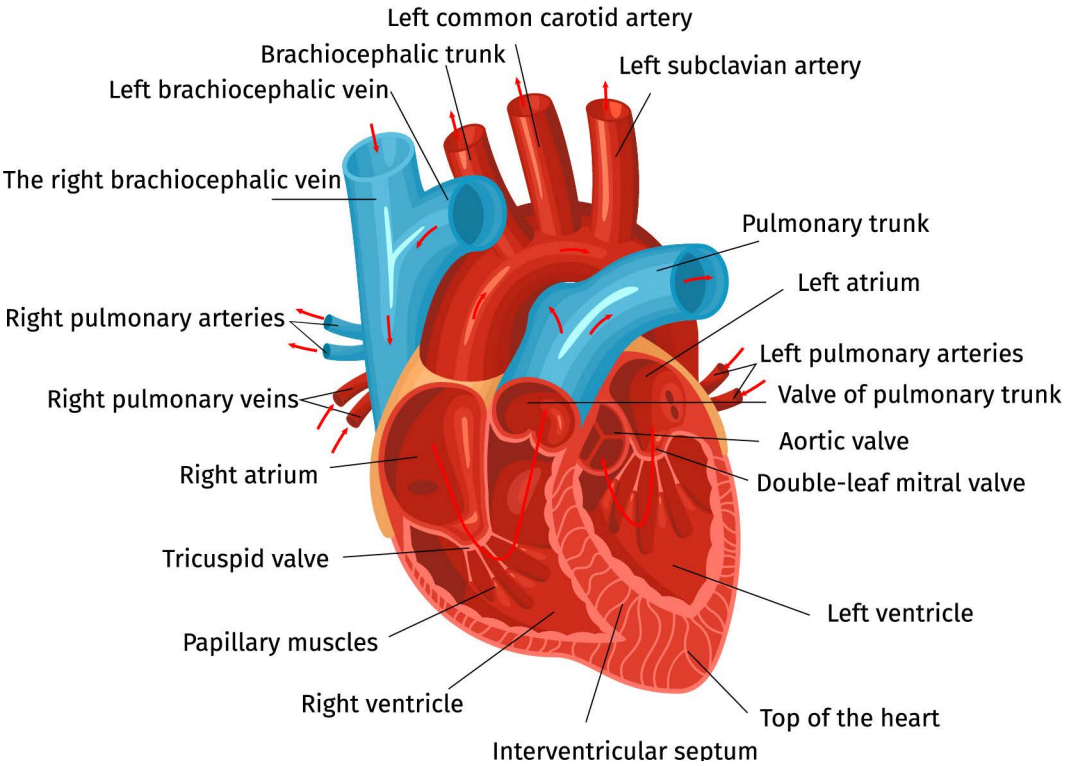
Genetic counselor: This is a professional who assesses individual or family risk for a variety of inherited conditions, such as genetic disorders and birth defects. The genetic counselor does not examine a person but, often, helps explain genetic testing results and helps clinical geneticists coordinate genetic testing.

Cardiovascular System

Heart and blood vessels



BLOOD CIRCULATION IN THE HEART



Clinical Characteristics

Structural Heart Abnormalities

Congenital heart defects (CHD): These are formed in fetal life and present at birth or shortly afterwards. CHDs are generally straightforward. Complex CHDs are not usually observed in individuals with Myhre syndrome except for a few individuals who have had Tetralogy of Fallot (TOF).

CHDs include the following:

- **An atrial septal defect (ASD):** A heart defect in which there is a hole in the wall (septum) that divides the upper chambers (atria) of the heart.
- **A ventricular septal defect (VSD):** A heart defect in which there is a hole in the wall (septum) that separates the two lower chambers (ventricles) of the heart.
- **Patent ductus arteriosus (PDA):** A heart defect in which there is a blood vessel (ductus) connecting the aorta and pulmonary artery. It is normal in a fetus but can persist abnormally after a child is born.

- **Obstructive defects of the left heart include:**
  - **juxtaductal aortic coarctation:** coarctation (narrowing) occurs most often in a short piece of the aorta near the ductus and thus is called 'juxtaductal' coarctation.
  - **long-segment aorta narrowing:** narrowing of the descending or abdominal aorta that is usually mild but can be more severe.
  - **aortic valve stenosis:** the valve between the lower left heart chamber and the body's main artery (aorta) may be narrowed and may not open fully.
  - **mitral valve stenosis:** a narrowing of the heart's mitral valve which may not open properly, blocking blood flow into the main pumping chamber of the heart (left ventricle).
  - Less common are obstructive defects of the right-side, such as **pulmonary valvar stenosis** (narrowing of the valve of the heart that allows blood to flow from the right side of the heart to the lungs) and **branch pulmonary artery stenosis** (narrowing of some of the parts of the pulmonary arteries that bring blood from the heart to the lungs).

Acquired Heart Issues

In contrast to CHDs, some heart problems occur after birth, usually after adolescence and into adulthood. They can be progressive (developing gradually or over time). Many persist and do not go away. Some may worsen following instrumentation (the use of tools, appliances, or apparatus in the treatment of a patient).

- **Pericardial disease:** the pericardium is a thin tissue sac that surrounds the heart. Pericardial disease can present as a short-term or recurrent effusion (fluid) or as chronic (persisting for a long time or recurring). Rarely, in the most severe form, it can progress to constrictive pericarditis in which the pericardial sac becomes thick and stiffened and restricts the filling of the heart; this requires surgical intervention.
- **Restrictive cardiomyopathy (RCM):** a form of heart muscle disease (cardiomyopathy) in which the chambers of the heart become stiff over time. This condition impacts the heart muscle, making it more challenging to pump blood throughout the body and lungs. Restrictive cardiomyopathy is the least common type in the general population and can be challenging to diagnose. It can be overlooked unless a cardiac catheterization is performed. This is an invasive procedure to examine how well your heart is pumping and requires the insertion of a catheter into a large blood vessel that leads to your heart. This measures the hemodynamics which refers to heart pressures and oxygenation.
- **Constrictive pericarditis** (stiff and thick pericardium) and restrictive cardiomyopathy (stiff heart muscle) can present similarly. They differ in cause and treatment. Doctors need to be aware of the differences and test appropriately.

- **Systemic hypertension:** refers to high blood pressure in the arteries that carry blood from your heart to your body's tissues.
- **Pulmonary hypertension:** refers to high blood pressure in the arteries of the lungs and leads to stress on the right side of the heart. It has been infrequently reported, which may reflect limited evaluations, reporting in medical literature, or the tendency for journal articles to report younger patients. Pulmonary hypertension may be more common with aging.
- **Peripheral vascular stenosis:** a circulatory condition in which narrowed blood vessels reduce blood flow to the limbs. It can affect the renal (kidney) or celiac arteries. The celiac artery is a blood vessel that branches off of the aorta and helps to send blood to certain organs (ex. stomach, liver, etc). Both affect blood flow to the limbs.

Treatment

Currently, there is no evidence that management of specific issues in Myhre syndrome differs from standard cardiac care. While some procedures are unavoidable, and necessary for survival in infancy, unnecessary instrumentation (the use of surgical tools) should be avoided as associated tissue trauma may induce stenosis (narrowing) and the scarring-type tissue response - unique to Myhre syndrome. The risks and benefits of any procedure should be thoroughly discussed with the cardiologist and the cardiothoracic surgeon.

Management Of Symptoms

All individuals with Myhre syndrome should be followed by a cardiologist who recognizes that their patient has a rare condition that requires special attention. Children should be followed by a pediatric cardiologist.

An echocardiogram or 'echo' with doppler (a non-invasive ultrasound of the heart) should be done at the time of diagnosis. Subsequent echoes should be performed every one to three years in patients whose first echocardiograms were normal. Baseline upper and lower body blood pressure measurement should be obtained.

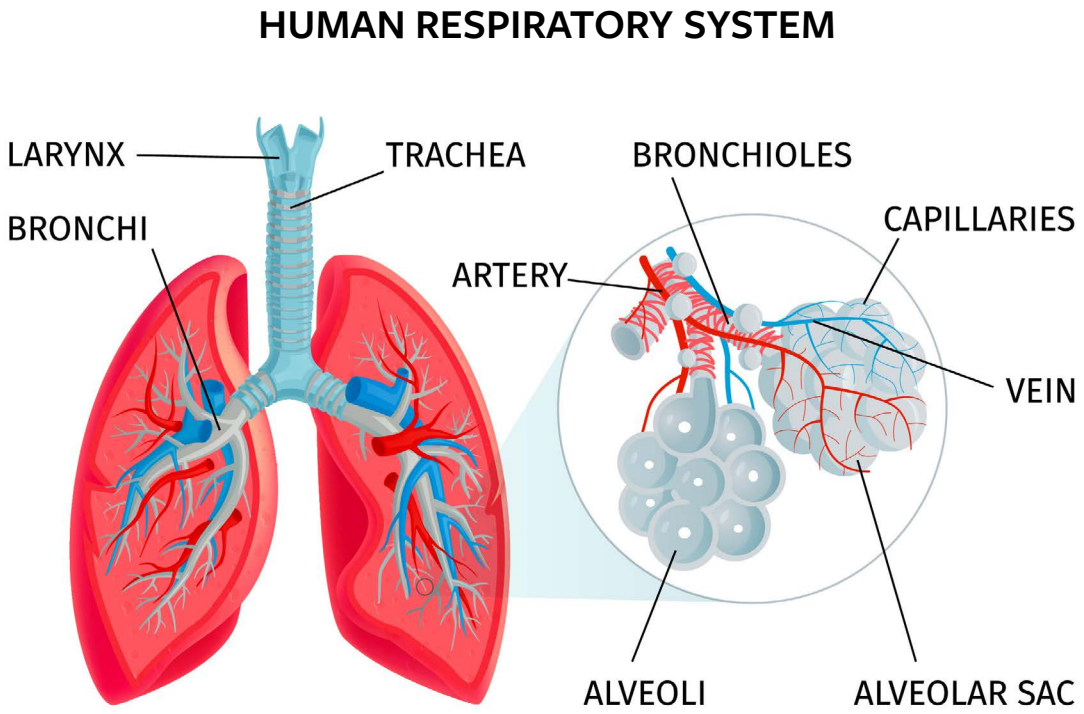
People who have abnormal cardiovascular findings at the time of initial diagnosis should consider more extensive imaging given the progressive nature of Myhre. One example is an MRI (magnetic resonance imaging), which is a medical imaging technique that uses radio waves to produce detailed images of almost every internal structure in the human body (including the organs, bones, muscles, and blood vessels). While MRIs are typically noninvasive and painless, sometimes a provider may order one 'with contrast ' that requires an IV through which dye will be injected to get a better picture of the structures of the heart to explain any symptoms or other findings.

Clinical Characteristics, Treatment & Management of Symptoms

To image the aorta well, MRA (magnetic resonance angiography) or CTA (computed tomography angiography) can be used. If a child has a heart or aorta abnormality, follow-up should be provided by a pediatric cardiologist who will provide patient-centered care. For adults diagnosed with a heart or aorta problem, follow-up should be provided by a cardiologist familiar with adult congenital heart disease (ACHD).

Respiratory System

Network of organs and tissues that help you breathe



Clinical Characteristics

Breathing issues are influenced by several factors or causes.

- **Airway narrowing:** typically involving the larynx and trachea, includes subglottic stenosis (a narrowing of the airway below the vocal cords and above the trachea) that can occur shortly after birth, or later. It is suspected that some types of intubations, if repeated and severe, might lead to this problem. Less common is narrowing of the upper airway (nasal cavities, oral cavity, pharynx, and larynx).
- **Choanal stenosis:** narrowing of a specific part of the nasal passage behind the nose.
- **Restrictive lung disease:** commonly seen in people with Myhre syndrome. It may occur from issues related to the lungs themselves or reduced compliance (flexibility) of the chest wall. Sometimes asthma is diagnosed in people with Myhre syndrome but often there is 'more to it' than typical asthma. With **restrictive pulmonary disease,** the lungs do not expand fully. With **obstructive lung disease,** the lungs do not expel the air fully. Both conditions can cause shortness of breath, exercise intolerance and when severe, low blood oxygen.

Treatment

Due to tracheal narrowing, some individuals with Myhre syndrome have required long-term tracheostomy which is a surgical procedure that creates on opening in the neck that opens into the air tube (trachea). Narrowing of the airway is not completely understood. It is suspected that it may be a congenital defect or follow many or traumatic intubations **(intubation is a procedure in which a tube is inserted into a person's airway. The tube keeps the trachea open so that air can get through and the individual can breathe either on their own or with the help of a machine (ventilator)).**

To avoid traumatic intubation, notify the care provider and anesthesiologist that experts in Myhre syndrome recommend using a size-smaller uncuffed endotracheal tube.

Elective (not completely medically necessary) tracheal surgery/intubation should be avoided.

Management Of Symptoms

If a person complains of any shortness of breath, oxygen saturation (level of oxygen in the blood) should be checked. If low, treatment should be provided. This may include oxygen or aerosol medications.

Pulmonary function tests (PFTs) should be completed annually or more often as needed for adults. PFT's refer to a range of breathing tests that measure how well your lungs are working. Children who can cooperate with testing and take instruction, often older than six, should have these tests done as well.

Evaluation for upper airway (trachea/throat) narrowing should be considered based on symptoms such as noisy breathing, severe snoring, increased work to breathe, and low level of oxygen in the blood. A pulmonologist or ear, nose, throat (ENT) physician can assess for airway narrowing by the least invasive (least damaging or traumatic to the body) method when signs of upper-airway obstruction might be present.

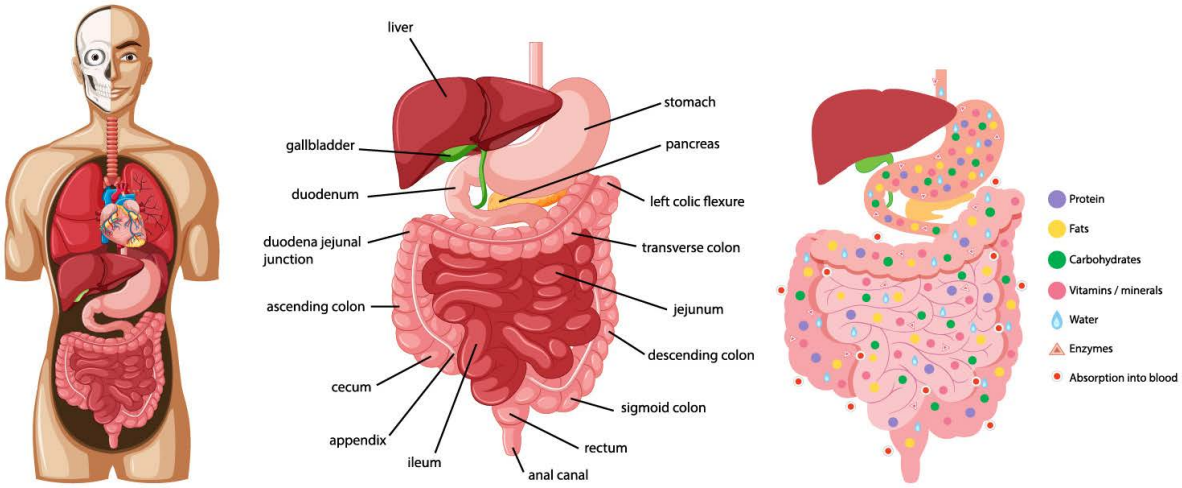
Pulmonologists can also assess lungs for evidence of restrictive and obstructive lung disease using oxygen saturation measurement, pulmonary function tests, chest x-rays, and occasionally more advanced imaging of the lungs.

People with Myhre syndrome and their close family members should not smoke or vape.

Gastrointestinal

Passageway of the digestive system that leads from the mouth to the anus

DIGESTIVE SYSTEM



Clinical Characteristics

- **Duodenal atresia:** a blockage of the duodenum (first part of the small intestine) which connects the stomach to the other intestinal segments called the jejunum and ileum. Together, they form a long hollow tube which digests food.
- **Pyloric stenosis:** thickening of the pylorus (the muscle at the end of the stomach before it connects to the intestines). When stenosis is present, the blockage results in severe and forceful (projectile) vomiting in the first few months of life.
- **Protein-losing enteropathy (PLE):** an extremely rare problem that is not part of Myhre syndrome itself but can occur with restrictive cardiomyopathy. It is a complicated problem in which serum proteins are lost inappropriately into the intestines. This leads to low protein in the blood. PLE in Myhre syndrome is a 'secondary' problem which differs from its occurrence in people with a problem of the lymphatics.
- **Severe constipation:** infrequent bowel movements or difficult passage of stools that persists for several weeks or longer.

- **Velopharyngeal insufficiency (VPI):** often caused by a soft palate that is too short or muscles of the palate that do not work well. Sometimes this can manifest as nasal speech or fluids coming out of the nose (especially when laughing).

Individuals with cleft palates or VPI should be referred to a craniofacial clinic because a multi-team approach is beneficial. If not available, a pediatric ENT doctor who works with a speech therapist is ideal.

Treatment

Aggressive management of constipation (through dietary means or medication if necessary) is recommended.

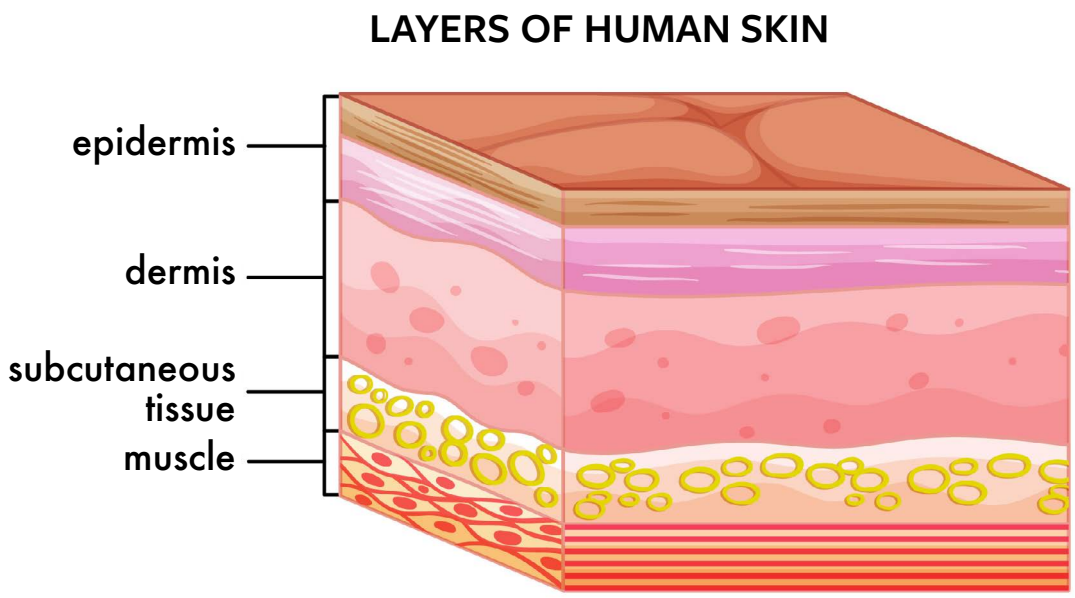
Management of Symptoms

In order to evaluate the gastrointestinal tract, endoscopy (a thin, flexible tube equipped with a light and camera (endoscope) may be inserted down the throat and into the tube that leads to the stomach). The tiny camera will examine the upper gastrointestinal tube until the small intestine (duodenum). This procedure should be approached with caution in individuals with Myhre syndrome due to risk of scarring. Noninvasive (external) 3D imaging may be preferred.

For any type of procedure on the gastrointestinal tract, minimal instrumentation (the use of tools, appliances, or apparatus in the treatment of a patient) is recommended. Following the procedure, adhesions (a band of scar tissue that joins two internal body surfaces that are not usually connected) can form, with fatal or serious consequences. GI interruptions such as pyloric stenosis or duodenal atresia require surgery.

Cutaneous

Skin



Clinical Characteristics

Thickening or stiffness of the skin throughout the body is seen in nearly all individuals with Myhre syndrome. Various terms used to describe the skin include thick, stiff, firm, rough, keratotic (a rough, scaly patch or bump on the skin), and inelastic (not elastic). Additional findings are minimal creasing of the facial skin, thick scars that resemble keloids (a thick raised scar), and other unusual scars. Skin changes may not be apparent in infancy; some may progress with age.

Treatment

There is no known treatment at this time.

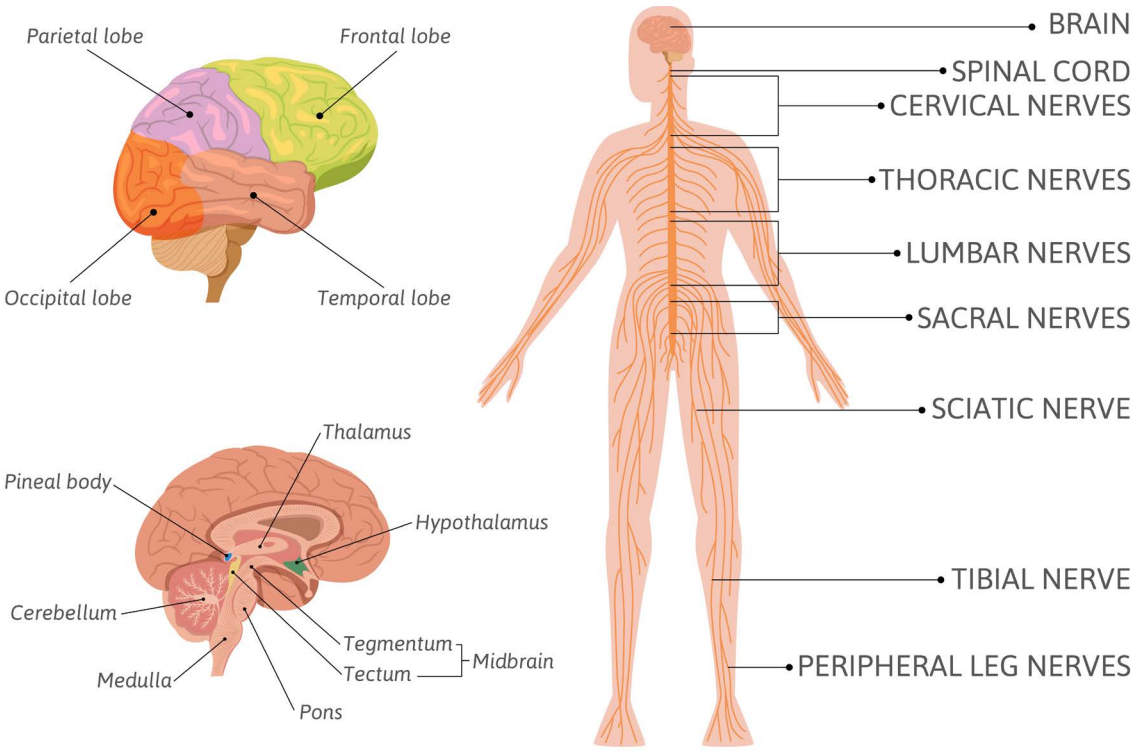
Management Of Symptoms

People with Myhre syndrome should follow up with their primary provider for any skin abnormalities.

Neuropsychiatric

Mental, emotional, and behavioral health as well as cognition which includes thinking, reasoning and memory related to the brain

BRAIN AND NERVOUS SYSTEM



Clinical Characteristics

- **Mild to moderate intellectual disability:** when a person's ability to learn at an expected level and function in daily life is limited. It is often based on the measured IQ, (intelligence quotient).
- **Developmental delay:** a lag in typical developmental skills compared to others of the same age. This occurs in all children with Myhre syndrome but can vary from mild to severe. Delays may occur in motor function (physical skills), speech and language, cognitive (thinking, reasoning, remembering), play, and social skills. Some individuals 'catch up' their skills over time to be age appropriate.

- **Social disability:** at some level occurs in almost all people with Myhre syndrome. This can improve over time. Some individuals may fulfill criteria for autism spectrum disorder.

Of note, acquired (not born with) and unrecognized hearing loss may also contribute to speech delays, as well as academic and social challenges.

Treatment

Neuropsychological evaluation may be indicated for those with autistic behaviors, high activity level, and or cognitive issues. In many areas, especially for school age children, this is also known as a PsychEd assessment.

Testing will see how your brain works. Testing will include reading, language usage, attention, learning, processing speed, reasoning, remembering, problem-solving, mood and personality and more. This information can be very helpful for the schools to help your child learn and to develop an IEP (individualized educational plan).

Children may qualify for and benefit from interventions used in the treatment of autism spectrum disorder, including applied behavior analysis (ABA). ABA therapy is targeted to the individual child's behavioral, social, and adaptive strengths and weaknesses and typically performed one on one with a board-certified behavior analyst.

Consultation with a developmental pediatrician may be helpful in guiding parents through appropriate behavior management strategies or providing prescription medications when necessary. Individualized behavioral therapy or pharmacologic (medication) treatment for anxiety, depression, or other mental health issues may be helpful to some people with Myhre syndrome. Please discuss with your primary care doctor if needed.

Management

The following information represents typical management recommendations for individuals with developmental delay, intellectual disability in the United States; standard recommendations may vary from country to country.

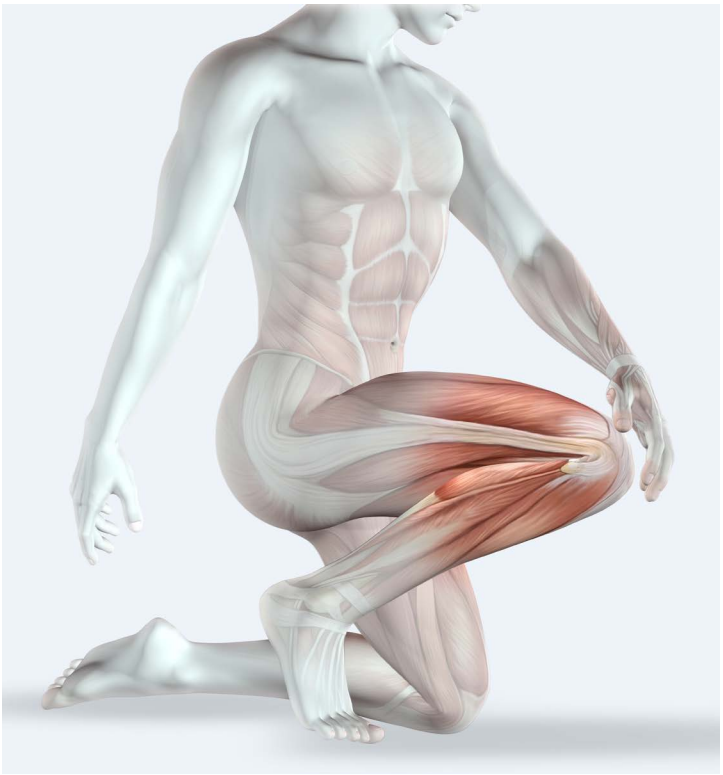
- **Ages 0-3 years**. Referral to an early intervention program is recommended for access to occupational, physical, speech, and feeding therapy. In the US, early intervention is a federally funded program available in all states administered through local public-school districts.
- **Ages 3-5 years.** In the US, developmental preschool through the local public school district is recommended. Before placement, an evaluation is made to determine needed services and therapies and an IEP is developed.

Clinical Characteristics, Treatment & Management of Symptoms

- **Ages 5-21 years.** In the US, an IEP based on the individual's level of function should be developed by the local public school district. Affected children are permitted to remain in the public school district until age 21. Discussion about transition plans including financial, vocation/employment, and medical arrangements should begin at age 12 years. Developmental pediatricians can aid with transition to adulthood.
- **All ages.** Consultation with a developmental pediatrician is recommended to ensure the involvement of appropriate community, state, and educational agencies and to support parents in maximizing quality of life. Consideration of private supportive therapies based on the affected individual's needs is recommended. Specific recommendations regarding type of therapy can be made by a developmental pediatrician.

Musculoskeletal System

Bones, muscles, and joints



Clinical Characteristics

Most infants with Myhre syndrome are small during pregnancy, and at birth. It is referred to as intrauterine growth restriction (IUGR) and small for gestational age (SGA).

- Short stature (reduced height for family potential) and a compact physique with normal head size becomes more apparent over time. Adult height is typically significantly less than what would be predicted from analyzing the parent's heights. There are some people with Myhre syndrome who have normal growth. Ongoing research is investigating the potential reason.
- Small hands and feet with short fingers (brachydactyly) are common.
- Posture may be distinctive with a straight spine, flexed (bent) elbows and bending forward at the hips.
- Reduced range of motion of large and small joints is characteristic and is exacerbated (gets worse) with age. Walking on tiptoes ('toe walking') is common.

Treatment

Consider physical therapy to keep joints mobile. However, no studies at this time have proven that this helps. Note: It is not known if passive range of motion exercises (when someone or something is creating the movement, such as a massage or physical therapist) keep joints more mobile over time.

Management Of Symptoms

Physical skill development and joint mobility should be monitored for any abnormalities.

At this time, there is no evidence that Myhre syndrome management of specific issues would differ from standard musculoskeletal care. However, any unnecessary instrumentation (the use of surgical tools) should be avoided as associated tissue trauma may induce stenosis (narrowing) and the scarring-type tissue response - unique to Myhre syndrome. The risks and benefits of any procedure should be thoroughly discussed with your primary care provider and the surgeon.

Immune System

Protects against bacteria, viruses and fungi

Clinical Characteristics

The immune system protects against germs such as bacteria, viruses, and fungi. A weakness in the immune system can contribute to increased infections. In individuals with Myhre syndrome, research is needed to determine if there is an increased susceptibility (more likely) to have an infection. There may be an immunoglobulin deficiency in Myhre syndrome (a health problem in which the body does not make enough immunoglobulin).

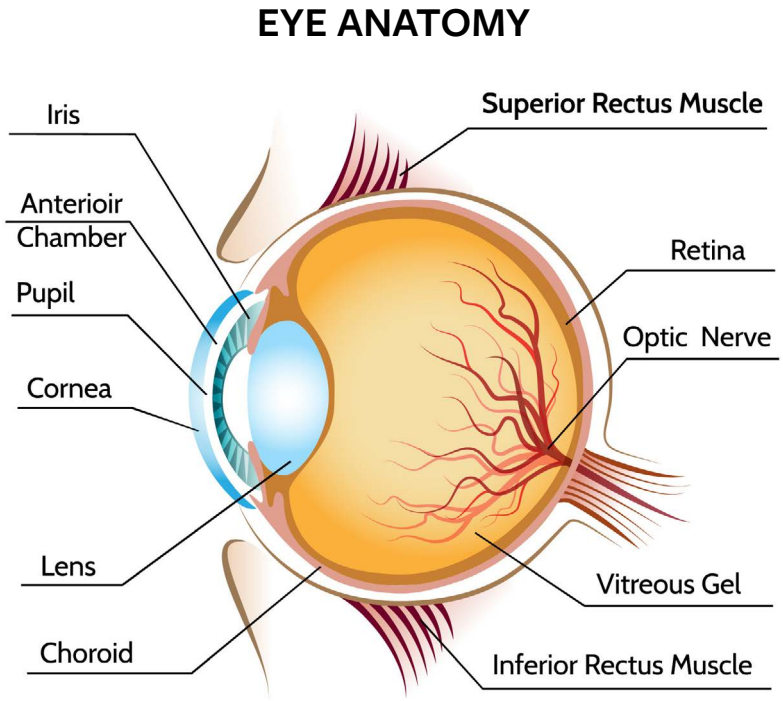
Treatments

Recurrent infections include otitis media (inner ear infections) and pneumonia (which involves the lungs). Both can be treated as needed by your providers.

Intravenous Immunoglobulin (IVIG) therapy can be used as a treatment for patients with persistent antibody deficiencies.

Ophthalmology

Eye and vision



Clinical Characteristics

At least one abnormal eye finding was reported in 53% (26/49) of affected individuals:

- **Strabismus** 13/53 (24%): misalignment of the eyes, causing one eye to deviate inward (esotropia) toward the nose, or outward (exotropia), while the other eye remains focused.
- **Refractive errors** in 17/53 (31%): refractive error means that the shape of your eye does not bend light correctly, resulting in a blurred image. The main types of refractive errors are myopia (nearsightedness), hyperopia (farsightedness), presbyopia (loss of near vision with age), and astigmatism (see below for definition)
- Other.
  - **Cataracts:** a cloudy area in the lens of your eye.
  - **Astigmatism:** the cornea (the clear front layer of your eye) or lens (an inner part of your eye that helps the eye focus) has a different shape than normal
  - **Optic nerve sheath meningioma (ONSM):** uncommon, benign (non-cancerous) neoplasms (tumors) originating from the meningothelial cells of the meninges

(specialized cells that are found in the brain and spinal cord that make up the meninges) surrounding the optic nerve. The tumor may arise from either the intraorbital or intracanalicular portions of the optic nerve where there is a meningeal sheath (a covering of the meninges).

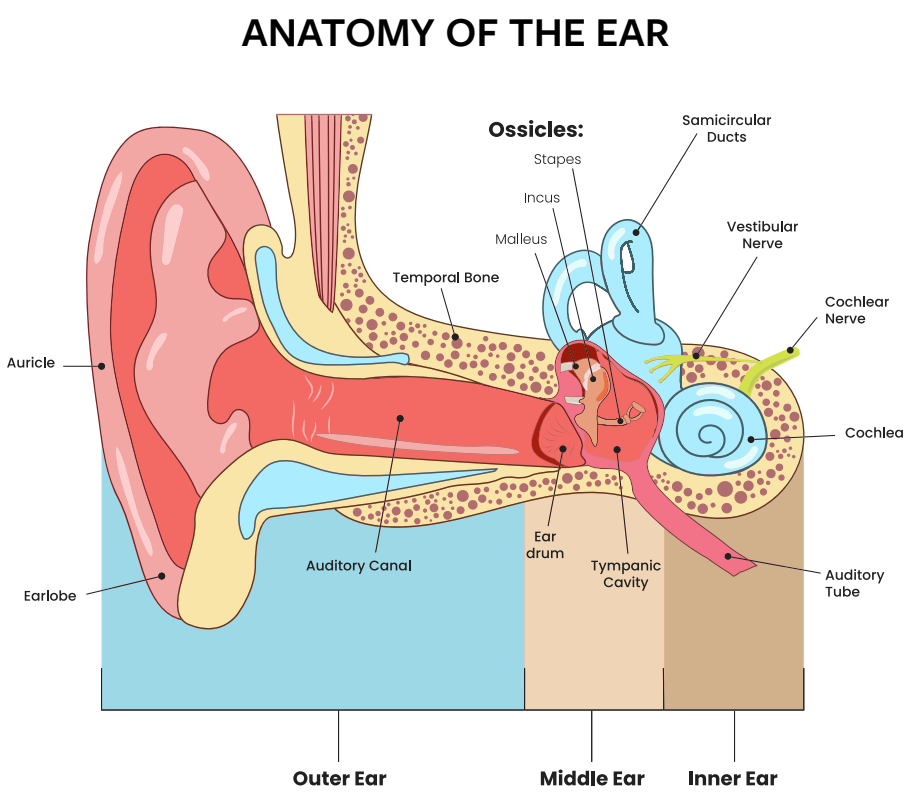
Treatment

Most individuals with Myhre syndrome benefit from glasses. Vision problems and 'lazy eye ' are common.

Management Of Symptoms

An annual evaluation (eye test) should be done by an ophthalmologist to evaluate for vision problems and medical problems with the eyes.

Hearing



Clinical Characteristics

Hearing loss is usually **conductive** (blockage of the normal movement of sound through the external ear or middle ear, preventing the inner ear to receive the sound), but can be **sensorineural** (abnormalities in the inner ear or the nerve which travels from the brain to the ear). Another type is called **mixed** hearing loss because there are elements of both conductive hearing loss and sensorineural hearing loss. The underlying cause of the hearing loss in Myhre is often unclear or unknown.

Most patients have a history of multiple inner ear infections, which require PE tubes in both ears. These can fall out or get clogged with ear wax. Many people with Myhre syndrome have been noted to have copious amounts of ear wax.

Of note, most infants pass their newborn hearing screen. Hearing loss usually becomes evident in early childhood when a formal hearing test (audiogram) is performed. Because there is a tendency to progress, hearing loss is typically present in adults.

Treatment

Appropriate hearing aids as required based upon the type and severity of hearing loss. Hearing loss can be progress and regular follow up is recommended.

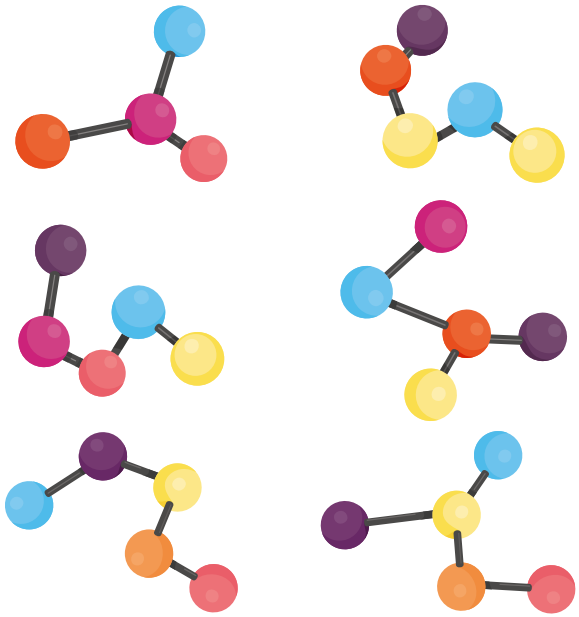
Frequent middle ear fluid – ear tubes as needed.

Management Of Symptoms

Annual hearing and ear exams or more often as needed.

Endocrine System

Hormones and the related glands



Clinical Characteristics

- Early or delayed puberty, usually normal in characteristic.
- Secondary amenorrhea in women, which refers to the absence of three or more periods in a row by someone who has had periods in the past. This should be evaluated by the primary care physician.
- Heavy menses (period)
- Diabetes has been reported in multiple individuals.
- Short stature

Management Of Symptoms

Evaluation by urine analysis, fasting glucose, and hemoglobin A1c on an annual basis after the second decade or sooner if there are symptoms of diabetes such as excessive thirst and frequent urination. Growth hormones have been utilized though it is not known if there is an overall increase in adult height.

Neoplasia

Uncontrolled, abnormal growth of cells or tissues in the body

Clinical Characteristics

An uncontrolled, abnormal growth of cells or tissues in the body which can include some types of cancer. The abnormal growth itself is called a neoplasm or tumor, which can be benign (growing slowly, and not spreading) or malignant (with uncontrollable cell growth that spreads locally or to distant sites). Neoplasia in Myhre syndrome was summarized in an article (Lin et al., 2020) which reported six patients.

- Endometrial carcinoma refers to cancer which involves uterus (womb). It has been reported in three women with Myhre syndrome.
- There were three other patients with very small tumors in the brain. These included an optic nerve sheath meningioma (a benign neoplasm originating from the tissue which surrounds the optic nerve to the eye). Another patient had a small mesencephalic glioma which is an infiltrating tumor at the base of the brain. A third patient had a small schwannoma (a tumor originating from the Schwann cells which are specialized cells found in the peripheral nervous system).

There may be other people with Myhre syndrome who have tumors that have not yet been reported in the medical literature.

Treatment

At this time, there is no evidence that in Myhre syndrome management of specific issues would differ from standard care. However, any unnecessary instrumentation (the use of surgical tools) should be avoided as associated tissue trauma may induce stenosis (narrowing) and the scarring-type tissue response - unique to Myhre syndrome. The risks and benefits of any procedure should be thoroughly discussed with the provider and the surgeon.

Management Of Symptoms

Monitoring for endometrial cancer should be considered as this has been reported in females with Myhre syndrome. The risks and benefits of hysterectomy (a surgical procedure to remove the womb or uterus) should be weighed against the risk of endometrial cancer in older women with Myhre syndrome. If hysterectomy is performed, monitor for symptoms that could be caused by banding (severe abdominal pain, no bowel movement) in the days/weeks after the procedure. If possible, avoid as after surgery thickening/scarring of the tissues is highly likely.

Prevention of secondary complications

Preventing damage to tissue is the single most important preventative measure

Extreme care with intubation and use of an endotracheal tube without a cuff (or careful monitoring of pressures with a cuff) may help prevent airway stenosis (narrowing). Alerting the anesthesiologist that experts in Myhre syndrome recommend utilizing a size-smaller tube if possible. Consideration should be given to a pre-operative visit with an ENT specialist who focuses on airways. Working with the anesthesiologist, they can determine if there are any existing airway issues. When possible, providers can consider whether there are alternatives to intubation (which refers to placement of a breathing tube in the airway). There are some noninvasive techniques such as using a 'bag and mask'. Whenever possible, use non-invasive approaches.

Limit abdominal and pelvic procedures as extensive adhesions (a band of scar tissue that joins two internal body surfaces that are not usually connected) may develop after the surgery.

Monitoring for endometrial cancer should be considered as this has been reported in females with Myhre syndrome. The risks and benefits of hysterectomy (a surgical procedure to remove the womb or uterus) should be weighed against the risk of endometrial cancer in older women with Myhre syndrome. If hysterectomy is performed, monitor for symptoms that could be caused by banding (severe abdominal pain, no bowel movement) in the days/weeks after the procedure. If possible, avoid as after surgery thickening/scarring of the tissues is highly likely.

Resources

Appointment Notes

Print and take this form to each of your appointments for easy reference and a history that is available at a glance.

Doctor name:	Follow up frequency:	Visit date:
Notes:		
Next appointment scheduled for:		

Overview of Care Team (page 1)

Use this template to keep track of the specialists you see. Print it out and keep handy, as well as sharing with a next of kin or family member.

Specialty	Doctor name	Clinic	Phone number	Email	Follow up frequency
Cardiology					
Dentist					
Endocrinology					
ENT					
Gastrointestinal					
Genetics					
Gynecology					
Nephrology & Hypertension					
Neuropsychology					
Occupational Therapy					

Overview of Care Team (page 2)

Use this template to keep track of the specialists you see. Print it out and keep handy, as well as sharing with a next of kin or family member.

Specialty	Doctor name	Clinic	Phone number	Email	Follow up frequency
Ophthalmology					
Physical Medicine & Rehab					
Physical Therapy					
Pulmonology					
Rheumatology					
Skin					
Sleep Medicine					
Speech Therapy					
Urology					

Myhre Syndrome Foundation – Medical Terminology List

Medical Terminology	Abbreviation	Definition
abdominal aortic aneurysm	**AAA**	a weak section of the lower part of the aorta; pressure causes it to bulge
ablation		the use of heat, chemicals, or cold to destroy tissues, tumors, or blood vessels
activities of daily living	**ADL**	daily self care activities such as bathing, dressing, eating, and hygiene; term used often in physical and occupational therapy
acute		sudden in onset (severe is implied sometimes, but not necessarily severe)
acute renal failure	**ARF**	acute kidney failure
ancillary		refers to diagnostic or therapeutic procedures that supplement the main tests or treatment
anterior		refers to the front such as the nose is on the anterior surface of the face
aorta		the main artery that supplies the blood to all other arteries in the body
artery		blood vessel that carries blood from the heart to organ or tissues
artifact		something that is seen in radiology but not present in reality
as needed	**PRN**	pharmacy term
at bedtime	**QHS**	pharmacy term
atresia		absent, underdevelopment or abnormal closure of a structure or opening
atrial fibrillation	**A-fib**	a type of heart arrhythmia involving the right side of the heart
atrophy		reduction in size of organ or structure
autosomal dominant		one way a genetic trait or disorder is passed down through families; if you get an abnormal gene from one parent, you will get the disease
autosomal recessive		one way a genetic trait or disorder is passed down through families; the child needs to inherit a copy of the defective gene or trait from each parent
balloon angioplasty		procedure using a small balloon to open narrow blood vessels
barium		a white, radio-opaque material that is visible with x-rays
basic metabolic profile	**BMP**	a lab test that gives a general metabolism overview
blood pressure	**BP**	a pressure of the blood in the circulatory system
bone density or DEXA scan		test to detect the density of your bones
both eyes	**OU**	pharmacy term
catheter		a long, thin, flexible tube
cerebral vascular accident	**CVA**	stroke
cerebrospinal fluid	**CSF**	clear, colorless fluid that surrounds the brain and spinal cord

Myhre Syndrome Foundation – Medical Terminology List

Medical Terminology	Abbreviation	Definition
chest pain	**CP**	pain in the chest area
chest x-ray	**CXR**	see x-ray
chief complaint	**CC**	the reason a patient is visiting the doctor in their own words; example...my chest hurts
chronic		persisting for a long time or constantly recurring
complete blood count	**CBC**	a lab test that counts red blood cells, white blood cells, and platelets in the blood
comprehensive metabolic profile	**CMP**	a lab test that measures general metabolism as well as liver function
computerized tomography	**CT**	medical imaging using x-rays to get detailed images inside the body; contrast may or may not be used
computerized tomography angiogram	**CTA**	a specialized CT that uses contrast to view blood vessels and other tissues within the body
continuous positive airway pressure	**CPAP**	common treatment for sleep apnea which keeps the airway open
contrast		dye or other substance that helps to show abnormal areas inside the body
critical care	**CC**	medical care for those with life-threatening injuries or illnesses
deep vein thrombosis	**DVT**	a blood clot of the deep veins
degenerative joint disease	**DJD**	medical term for what is commonly known in lay terms as arthritis
diabetes mellitus	**DM**	a disease in which the body is unable to produce or unable to respond normally to insulin resulting in abnormal metabolism of carbohydrates
distal		parts of the body located away from the center of the body; your hands are distal to your elbows
do not intubate	**DNI**	an advanced directive which states the patient does not want a breathing tube
do not resuscitate	**DNR**	an advanced directive which states a person does not want CPR
dyspnea on exertion	**DOE**	shortness of breath upon exertion
electrocardiogram	**EKG**	a test used to measure the electrical activity of the heart
electroencephalogram	**EEG**	a test used to measure electrical activity within the brain
embolism		a blockage of a blood vessel
endovascular procedure		a wire or catheter in inserted into the blood vessels through a small incision by a specialized doctor called an interventional radiologist; minimally invasive
every day	**QD**	pharmacy term
every evening	**QPM**	pharmacy term
every morning	**QAM**	pharmacy term
every other day	**QOD**	pharmacy term

Myhre Syndrome Foundation – Medical Terminology List

Medical Terminology	Abbreviation	Definition
fibrosis		abnormal healing in which connective tissue replaces normal tissues
fluoroscopy		a real time x-ray that guides a doctor in a procedure such as setting a bone
four times a day	**QID**	pharmacy term
gain of function		an increased or new response from the body that is produced by the atypical structure of SMAD4 gene associated with Myhre Syndrome
Gastroesophageal Reflux Disease	**GERD**	a condition in which stomach acid and contents rise into the esophagus
gene		small molecules within our bodies that provide instructions that allow us to grow and live; DNA is needed in order to create genes
headache	**HA**	
history of present illness	**HPI**	a type of doctor appointment which is usually required before surgery which involves taking both the patient's history and doing a physical exam
Hyperlipidemia		high cholesterol
hypertension	**HTN**	high blood pressure
incision and drainage	**I&D**	opening up an abscess and draining it
inferior		refers to below; the feet are inferior to the knees
intensive care unit	**ICU**	a specialized unit at the hospital for patients who are acutely unwell and require critical medical care
intramuscular	**IM**	a shot in the muscle
joint	**JT**	
lateral		to the side of or away from the middle of the body
left	**LT**	
left eye	**OS**	pharmacy term
left lower quadrant	**LLQ**	the left lower area of the abdomen
left upper quadrant	**LUQ**	the left upper area of the abdomen
liver function tests	**LFT**	a lab which measures the function of the liver
low back pain	**LBP**	
Magnetic Resonance Angiogram	**MRA**	a type of MRI that looks specifically at blood vessels; uses IV contrast
Magnetic Resonance Imaging	**MRI**	a type of imaging using magnetic fields to get a detailed image of the body; contrast may be used to get clearer images
Massachusetts General Hospital	**MGH**	
medial		towards the middle of the body

Myhre Syndrome Foundation – Medical Terminology List

Medical Terminology	Abbreviation	Definition
milligrams	**MG**	a measurement that is often used for medicine in pharmacy
milliliters	**ml**	a liquid measurement used for medicine in pharmacy
mitral valve prolapse	**MVP**	the two valve flaps of the mitral valve do not close evenly or smoothly. The mitral valve is between the left atrium and ventricle of the heart
nausea vomiting	**N/V**	
non sustained ventricular tachycardia	**NSVT**	a type of heart arrhythmia of the left side that is not sustained
normal sinus rhythm	**NSR**	normal heart beat
nothing by mouth	**NPO**	instructions often given prior to a procedure meaning nothing orally
occult		refers to a diagnosis that the doctor cannot see on one or more images; occult fracture
occupational therapy	**OT**	therapy which focuses on enabling people to do the things they need in order to live their daily lives
oral	**PO**	pharmacy term
periumbilical		towards or nearest to the center of the body
physical therapy	**PT**	a type of therapy which uses exercises to help people regain or improve their physical abilities
platelets	**Plt**	a component of the blood
Positron Emission Tomography	**PET Scan**	an imaging technique that looks for changes in metabolic processes seen in cancer, bone formation, and other processes
posterior		refers to the back; the spine is on the posterior surface of the body
potassium	**K**	a mineral necessary for body function
premature ventricular contraction	**PVC**	a common type of heart arrhythmia involving the left ventricle
proximal		closer to the center of the body; your shoulder is proximal to your hand
pulmonary embolism	**PE**	a blood clot of the lungs
pulmonary function test	**PFT**	lung function test
pulse	**P**	the number of times a heart beats per minute; can be felt in various locations of the body
pupils equal round and reactive to light and accommodation	**PERRLA**	An abbreviation doctors use to indicate the eyes are functioning normally
rebound	**REB**	the return of response upon withdrawal of the stimulus; often used to describe a response to abdominal pain examination
review of systems	**ROS**	an inventory of the body systems obtained through a series of questions in order to identify signs or symptoms which the patient may be experiencing
right	**RT**	
right eye	**OD**	pharmacy term

Myhre Syndrome Foundation – Medical Terminology List

Medical Terminology	Abbreviation	Definition
right lower quadrant	**RLQ**	right lower area of the abdomen
right upper quadrant	**RUQ**	right upper area of the abdomen
rule out	**R/O**	a medical term meaning the condition has been ruled out
sclerosis		stiffening of the tissue
shortness of breath	**SOB**	having difficulty breathing
SMAD4	**SMAD4**	the gene that is atypical in individuals with Myhre Syndrome
sodium	**NA**	a mineral necessary for body function
speech therapy	**ST**	a therapist who works with speech and language disorders as well as swallowing
status post	**s/p**	a treatment or diagnosis that a patient has previously experienced such as status post appendix removal
stenosis		an abnormal narrowing
stent		an expandable metal or plastic tube used to hold open a blood vessel from the inside
subcutaneous	**SQ**	a shot under the skin
superior		location meaning above; the head is superior to the chest
temperature	**T**	
three times a day	**TID**	pharmacy term
twice a day	**BID**	pharmacy term
ultrasound	**US**	a type of radiology exam using ultrasound waves; can be used to look at soft tissues such as organs or for fluid accumulations
units	**U**	a measurement used in pharmacy
upper respiratory infection	**URI**	an infection of the upper airways
urinalysis	**UA**	lab test in which urine is analyzed
urinary tract infection	**UTI**	an infection of the urinary tract
urine culture	**UC**	lab test in which a culture of urine is taken to see if any abnormal bacteria grows
ventricular tachycardia	**VT**	a type of heart arrhythmia involving the left side of the heart
vital signs	**VS**	temperature, pulse, blood pressure, respiratory rate, and sometimes oxygen saturation
vital signs stable	**VSS**	normal or stable vital signs
weight	**Wt**	
x-ray		a type of imaging used to visualize mostly bones; can also see fluid in the chest or other body areas