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Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome Overview

Synonyms: Berdon Syndrome, MMHS

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Summary

The purpose of this overview is to increase the awareness of clinicians regarding megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) and its genetic causes and management.

Goal 1

Describe the clinical characteristics of MMIHS.

Goal 2

Review the genetic causes of MMIHS.

Goal 3

Provide an evaluation strategy to identify the genetic cause of MMIHS in a proband (when possible).

Goal 4

Review management of MMIHS.

Goal 5

Inform genetic counseling of family members of an individual with MMIHS.

1. Clinical Characteristics of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is characterized by megacystis (bladder distention in the absence of mechanical obstruction), microcolon, and intestinal hypoperistalsis (dysmotility). This rare disorder is associated with significant morbidity and mortality.

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MMIHS may be suspected prenatally secondary to findings of fetal megacystis on prenatal ultrasound. Affected infants present shortly after birth with symptoms of bowel and bladder obstruction. The most common presenting symptom is abdominal distention that is secondary to a massively dilated bladder in the absence of mechanical obstruction with or without dilated bowel loops. Other manifestations include bilious emesis, failure to pass meconium, and inability to spontaneously void requiring catheterization [Puri & Shinkai 2005, Puri & Gosemann 2012, Soh et al 2015, Wymer et al 2016, Hugar et al 2018, Prathapan et al 2021, Pellegrino et al 2024].

Infants and children with MMIHS have myopathic dysfunction of bladder and associated urologic comorbidities that include urinary retention, febrile urinary tract infections, vesicoureteral reflux (VUR), and hydronephrosis with resultant risk of kidney failure [Wymer et al 2016, Hugar et al 2018, Pellegrino et al 2024]. Gastrointestinal complications of MMIHS include microcolon, intestinal dysmotility, and associated gastrointestinal comorbidities including malrotation and complications such as short bowel syndrome and recurrent symptomatic and radiographic evidence of bowel obstruction in the absence of mechanical obstruction, known as chronic intestinal pseudo-obstruction (CIPO).

Intestinal dysfunction ultimately leads to nutritional compromise and intestinal failure resulting in dependence on total parenteral nutrition (TPN). Subsequently individuals may develop complications from TPN including central line infections, liver dysfunction, and liver failure. Multivisceral or isolated intestinal transplantation should be considered for those who continue to have nutritional failure and are unable to tolerate TPN as a result of liver failure or inability to maintain central venous access [De Sousa et al 2016, Wymer et al 2016, Prathapan et al 2021].

The prognosis for individuals with MMIHS, in light of its variable genetic causes, has not been well elucidated. Data on individuals prior to molecular diagnosis suggest a poor and often fatal prognosis especially within the first year of life. Sepsis followed by multiorgan failure and malnutrition have been reported as the most frequent causes of death [Gosemann & Puri 2011].

Specialized centers with multidisciplinary care, intestinal rehabilitation, TPN management, and multivisceral transplantation have been credited for improving survival rates from 12.6% (1976-2004) to 55.6% (2004-2011) [Gosemann & Puri 2011, Puri & Gosemann 2012]. A Japanese nationwide survey reported five- and ten-year survival rates to be 63% and 57%, respectively [Soh et al 2015].

In a recent single-center long-term follow up of children with and without intestinal transplant, survival at five, ten, and 20 years was 100%, 100%, and 86%, respectively [Prathapan et al 2021]. All children with intestinal transplant, with the exception of one, were tolerating enteral feeds and did not have significantly different growth parameters or laboratory assessment of liver function when compared to children who were not transplanted and dependent on TPN [Prathapan et al 2021].

Establishing the Clinical Diagnosis of MMIHS

Prenatal Imaging Features of MMIHS

In a systematic review, prenatal diagnosis of MMIHS was suspected in 26% of individuals using prenatal ultrasound findings [Tuzovic et al 2014].

Grossly dilated bladder with or without hydroureteronephrosis in the setting of normal or increased amniotic fluid volume may be found on the second trimester prenatal ultrasound [Puri & Gosemann 2012, Machado et al 2013, Tuzovic et al 2014, De Sousa et al 2016, Fontanella et al 2019]. Prenatal bladder manifestations of megacystis with or without hydroureteronephrosis are an initial presenting finding in 88% of individuals [Tuzovic et al 2014].

Gastrointestinal abnormalities on prenatal ultrasound are less common (24%) and include gastric distention (visible in the second trimester) and dilated bowel loops (visible in the third trimester) [Tuzovic et al 2014].

Dilated esophagus and microcolon have been reported using fetal MRI [Munch et al 2009, Machado et al 2013].

Postnatal Clinical and Imaging Features of MMIHS

Clinical features include signs and symptoms of bowel and bladder obstruction [Gosemann & Puri 2011, Puri & Gosemann 2012, Hugar et al 2018, Pellegrino et al 2024]. The following are the most common:

- Abdominal distention
- Absent or decreased bowel sounds
- Bilious emesis
- Failure to pass meconium
- Inability to void requiring catheterization

Imaging features

- Abdominal radiograph shows gastric distention and dilatation of small bowel loops with paucity of distal gas [Ballisty et al 2013].
- Fluoroscopic upper-gastrointestinal series reveals dilated stomach and small intestine with associated malrotation [Ballisty et al 2013].
- Contrast enema demonstrates a small-caliber colon (microcolon) and may show an associated malrotation [Ballisty et al 2013, Wymer et al 2016].
- Urologic findings on kidney/bladder ultrasound and cystography include a dilated bladder with large capacity, hydroureteronephrosis, and VUR. [Ballisty et al 2013, Machado et al 2013, Hugar et al 2018, Pellegrino et al 2024]. Kidney scarring and acontractile bladder on kidney/bladder scan and urodynamic studies have been reported [Hugar et al 2018].

Differential Diagnosis of MMIHS

Table 1. Differential Diagnosis of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Presenting Symptom in MMIHS	Differential Diagnosis	Distinguishing Clinical Features
Fetal megacystis	Lower urinary tract obstruction	Imaging or cystoscopy shows posterior urethral valves or urethral atresia/stenosis.
Obstructive symptoms (e.g., abdominal distention, bilious emesis, failure to pass meconium)	Hirschsprung disease	Absence of megacystis; rectal biopsy shows absence of ganglion cells.
	Small bowel atresia or colonic atresia	Absence of microcolon; isolated colonic atresia w/o megacystis
	Anorectal malformation	Abnormal anal position/caliber; clinical features of VACTERL association
	Meconium ileus/plug	Family history of cystic fibrosis; poor weight gain; pancreatic insufficiency
	Hypothyroidism	Absence of megacystis & microcolon; laboratory evidence of hypothyroidism
	Sepsis	Absence of megacystis & microcolon; laboratory evidence of sepsis
	Prenatal & intrapartum medication exposure (e.g., magnesium sulfate, opioids)	Absence of megacystis & microcolon
	Diabetic embryopathy	Absence of megacystis

Table 1. continued from previous page.

Presenting Symptom in MMIHS	Differential Diagnosis	Distinguishing Clinical Features
Fetal megacystis & obstructive symptoms	Prune belly sequence [1]	Absence of microcolon
	Multisystemic smooth muscle dysfunction syndrome (MSMDS) [1]	Mydriasis, vascular abnormalities, absence of microcolon

VACTERL = (*v*ertebral anomalies, *a*nal anomalies, *c*ardiac defects, *t*racheoesophageal fistula with *e*sophageal atresia, *r*enal anomalies, and *l*imb anomalies)
1. Isolated (without additional features of MMIHS)

2. Genetic Causes of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Table 2. Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome: Genes and Distinguishing Clinical Features

Gene [1]	% of All MMIHS	MOI	Distinguishing Clinical Features	Other
ACTG2	44.1%	AD	Classic features of MMIHS (e.g., megacystis, microcolon, intestinal dysmotility)	• Greater disease severity reported in probands w/*de novo* (vs inherited) pathogenic variant • Parental somatic & gonadal mosaicism reported
ATP2B4 [2]	1 person	AD	Mild disease process w/presentation in later infancy	
LMOD1 [3]	1 person	AR	Classic features of MMIHS	Large del/dups not reported to date
MYH11 [4]	7 persons	AR	• Overlapping features of MMIHS & prune belly sequence (1 person) • Overlapping features of MMIHS & MSMDS (1 person)	Large del/dups not assoc w/MMIHS to date
MYL9 [5]	4 persons	AR	• Mydriasis • No vascular smooth muscle dysfunction [6]	Homozygous partial-gene deletion reported [7]
MYLK [8]	2 families (3 persons)	AR	No vascular smooth muscle dysfunction [6]	Large del/dups not assoc w/MMIHS to date
PDCL3 [9]	2 persons [10]	AR	Overlapping features of MMIHS & prune belly sequence (1 person)	

Table 2. continued from previous page.

Gene [1]	% of All MMIHS	MOI	Distinguishing Clinical Features	Other
Unknown [11]	~55%	NA		

AD = autosomal dominant; AR = autosomal recessive; del/dups = deletions/duplications; MMIHS = megacystis-microcolon-intestinal hypoperistalsis syndrome; MOI = mode of inheritance; MSMDS = multisystemic smooth muscle dysfunction syndrome; NA = not applicable

1. Genes are listed alphabetically.
2. Kalsbeek et al [2022]
3. Halim et al [2017b]
4. Gauthier et al [2015], Yetman & Starr [2018], Kloth et al [2019], Wang et al [2019], Billon et al [2020]
5. Moreno et al [2018], Billon et al [2020], Kandler et al [2020]
6. Vascular smooth muscle dysfunction including aortic aneurysms or dissection has not been reported.
7. Moreno et al [2018] identified a homozygous intragenic 6,964-bp deletion of intron 3, exon 4, and 3' UTR in *MYL9* in one of two affected sibs.
8. Halim et al [2017a]
9. Billon et al [2020]
10. One reported individual resulted in fetal death, and one was terminated during pregnancy.
11. A heterozygous variant in *CHRNA3* or *CHRNB4* was identified in four persons with MMIHS; however, the specific variants were not reported [Kalsbeek et al 2022].

3. Evaluation Strategy to Identify the Genetic Cause of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Establishing a specific genetic cause of megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS):

- Can aid in discussions of prognosis (which are beyond the scope of this *GeneReview*) and genetic counseling;
- Usually involves a medical history, physical examination, laboratory testing, family history, and genomic/genetic testing.

Medical history. The following medical history should raise concern for MMIHS:

- Fetal megacystis on prenatal ultrasound in the setting of normal or increased amniotic fluid specifically in the second or third trimester of pregnancy
- Clinical symptoms of bowel and bladder obstruction shortly after birth characterized by abdominal distention, abnormal bowel sounds, bilious emesis, failure to pass meconium, and inability to void spontaneously requiring catheterization [Devavarapu et al 2024]

Physical examination. Dilated pupils (mydriasis) suggest *MYL9*-related MMIHS. Dilated pupils (mydriasis) and vascular smooth muscle dysfunction (e.g., aortic aneurysm, aortic dissection) should raise concern for *MYH11*-related MMIHS (see Table 2).

Family history. A three-generation family history should be taken, with attention to the following:

- Manifestations of MMIHS, bowel/bladder dysfunction, chronic intestinal pseudo-obstruction (CIPO), and multisystemic smooth muscle dysfunction syndrome (MSMDS), as well as familial forms of myopathy, neuropathy, mitochondrial diseases, and other conditions that affect the enteric nervous system or smooth muscle
- Parental consanguinity
- Recurrent fetal loss

Genomic/genetic testing. Molecular genetic testing approaches can include a combination of **gene-targeted testing** (multigene panel, single gene testing) and **comprehensive genomic testing** (exome sequencing, genome

sequencing). Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas comprehensive genomic testing does not.

- **A multigene panel** that includes some or all of the genes listed in Table 1 is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

  For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

- **Serial single-gene testing** can be considered if clinical findings and/or family history indicate that pathogenic variants in a particular gene are most likely (see Table 2).

- **Comprehensive genomic testing** does not require the clinician to determine which gene is likely involved. **Exome sequencing** is most commonly used; **genome sequencing** is also possible.

  For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

4. Management of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), the evaluations summarized in this section (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Urology

- Urodynamic studies to evaluate the degree of bladder dysfunction (e.g., enlarged bladder capacity for age, detrusor acontractility with failure to empty) [Wymer et al 2016, Hugar et al 2018]
- Voiding cystourethrogram to evaluate for outlet obstruction, vesicoureteral reflux (VUR), and bladder capacity [Wymer et al 2016, Pellegrino et al 2024]
- Kidney and bladder ultrasound to evaluate for hydronephrosis and renal parenchyma
- Laboratory evaluation of kidney function (blood urea nitrogen, creatinine, glomerular filtration rate) and electrolytes (potassium, phosphorus, calcium)

Gastroenterology

- Bowel imaging: abdominal radiograph, contrast enema, and fluoroscopic upper gastrointestinal series. Computed tomography examination of the abdomen may be indicated to evaluate for a mechanical obstruction.
- Laboratory monitoring of liver enzymes (aspartate transaminase, alanine transaminase, alkaline phosphatase), cholestasis (total and direct bilirubin), and liver function (prothrombin time, partial thromboplastin time, international normalized ratio, albumin)

- Laboratory evaluation of macronutrient (carbohydrates, fat, protein) and micronutrient (vitamins, minerals) deficiencies in the setting of intestinal dysfunction and progressive malabsorption
- Nutrition evaluation and close monitoring of growth parameters

Cardiology. Cardiology evaluation with echocardiogram in individuals with *MYH11* pathogenic variants that raise suspicion of multisystemic smooth muscle dysfunction syndrome (MSMDS) [Yetman & Starr 2018]

Genetic. Consultation with a medical geneticist, certified genetic counselor, or certified advanced genetic nurse to inform affected individuals and their families about the nature, mode of inheritance, and implications of MMIHS in order to facilitate medical and personal decision making

Other. Ophthalmologic evaluation for mydriasis

Treatment of Manifestations

Myopathic bladder dysfunction and associated urologic comorbidities. Clean intermittent catheterizations or vesicostomy to ensure bladder decompression and prevent kidney scarring and failure [Pellegrino et al 2024].

Bowel dysfunction, microcolon, intestinal dysmotility, and associated gastrointestinal comorbidities (malrotation, short bowel syndrome, recurrent non-mechanical bowel obstruction):

- Surgical interventions such as enterostomies (e.g., gastrostomy, jejunostomy) for nutrition administration and proximal bowel decompression [Puri & Gosemann 2012, Soh et al 2015, De Sousa et al 2016, Wymer et al 2016, Thapar et al 2018, Devavarapu et al 2024]
- Bowel diversion (e.g., ileostomy, colostomy) for distal bowel decompression [Puri & Gosemann 2012, Soh et al 2015, De Sousa et al 2016, Wymer et al 2016, Thapar et al 2018, Devavarapu et al 2024]
- Total parenteral nutrition (TPN) when appropriate for malnutrition as a result of intestinal failure from intestinal dysmotility
- Multivisceral or isolated intestinal transplantation should be considered for those who continue to have nutritional failure and are unable to tolerate TPN because of complications (e.g., liver dysfunction and cholestasis, lack of adequate central venous access, recurrent central line-associated bloodstream infections) [Huang et al 2013, De Sousa et al 2016, Wymer et al 2016, Thapar et al 2018, Devavarapu et al 2024].

Vascular smooth muscle dysfunction in individuals with *MYH11* and *ACTA2* pathogenic variants that cause concern for MSMDS [Yetman & Starr 2018]:

- Referral to cardiologist and monitoring for pulmonary hypertension, aortic dilatation, and patent ductus arteriosus
- Referral to neurologist for evaluation for abnormal cerebral vasculature [Yetman & Starr 2018]

Surveillance

The prognosis for individuals with MMIHS in light of its variable genetic causes has not been well elucidated. Data on individuals prior to molecular diagnosis suggests a poor and often fatal prognosis within the first year of life.

The evaluation and management are primarily supportive. Specialized centers offer multidisciplinary medical and surgical models of care including comprehensive TPN management and multivisceral transplantation.

Goals of bladder management include bladder decompression and subsequent monitoring and prevention of kidney failure.

Goals of bowel management include providing means of nutrition in the setting of intestinal dysmotility via enteral or parenteral means while monitoring for nutritional failure and TPN-associated complications (line infections, liver disease).

Agents/Circumstances to Avoid

Treatment/medications to be avoided or limited include those that diminish bowel and bladder motility.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

5. Genetic Counseling of Family Members of an Individual with Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) caused by pathogenic variants in *ACTG2* is typically inherited in an autosomal dominant manner. Apparent autosomal recessive inheritance has been reported in one family in which two sibs with intestinal pseudo-obstruction and megacystis were found to have biallelic *ACTG2* variants while their heterozygous parents were asymptomatic [Matera et al 2021]. Further study is needed to confirm that the *ACTG2* variants segregating in this family are causative of the phenotype in the affected sibs.

MMIHS caused by biallelic pathogenic variants in *LMOD1*, *MYH11*, *MYL9*, *MYLK*, or *PDCL3* is inherited in an autosomal recessive manner.

MMIHS caused by a heterozygous pathogenic variant in *ATP2B4* is inherited in an autosomal dominant manner.

Autosomal Dominant Inheritance – Risk to Family Members

Parents of a proband

- Some individuals diagnosed with autosomal dominant MMIHS have the disorder as the result of a *de novo* pathogenic variant [Wangler et al 2014].
- Some individuals diagnosed with MMIHS inherited a pathogenic variant from a parent. The severity of clinical findings may vary within a family; a parent may be asymptomatic or have a milder phenotype [Wangler et al 2014].
- If the proband appears to be the only affected family member (i.e., a simplex case), molecular genetic testing is recommended for the parents of the proband to evaluate their genetic status and inform recurrence risk assessment.

- If the pathogenic variant identified in the proband is not identified in either parent and parental identity testing has confirmed biological maternity and paternity, the following possibilities should be considered:
  - The proband has a *de novo* pathogenic variant.
  - The proband inherited a pathogenic variant from a parent with gonadal (or somatic and gonadal) mosaicism.* Parental somatic and gonadal mosaicism have been reported in *ACTG2*-related MMIHS [Tuzovic et al 2015, Milunsky et al 2017]. Note: Testing of parental leukocyte DNA may not detect all instances of somatic mosaicism and will not detect a pathogenic variant that is present in the germ (gonadal) cells only.

    * A parent with somatic and gonadal mosaicism for an *ACTG2* pathogenic variant may be mildly/minimally affected.
- The family history of some individuals diagnosed with autosomal dominant MMIHS may appear to be negative because of failure to recognize the disorder in family members because of a milder phenotypic expression, early death of the parent before the onset of symptoms, or late onset of the disease in the affected parent. Therefore, an apparently negative family history cannot be confirmed unless molecular genetic testing has demonstrated that neither parent is heterozygous for the MMIHS-related pathogenic variant identified in the proband.

Sibs of a proband. The risk to sibs depends on the clinical/genetic status of a proband's parents:

- If a parent of the proband is affected and/or is known to have the autosomal dominant MMIHS-related pathogenic variant identified in the proband, the risk to the sibs of inheriting the pathogenic variant is 50%.
- Clinical severity and phenotype may differ between family members with the same MMIHS-related pathogenic variant; thus, age of onset and/or progression may not be predictable in heterozygous sibs.
- If the MMIHS-related pathogenic variant detected in the proband cannot be detected in the leukocyte DNA of either parent, the recurrence risk to sibs is slightly greater than that of the general population because of the possibility of parental gonadal mosaicism [Tuzovic et al 2015, Milunsky et al 2017].
- If the parents have not been tested for the MMIHS-related pathogenic variant but are clinically unaffected, the risk to the sibs of a proband appears to be low. However, sibs of a proband with clinically unaffected parents are still presumed to be at increased risk for MMIHS because of the possibility of parental gonadal mosaicism or reduced penetrance in a heterozygous parent.

Offspring of a proband. Each child of an individual with autosomal dominant MMIHS has a 50% chance of inheriting the MMIHS-related pathogenic variant.

Other family members. The risk to other family members depends on the status of the proband's parents: if a parent has the MMIHS-related pathogenic variant, the parent's family members may be at risk.

Autosomal Recessive Inheritance – Risk to Family Members

Parents of a proband

- The parents of an affected individual are presumed to be heterozygous for an MMIHS-related pathogenic variant.
- If a molecular diagnosis has been established in the proband, molecular genetic testing is recommended for the parents of a proband to confirm that both parents are heterozygous for an MMIHS-related pathogenic variant and to allow reliable recurrence risk assessment.
- If a pathogenic variant is detected in only one parent and parental identity testing has confirmed biological maternity and paternity, it is possible that one of the pathogenic variants identified in the proband occurred as a *de novo* event in the proband or as a postzygotic *de novo* event in a mosaic parent

[Jónsson et al 2017]. If the proband appears to have homozygous pathogenic variants (i.e., the same two pathogenic variants), additional possibilities to consider include:
    - A single- or multiexon deletion in the proband that was not detected by sequence analysis and that resulted in the artifactual appearance of homozygosity;
    - Uniparental isodisomy for the parental chromosome with the pathogenic variant that resulted in homozygosity for the pathogenic variant in the proband.
- Heterozygotes (carriers) are not at risk for MMIHS.

Sibs of a proband

- If both parents are known to be heterozygous for an MMIHS-related pathogenic variant, each sib of an affected individual has at conception a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.
- Heterozygotes (carriers) are not at risk for MMIHS.

Offspring of a proband. The offspring of an individual with autosomal recessive MMIHS are obligate heterozygotes (carriers) for an MMIHS-related pathogenic variant.

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of an MMIHS-related pathogenic variant.

Carrier detection. Carrier testing for at-risk relatives requires prior identification of the MMIHS-related pathogenic variants in the family.

Related Genetic Counseling Issues

Evaluation of relatives at risk. It is appropriate to clarify the genetic status of apparently asymptomatic younger at-risk relatives of an affected individual, as early diagnosis may help prevent unnecessary surgery for symptoms of intestinal obstruction and may allow early evaluation of bladder function, the urinary tract (for evidence of dilatation), and kidney function. Evaluations can include:

- Molecular genetic testing if the pathogenic variant(s) in the family are known;
- Abdominal or bladder ultrasound and contrast enema if the pathogenic variant(s) in the family are not known. Evidence of megacystis (on the abdominal or bladder ultrasound) and microcolon (on the contrast enema) are highly suggestive of MMIHS.

Family planning

- The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected or are at risk of having an MMIHS-related pathogenic variant.
- It is appropriate to offer molecular genetic testing for reproductive partners of individuals known to be heterozygous for a pathogenic variant associated with autosomal recessive MMIHS, particularly if consanguinity is likely.

Prenatal Testing and Preimplantation Genetic Testing

Molecular genetic testing. Once the MMIHS-related pathogenic variant(s) have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.

Prenatal ultrasound. See Prenatal Imaging Features of MMIHS.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal and preimplantation genetic testing. While most health care professionals would consider use of prenatal and preimplantation genetic testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **MMIHS Foundation**
  mmihs.org
- **Children's Organ Transplant Association**
  Phone: 800-366-2682
  Fax: 812-336-8885
  Email: cota@cota.org
  cota.org
- **International Foundation for Functional Gastrointestinal Disorders (IFFGD)**
  Phone: 414-964-1799
  iffgd.org
- **International Foundation for Functional Gastrointestinal Disorders (IFFGD) - ABOUT KIDS GI**
  aboutkidsgi.org
- **National Digestive Diseases Information Clearinghouse (NDDIC)**
  Intestinal Pseudo-obstruction
- **National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)**
  Phone: 301-496-3583
  niddk.nih.gov
- **Prune Belly Syndrome Network**
  Phone: 855-ASK-PBSN
  prunebelly.org
- **Pull-thru Network**
  Phone: -309-262-0786
  Email: info@pullthrunetwork.org
  pullthrunetwork.org
- **The Oley Foundation**
  Phone: 518-262-5079
  Email: info@oley.org
  oley.org
- **United Ostomy Associations of America, Inc.**

Phone: 800-826-0826

ostomy.org

Chapter Notes

Author Notes

Lusine Ambartsumyan's web page

Lusine Ambartsumyan specializes in the diagnosis and management of individuals with Hirschsprung disease, anorectal malformation, refractory constipation, neurogenic bowel, gastroparesis, chronic intestinal pseudo-obstruction, achalasia, and scleroderma. Her clinical and research interests include mechanisms of fecal continence in children with functional and organic defecation disorders, specifically children with anorectal malformations, neurogenic bowel, and postsurgical Hirschsprung disease.

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Countless patients and families who have entrusted our gastrointestinal motility program with their care.

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