

# Intestinal Pseudo-Obstruction

Subjects: **Genetics & Heredity**

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Intestinal pseudo-obstruction is a condition characterized by impairment of the muscle contractions that move food through the digestive tract.

genetic conditions

## 1. Introduction

Intestinal pseudo-obstruction can occur at any time of life, and its symptoms range from mild to severe. The condition may arise from abnormalities of the gastrointestinal muscles themselves (myogenic) or from problems with the nerves that control the muscle contractions (neurogenic).

Intestinal pseudo-obstruction leads to a buildup of partially digested food in the intestines. This buildup can cause abdominal swelling (distention) and pain, nausea, vomiting, and constipation or diarrhea. Affected individuals experience loss of appetite and impaired ability to absorb nutrients, which may lead to malnutrition. These symptoms resemble those of an intestinal blockage (obstruction), but in intestinal pseudo-obstruction no blockage is found.

Depending on the cause of intestinal pseudo-obstruction, affected individuals can have additional signs and symptoms. Some people with intestinal pseudo-obstruction have bladder dysfunction such as an inability to pass urine. Other features may include decreased muscle tone (hypotonia) or stiffness (spasticity) of the torso and limbs, weakness in the muscles that control eye movement (ophthalmoplegia), intellectual disability, seizures, unusual facial features, or recurrent infections.

When intestinal pseudo-obstruction occurs by itself, it is called primary or idiopathic intestinal pseudo-obstruction. The disorder can also develop as a complication of another health problem; in these cases, it is called secondary intestinal pseudo-obstruction. The condition can be episodic (acute) or persistent (chronic).

## 2. Frequency

The overall prevalence of intestinal pseudo-obstruction is unknown. Researchers in Japan have estimated the prevalence of chronic intestinal pseudo-obstruction in that country as 9 cases per million people.

## 3. Causes

In some individuals with primary intestinal pseudo-obstruction, the condition is caused by genetic changes affecting the *FLNA* or *ACTG2* gene.

The protein produced from the *FLNA* gene, filamin A, attaches (binds) to proteins called actins and helps them form the branching network of filaments that make up the cytoskeleton, which gives structure to cells and allows them to change shape and move. *FLNA* gene mutations that cause intestinal pseudo-obstruction are thought to reduce levels of the filamin A protein or impair its function. Research suggests that decreased filamin A function may affect the shape of cells in the smooth muscles of the gastrointestinal tract during development before birth, causing abnormalities in the layering of these muscles. Smooth muscles line the internal organs; they contract and relax without being consciously controlled. In the gastrointestinal tract, abnormal layering of these muscles interferes with the ability to produce the coordinated waves of contractions (peristalsis) that move food along during digestion.

Deletions or duplications of genetic material can affect all or part of the *FLNA* gene, and may also include adjacent genes on the X chromosome. Changes in adjacent genes may account for some of the other signs and symptoms that can occur with intestinal pseudo-obstruction.

The *ACTG2* gene provides instructions for making a member of the actin family called gamma ( $\gamma$ )-2 actin. The  $\gamma$ -2 actin protein is found in smooth muscle cells of the intestinal and urinary tracts. It is necessary for contraction of the smooth muscles in the intestines and bladder. These contractions move food through the intestines as part of the digestive process and empty urine from the bladder. *ACTG2* gene mutations hinder the formation of actin filaments in the cytoskeleton and reduce the ability of smooth muscles in the intestines and bladder to contract, leading to the signs and symptoms of intestinal pseudo-obstruction.

Secondary intestinal pseudo-obstruction occurs as a complication of other disorders that damage muscles or nerves in the intestinal tract, such as Parkinson disease, type 2 diabetes, various types of muscular dystrophy, or Kawasaki disease. Additionally, the condition is a characteristic feature of certain inherited syndromes such as megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) or mitochondrial neurogastrointestinal encephalopathy disease (MNGIE disease). Infections, surgery, or certain drugs can also cause secondary intestinal pseudo-obstruction.

Mutations in other genes involved in smooth muscle contraction can also cause intestinal pseudo-obstruction. Studies suggest that mutations in additional genes that have not been identified can also result in this condition. In some affected individuals, the cause of intestinal pseudo-obstruction is unknown.

### 3.1. The genes and chromosome associated with Intestinal pseudo-obstruction

- ACTG2
- FLNA

- MYH11
- x chromosome

## **I** 4. Inheritance

Intestinal pseudo-obstruction is often not inherited, and most affected individuals do not have a family history of the disorder. When it does run in families, it can have different inheritance patterns.

Intestinal pseudo-obstruction caused by *FLNA* gene mutations is inherited in an X-linked recessive pattern. The *FLNA* gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Intestinal pseudo-obstruction caused by *ACTG2* gene mutations is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Some other cases of intestinal pseudo-obstruction are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **I** 5. Other Names for This Condition

- chronic idiopathic intestinal pseudo-obstruction
- CIIP
- CIPO
- congenital short bowel syndrome
- enteric neuropathy
- familial visceral myopathy
- familial visceral neuropathy

- IPO
- paralytic ileus
- pseudo-obstruction of intestine
- pseudointestinal obstruction syndrome
- pseudoobstructive syndrome

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