



Strømme Syndrome

Synonyms: Apple Peel Syndrome with Microcephaly and Ocular Anomalies, Jejunal Atresia with Microcephaly and Ocular Anomalies

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Summary

Clinical characteristics

Strømme syndrome is a clinically variable disorder characterized primarily by small bowel intestinal atresia (including apple peel intestinal atresia), microcephaly, developmental delay and/or intellectual disability, structural brain anomalies, and ocular, genitourinary, and cardiac anomalies. A highly variable clinical presentation is observed among affected individuals that may range from mid-gestation lethality, to multisystem involvement with features implicated in the ciliopathies, to nonsyndromic microcephaly with developmental delay. Apple peel intestinal atresia, a rare form of small bowel atresia involving the proximal jejunum near the ligament of Treitz, occurs in some individuals. Intestinal atresia in individuals with Strømme syndrome can involve the duodenum, jejunum, or multiple segments.

Diagnosis/testing

The diagnosis of Strømme syndrome is established in a proband with characteristic features and biallelic *CENPF* pathogenic variants identified by molecular genetic testing.

Management

Treatment: Individualized care by a multidisciplinary team; surgical treatment of gastrointestinal atresia; developmental and educational support; standard treatment for ocular anomalies, vision issues, renal anomalies, and cardiac anomalies; social work involvement and care coordination as needed.

Surveillance: Assess growth, feeding, and development at each visit. Follow up for ophthalmologic manifestations and vision issues as recommended by ophthalmologist and low-vision clinic.

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Genetic counseling

Strømme syndrome is inherited in an autosomal recessive manner. If both parents are known to be heterozygous for a *CENPF* 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. Once the *CENPF* pathogenic variants have been identified in an affected family member, carrier testing for at-risk relatives and prenatal/preimplantation genetic testing are possible.

Diagnosis

No consensus clinical diagnostic criteria for Strømme syndrome have been published.

Suggestive Findings

Strømme syndrome **should be suspected** in individuals with the following clinical, imaging, and family history findings.

Clinical findings

- Small bowel intestinal atresia, in particular apple peel intestinal atresia
- Microcephaly
- Mild-to-moderate developmental delay and/or intellectual disability
- Various ocular anomalies including anterior segment anomalies and microphthalmia
- Genitourinary anomalies including hypoplastic kidney, horseshoe kidney, hydroureteronephrosis, and/or cryptorchidism

Imaging findings

- Brain MRI may reveal corpus callosum agenesis, hydrocephalus, pachygyria, lissencephaly, holoprosencephaly, cerebral and cerebellar hypoplasia.
- Abdominal imaging findings may include hypoplastic kidney, horseshoe kidney, hydroureteronephrosis, and/or accessory spleen.

Family history is consistent with autosomal recessive inheritance (e.g., affected sibs and/or parental consanguinity). Absence of a known family history does not preclude the diagnosis.

Establishing the Diagnosis

The diagnosis of Strømme syndrome **is established** in a proband with suggestive findings and biallelic pathogenic (or likely pathogenic) variants in *CENPF* identified by molecular genetic testing (see Table 1).

Note: (1) Per ACMG/AMP variant interpretation guidelines, the terms "pathogenic variants" and "likely pathogenic variants" are synonymous in a clinical setting, meaning that both are considered diagnostic, and both can be used for clinical decision making [Richards et al 2015]. Reference to "pathogenic variants" in this section is understood to include any likely pathogenic variants. (2) Identification of biallelic *CENPF* variants of uncertain significance (or of one known *CENPF* pathogenic variant and one *CENPF* variant of uncertain significance) does not establish or rule out the diagnosis.

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

Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Individuals with the distinctive findings described in Suggestive Findings are likely to be

diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from many other inherited disorders with microcephaly and/or intellectual disability are more likely to be diagnosed using genomic testing (see Option 2).

Option 1

Single-gene testing. Sequence analysis of *CENPF* is performed first to detect small intragenic deletions/insertions and missense, nonsense, and splice site variants. Note: Depending on the sequencing method used, single-exon, multiexon, or whole-gene deletions/duplications may not be detected. If only one or no variant is detected by the sequencing method used, the next step is to perform gene-targeted deletion/duplication analysis to detect exon and whole-gene deletions or duplications.

A ciliopathies multigene panel that includes *CENPF* and other genes of interest (see Differential Diagnosis) 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](#).

Option 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](#).

Table 1. Molecular Genetic Testing Used in Strømme Syndrome

Gene ¹	Method	Proportion of Pathogenic Variants ² Detectable by Method
<i>CENPF</i>	Sequence analysis ³	100% ⁴
	Gene-targeted deletion/duplication analysis ⁵	None reported ⁶

1. See Table A. Genes and Databases for chromosome locus and protein.

2. See Molecular Genetics for information on variants detected in this gene.

3. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click [here](#).

4. Waters et al [2015], Filges et al [2016], Ozkinay et al [2017], Al-Dewik et al [2019], Kahrizi et al [2019], Maddirevula et al [2019], Monies et al [2019], Alghamdi et al [2020], Caridi et al [2020], Al-Hamed et al [2022], Cappuccio et al [2022], Ho et al [2022]

5. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.

6. To date, no large exon or multiexon deletions or duplications have been reported.

Clinical Characteristics

Clinical Description

Initially believed to be pathognomonic of Strømme syndrome, small intestine atresia is now considered a distinctive but nonobligatory feature. A highly variable clinical presentation is observed among affected individuals that may range from mid-gestation lethality, to multisystem involvement with features implicated in the ciliopathies, to nonsyndromic microcephaly with developmental delay.

To date, at least 26 individuals have been identified with pathogenic variants in *CENPF* [Waters et al 2015, Filges et al 2016, Ozkinay et al 2017, Al-Dewik et al 2019, Kahrizi et al 2019, Maddirevula et al 2019, Monies et al 2019, Palombo et al 2020, Alghamdi et al 2020, Caridi et al 2020, Al-Hamed et al 2022, Blue et al 2022, Cappuccio et al 2022, Ho et al 2022]. The following description of the phenotypic features associated with Strømme syndrome is based on 25 individuals with clinical descriptions from these reports.

Table 2. Strømme Syndrome: Frequency of Select Features

Feature	Proportion of Persons w/Feature	Comment	
Intestinal atresia	Small bowel intestinal atresia	14/25	Often assoc w/malrotation
	Duodenal atresia	8/16 ¹	
	Jejunal atresia	4/16 ¹	
	Multiple segment atresia	3/16 ¹	
Neurodevelopmental	Microcephaly	21/23	
	Developmental delay / intellectual disability	13/14	
	Structural brain anomalies	9/15	Corpus callosum agenesis, hydrocephalus, pachygyria, lissencephaly, holoprosencephaly, cerebral & cerebellar hypoplasia
Ophthalmologic	Anterior segment anomalies	9/14	Peters anomaly, corneal opacity w/or w/o lens adhesions, sclerocornea, atrophy of iris villi, cornea-peripheral anterior synechiae, cataract, iris coloboma, microcornea, irregular & dilated pupil
	Microphthalmia	8/14	Unilateral or bilateral
Genitourinary anomalies	Hypoplastic kidney	6/16	
	Cryptorchidism	4/9	
Other	Congenital heart disease	5/18 ²	Septal defects, patent ductus arteriosus, coarctation of aorta, & Ebstein-like tricuspid valve
	Polydactyly	2/25	Preaxial
	Accessory spleen	2/11	

1. Three of the individuals with intestinal atresia reported in the literature did not have the affected segment specified and are therefore excluded from the denominator.

2. Physiologic patent ductus arteriosus due to prematurity is not included.

Gastrointestinal Features

Small bowel atresia. Duodenum is the most commonly involved region in Strømme syndrome-related small bowel atresia, although jejunal and ileal atresia have also been reported [Waters et al 2015, Filges et al 2016, Ozkinay et al 2017, Alghamdi et al 2020, Caridi et al 2020, Cappuccio et al 2022]. The majority of Strømme syndrome-related small bowel atresia are identified through abnormal antenatal ultrasound scans or in infants who presented with vomiting shortly after birth. As with nonsyndromic intestinal atresia, Strømme syndrome-related small bowel atresia is often accompanied by malrotation and premature delivery.

Apple peel intestinal atresia, a rare form of small bowel atresia, is considered a highly specific but nonobligatory feature of Strømme syndrome. It is classically defined as atresia of the proximal jejunum near the ligament of Treitz that ends in a blind segment and a distal unused segment supplied by branches from the right colic or ileocolic artery and is associated with a mesenteric defect. The distal small bowel is wrapped around its blood supply in a spiral manner that resembles an apple peel configuration.

Apple peel intestinal atresia is managed by resection of the atretic segment with subsequent anastomosis. The underlying insecure vasculature and the need for bowel preservation have contributed to challenges in surgical treatment, unfavorable prognosis, and a higher risk of short bowel syndrome. Affected individuals may require prolonged total parental nutrition, which may be complicated by cholestasis, sepsis, and multisystem organ failure. Persistent malabsorption and poor weight gain after surgical intervention have been described in individuals with Strømme syndrome-related small bowel atresia [Filges et al 2016].

Ophthalmologic Features

Anterior segment anomalies including Peters anomaly, corneal opacity with or without lens adhesions, sclerocornea, atrophy of the iris villi, cornea-peripheral anterior synechiae, cataract, iris coloboma, microcornea, and irregular and dilated pupil have been reported in affected individuals [Filges et al 2016, Ozkinay et al 2017, Caridi et al 2020, Cappuccio et al 2022].

Other ophthalmologic features including unilateral or bilateral microphthalmia and esotropia have also been reported in individuals with Strømme syndrome [Filges et al 2016, Ozkinay et al 2017, Caridi et al 2020, Ho et al 2022]. Abnormal visual evoked potential associated with excavation of the optic disc was reported in one individual [Cappuccio et al 2022]. Unilateral poor vision and blindness were reported in three individuals [Filges et al 2016, Ho et al 2022].

Neurodevelopmental Features

Developmental delay and/or intellectual disability ranging from mild-to-moderate severity is frequently described in individuals with Strømme syndrome, although one adult with normal development and no learning difficulties has been reported [Ho et al 2022]. In individuals in whom intelligence quotient testing was performed, scores have ranged from 40 to 83 [Filges et al 2016, Kahrizi et al 2019, Alghamdi et al 2020, Cappuccio et al 2022].

Neuroimaging may reveal various structural anomalies including hydrocephalus, corpus callosum agenesis, pachygyria, lissencephaly, holoprosencephaly, and cerebral and cerebellar atrophy [Waters et al 2015, Ozkinay et al 2017, Maddirevula et al 2019, Caridi et al 2020, Cappuccio et al 2022].

Microcephaly (head circumference ≥ 2 SD below the mean for age and sex) is often detected antenatally or is present at birth.

Genitourinary Features

The renal phenotype observed in Strømme syndrome is highly variable. Structural renal anomalies reported include single kidney, hypoplastic kidneys, horseshoe kidneys, and hydroureteronephrosis [Waters et al 2015,

Filges et al 2016, Maddirevula et al 2019, Cappuccio et al 2022]. End-stage kidney disease requiring dialysis and kidney transplant was reported in one affected individual [Caridi et al 2020].

Undescended and retractile testis have been reported in affected individuals [Maddirevula et al 2019, Alghamdi et al 2020, Cappuccio et al 2022].

Other Features

Growth. The majority of affected individuals were born prematurely, which may be due to underlying intestinal atresia and polyhydramnios. Strømme syndrome-related small bowel atresia contributes to malabsorption and poor weight gain; however, individuals without intestinal atresia have also been reported to have poor weight gain [Filges et al 2016, Ozkinay et al 2017, Cappuccio et al 2022].

Congenital heart disease including atrial septal defect, ventricular septal defect, patent ductus arteriosus, bicuspid aortic valve, Ebstein-like tricuspid valvular dysplasia, and coarctation of aorta have been reported [Filges et al 2016, Ozkinay et al 2017, Alghamdi et al 2020, Cappuccio et al 2022].

Musculoskeletal anomalies. Preaxial polydactyly, platyspondyly, and xiphoid cleft have been reported in affected individuals [Filges et al 2016, Ho et al 2022].

Dysmorphic craniofacial features observed in Strømme syndrome are highly variable. Recurrently reported features include receding forehead, broad and high nasal root, anteverted nares, short palpebral fissure, deep-set eyes, wide mouth, micrognathia, facial asymmetry, and low-set and large ears [Waters et al 2015, Filges et al 2016, Ozkinay et al 2017, Maddirevula et al 2019, Alghamdi et al 2020, Caridi et al 2020, Cappuccio et al 2022, Ho et al 2022].

Accessory spleen has been reported in two individuals [Waters et al 2015, Filges et al 2016].

Prognosis. The prognosis for Strømme syndrome is highly variable, ranging from mid-gestation lethality to nonsyndromic developmental delay and microcephaly.

Genotype-Phenotype Correlations

No genotype-phenotype correlations have been identified.

Nomenclature

Strømme syndrome has also been referred to as primary ciliary dyskinesia 31 (CILD31).

Prevalence

Strømme syndrome is rare, and the exact prevalence is unknown. To date, at least 26 individuals with molecularly confirmed Strømme syndrome have been reported.

Genetically Related (Allelic) Disorders

No phenotypes other than those discussed in this *GeneReview* are known to be associated with germline pathogenic variants in *CENPF*.

Differential Diagnosis

Strømme syndrome. Because Strømme syndrome is associated with a highly variable clinical presentation, phenotypic features are often not sufficient to diagnose the condition. All disorders that fall within the spectrum of ciliopathies should be considered in the differential diagnosis.

Intestinal atresia. Syndromes of interest in the differential diagnosis of intestinal atresia are summarized in Table 3.

Table 3. Genes of Interest in the Differential Diagnosis of Intestinal Atresia

Gene	Disorder	MOI	Distinctive Features
<i>MYCN</i>	Feingold syndrome 1 (FS1)	AD	Unlike Strømme syndrome, FS1 is assoc w/: <ul style="list-style-type: none"> • Digital anomalies incl toe syndactyly, thumb hypoplasia, & brachymesophalangy; • Tracheoesophageal atresia.
<i>PI4KA</i>	<i>PI4KA</i> -related multiple intestinal atresia ± immunodeficiency (See <i>PI4KA</i> -Related Disorder.)	AR	Unlike Strømme syndrome, <i>PI4KA</i> -related disorder may be assoc w/ immunodeficiency.
<i>RFX6</i>	Mitchell-Riley syndrome (OMIM 615710)	AR	Unlike Strømme syndrome, Mitchell-Riley syndrome is assoc w/: <ul style="list-style-type: none"> • GI involvement incl cholestasis, gallbladder aplasia or hypoplasia, & hypoplastic or annular pancreas; • Neonatal or childhood onset diabetes.
<i>TTC7A</i>	Gastrointestinal defects & immunodeficiency syndrome 1 (GIDID1) (OMIM 243150)	AR	Unlike Strømme syndrome, GIDID1 is assoc w/: <ul style="list-style-type: none"> • GI involvement (e.g., hepatitis, omphalocele); • Immunodeficiency w/thymus hypoplasia.

AD = autosomal dominant; AR = autosomal recessive; GI = gastrointestinal; MOI = mode of inheritance

Management

No clinical practice guidelines for Strømme syndrome have been published.

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with Strømme syndrome, the evaluations summarized in Table 4 (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Table 4. Recommended Evaluations Following Initial Diagnosis in Individuals with Strømme Syndrome

System/Concern	Evaluation	Comment
Gastrointestinal/Feeding	Gastroenterologist / GI surgeon / nutrition / feeding team eval	To incl eval of intestinal atresia & feeding difficulties
Neurologic	Neurologic eval	Consider brain MRI to delineate structural brain anomalies if there is evidence of neurologic abnormalities or DD.
Development	Developmental assessment	<ul style="list-style-type: none"> • To incl motor, adaptive, cognitive, & speech/ language eval • Eval for early intervention / special education
Ophthalmologic	Ophthalmologic exam	To assess for structural eye anomalies & visual impairment
Genitourinary anomalies	<ul style="list-style-type: none"> • Renal ultrasound eval for structural anomalies & parenchymal disease • Physical exam for undescended testes in males • Lab assessment of renal function incl CBC, BUN, creatinine, & electrolytes 	

Table 4. continued from previous page.

System/Concern	Evaluation	Comment
Congenital heart disease	Echocardiogram	To assess valvular & anatomic defects
Genetic counseling	By genetics professionals ¹	To inform affected persons & their families re nature, MOI, & implications of Strømme syndrome to facilitate medical & personal decision making
Family support & resources	Assess need for: <ul style="list-style-type: none"> Community or online resources such as Parent to Parent; Social work involvement for parental support; Home nursing referral. 	

BUN = blood urea nitrogen; CBC = complete blood count; DD = developmental delay; GI = gastrointestinal; MOI = mode of inheritance

1. Medical geneticist, certified genetic counselor, certified advanced genetic nurse

Treatment of Manifestations

Supportive care to improve quality of life, maximize function, and reduce complications is recommended. This can include multidisciplinary care by specialists in neurology, speech-language pathology, occupational therapy, physical therapy, feeding, ophthalmology, surgery, nephrology, developmental pediatrics, and clinical genetics (see Table 5).

Table 5. Treatment of Manifestations in Individuals with Strømme Syndrome

Manifestation/Concern	Treatment	Considerations/Other
Intestinal atresia	Surgical treatment of gastrointestinal atresia	Per gastroenterologist / GI surgeon
Developmental delay / Intellectual disability	See Developmental Delay / Intellectual Disability Management Issues.	
Ophthalmologic	Per ophthalmologist	
Renal anomalies	Per renal consultants	
Cardiac anomalies	Per cardiac consultants	
Family/Community	<ul style="list-style-type: none"> Ensure appropriate social work involvement to connect families w/local resources, respite, & support. Coordinate care to manage multiple subspecialty appointments, equipment, medications, & supplies. 	<ul style="list-style-type: none"> Ongoing assessment of need for palliative care involvement &/or home nursing Consider involvement in adaptive sports or Special Olympics.

GI = gastrointestinal

Developmental Delay / Intellectual Disability Management Issues

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 as well as infant mental health services, special educators, and sensory impairment specialists. In the US, early intervention is a federally funded program available in all states that provides in-home services to target individual therapy needs.

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 individualized education plan (IEP) is developed for those who qualify based on established motor, language, social, or cognitive delay. The early intervention program typically assists with this transition. Developmental preschool is center based; for children too medically unstable to attend, home-based services are provided.

All ages. Consultation with a developmental pediatrician is recommended to ensure the involvement of appropriate community, state, and educational agencies (US) and to support parents in maximizing quality of life. Some issues to consider:

- IEP services:
 - An IEP provides specially designed instruction and related services to children who qualify.
 - IEP services will be reviewed annually to determine whether any changes are needed.
 - Special education law requires that children participating in an IEP be in the least restrictive environment feasible at school and included in general education as much as possible, when and where appropriate.
 - Vision consultants should be a part of the child's IEP team to support access to academic material.
 - PT, OT, and speech services will be provided in the IEP to the extent that the need affects the child's access to academic material. Beyond that, private supportive therapies based on the affected individual's needs may be considered. Specific recommendations regarding type of therapy can be made by a developmental pediatrician.
 - As a child enters the teen years, a transition plan should be discussed and incorporated in the IEP. For those receiving IEP services, the public school district is required to provide services until age 21.
- A 504 plan (Section 504: a US federal statute that prohibits discrimination based on disability) can be considered for those who require accommodations or modifications such as front-of-class seating, assistive technology devices, classroom scribes, extra time between classes, modified assignments, and enlarged text.
- Developmental Disabilities Administration (DDA) enrollment is recommended. DDA is a US public agency that provides services and support to qualified individuals. Eligibility differs by state but is typically determined by diagnosis and/or associated cognitive/adaptive disabilities.
- Families with limited income and resources may also qualify for supplemental security income (SSI) for their child with a disability.

Motor Dysfunction

Gross motor dysfunction

- Physical therapy is recommended to maximize mobility and to reduce the risk for later-onset orthopedic complications (e.g., contractures, scoliosis, hip dislocation).
- Consider use of durable medical equipment and positioning devices as needed (e.g., wheelchairs, walkers, bath chairs, orthotics, adaptive strollers).
- For muscle tone abnormalities including hypertonia or dystonia, consider involving appropriate specialists to aid in management of baclofen, tizanidine, Botox[®], anti-parkinsonian medications, or orthopedic procedures.

Fine motor dysfunction. Occupational therapy is recommended for difficulty with fine motor skills that affect adaptive function such as feeding, grooming, dressing, and writing.

Oral motor dysfunction should be assessed at each visit and clinical feeding evaluations and/or radiographic swallowing studies should be obtained for choking/gagging during feeds, poor weight gain, frequent respiratory illnesses, or feeding refusal that is not otherwise explained. Assuming that the child is safe to eat by mouth,

feeding therapy (typically from an occupational or speech therapist) is recommended to help improve coordination or sensory-related feeding issues. Feeds can be thickened or chilled for safety. When feeding dysfunction is severe, an NG-tube or G-tube may be necessary.

Communication issues. Consider evaluation for alternative means of communication (e.g., [augmentative and alternative communication](#) [AAC]) for individuals who have expressive language difficulties. An AAC evaluation can be completed by a speech-language pathologist who has expertise in the area. The evaluation will consider cognitive abilities and sensory impairments to determine the most appropriate form of communication. AAC devices can range from low-tech, such as picture exchange communication, to high-tech, such as voice-generating devices. Contrary to popular belief, AAC devices do not hinder verbal development of speech, but rather support optimal speech and language development.

Surveillance

Table 6. Recommended Surveillance for Individuals with Strømme Syndrome

System/Concern	Evaluation	Frequency
Growth/Feeding	<ul style="list-style-type: none"> • Measurement of growth parameters • Eval of nutritional status & oral intake 	At each visit
Development	Monitor developmental progress & educational needs.	
Ophthalmologic	Eval of structural eye anomalies	Per treating ophthalmologist
	Evaluate for changes in vision.	Per low-vision clinic
Family/Community	Assess family need for social work support (e.g., palliative/respite care, home nursing, other local resources), care coordination, or follow-up genetic counseling if new questions arise (e.g., family planning).	At each visit

Evaluation of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

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.

Genetic Counseling

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

Strømme syndrome is inherited in an autosomal recessive manner.

Risk to Family Members

Parents of a proband

- The parents of an affected child are presumed to be heterozygous for a *CENPF* pathogenic variant.

- Molecular genetic testing is recommended for the parents of a proband to confirm that both parents are heterozygous for a *CENPF* 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 asymptomatic and are not at risk of developing the disorder.

Sibs of a proband

- If both parents are known to be heterozygous for a *CENPF* 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 asymptomatic and are not at risk of developing the disorder.

Offspring of a proband. The offspring of an individual with Strømme syndrome are obligate heterozygotes (carriers) for a pathogenic variant in *CENPF*.

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of a *CENPF* pathogenic variant.

Carrier Detection

Carrier testing for at-risk relatives requires prior identification of the *CENPF* pathogenic variants in the family.

Related Genetic Counseling Issues

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 carriers or are at risk of being carriers.

Prenatal Testing and Preimplantation Genetic Testing

Once the *CENPF* pathogenic variants have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal 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](#).

No specific resources for Strømme Syndrome have been identified by *GeneReviews* staff.

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Strømme Syndrome: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
CENPF	1q41	Centromere protein F	CENPF @ LOVD	CENPF	CENPF

Data are compiled from the following standard references: gene from [HGNC](#); chromosome locus from [OMIM](#); protein from [UniProt](#). For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click [here](#).

Table B. OMIM Entries for Strømme Syndrome ([View All in OMIM](#))

243605	STROMME SYNDROME; STROMS
600236	CENTROMERIC PROTEIN F; CENPF

Molecular Pathogenesis

CENPF encodes centromere protein F (CENPF), which is involved in kinetochore function and chromosome segregation through association with kinetochore and mitotic spindles. CENPF is also essential in ciliogenesis and ciliary function [Waters et al 2015, Filges et al 2016, Cappuccio et al 2022].

Mechanism of disease causation. Loss of function (i.e., haploinsufficiency) leading to anomalies in cell division processes, ciliogenesis, and ciliary function [Filges et al 2016, Cappuccio et al 2022]

Chapter Notes

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