

# Melnick-Needles Syndrome

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Melnick-Needles syndrome is a disorder involving abnormalities in skeletal development and other health problems.

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## 1. Introduction

It is a member of a group of related conditions called otopalatodigital spectrum disorders, which also includes otopalatodigital syndrome type 1, otopalatodigital syndrome type 2, frontometaphyseal dysplasia, and terminal osseous dysplasia. In general, these disorders involve hearing loss caused by malformations in the tiny bones in the ears (ossicles), problems in the development of the roof of the mouth (palate), and skeletal abnormalities involving the fingers and/or toes (digits).

Melnick-Needles syndrome is usually the most severe of the otopalatodigital spectrum disorders. People with this condition are usually of short stature, have an abnormal curvature of the spine (scoliosis), partial dislocation (subluxation) of certain joints, and unusually long fingers and toes. They may have bowed limbs; underdeveloped, irregular ribs that can cause problems with breathing; and other abnormal or absent bones.

Characteristic facial features may include bulging eyes with prominent brow ridges, excess hair growth on the forehead, round cheeks, a very small lower jaw and chin (micrognathia), and misaligned teeth. One side of the face may appear noticeably different from the other (facial asymmetry). Some individuals with this disorder have hearing loss.

In addition to skeletal abnormalities, individuals with Melnick-Needles syndrome may have obstruction of the ducts between the kidneys and bladder (ureters) or heart defects.

Males with Melnick-Needles syndrome generally have much more severe signs and symptoms than do females, and in almost all cases die before or soon after birth.

## 2. Frequency

Melnick-Needles syndrome is a rare disorder; fewer than 100 cases have been reported worldwide.

## 3. Causes

Mutations in the *FLNA* gene cause Melnick-Needles syndrome.

The *FLNA* gene provides instructions for producing the protein filamin A, which helps build the network of protein filaments (cytoskeleton) that gives structure to cells and allows them to change shape and move. Filamin A binds to another protein called actin, and helps the actin to form the branching network of filaments that make up the cytoskeleton. Filamin A also links actin to many other proteins to perform various functions within the cell.

A small number of mutations in the *FLNA* gene have been identified in people with Melnick-Needles syndrome. These mutations are described as "gain-of-function" because they appear to enhance the activity of the filamin A protein or give the protein a new, atypical function. Researchers believe that the mutations may change the way the filamin A protein helps regulate processes involved in skeletal development, but it is not known how changes in the protein relate to the specific signs and symptoms of Melnick-Needles syndrome.

### 3.1. The Gene Associated with Melnick-Needles Syndrome

FLNA

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## 4. Inheritance

This condition is inherited in an X-linked dominant pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

## 5. Other Names for This Condition

- Melnick-Needles osteodysplasty
- MNS
- osteodysplasty of Melnick and Needles

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