

Pachyonychia congenita

Description

Pachyonychia congenita is a condition that primarily affects the skin and nails. The signs and symptoms of this condition usually become apparent within the first few years of life.

Almost everyone with pachyonychia congenita develops very painful calluses on the soles of the feet. This condition is known as plantar keratoderma. Calluses usually begin to form on the feet in childhood when kids first start to walk. The calluses can make walking painful or impossible. In some affected individuals, blisters, bundles of blood vessels and nerves (neurovascular structures), or a deep itch may develop under or near the calluses, increasing pain and discomfort.

Most people with pachyonychia congenita also show some signs of hypertrophic nail dystrophy, which causes the fingernails and toenails to become thick and abnormally shaped. The number of affected nails varies.

Pachyonychia congenita can have several additional features. These features include thickened skin on the palms of the hands (palmar keratoderma), which can be painful; thick, white patches on the tongue and inside of the cheeks (oral leukokeratosis); bumps that develop around hair follicles (follicular keratoses) on the elbows, knees, and waistline; cysts in the armpits, groin, back, or scalp; and excessive sweating on the palms and soles (palmoplantar hyperhidrosis).

Some affected individuals also develop widespread cysts called steatocystomas, which are filled with an oily substance called sebum that normally lubricates the skin and hair. Some babies with pachyonychia congenita have prenatal or natal teeth, which are teeth that are present at birth or in early infancy. Some babies and children with pachyonychia congenita have pain in one or both ears when beginning to eat or drink. Pachyonychia congenita can also affect the voice box (larynx), causing hoarseness or breathing problems.

Researchers used to classify pachyonychia congenita as either PC-1 or PC-2 based on the genetic cause and pattern of signs and symptoms. However, as more affected individuals were identified, it became clear that the signs and symptoms of the types overlapped considerably. Pachyonychia congenita is now classified into five types based on the gene that is altered.

Frequency

Pachyonychia congenita is a very rare disorder, although its exact prevalence is unknown.

Causes

Variants (also called mutations) in the *KRT6A*, *KRT6B*, *KRT6C*, *KRT16*, or *KRT17* genes cause pachyonychia congenita.

When pachyonychia congenita is caused by variants in the *KRT6A* gene, it is classified as PC-K6a. Similarly, *KRT6B* gene variants cause PC-K6b, *KRT6C* gene variants cause PC-K6c, *KRT16* gene variants cause PC-K16, and *KRT17* gene variants cause PC-K17.

All of the involved genes provide instructions for making tough, fibrous proteins called keratins. These proteins form networks that provide strength and resilience to the tissues that make up the skin, hair, and nails.

Variants in keratin genes alter the structure of keratin proteins. The altered proteins are unable to form strong, stable networks within cells. Without this network, skin cells become fragile and are easily damaged, making the skin less resistant to friction and minor trauma. In people with pachyonychia congenita, normal activities such as standing and walking cause skin cells to break down, resulting in the formation of severe, painful blisters and calluses. Defective keratins also disrupt the growth and function of cells in the hair follicles and nails, resulting in the other features of pachyonychia congenita.

[Learn more about the genes associated with Pachyonychia congenita](#)

- KRT16
- KRT17
- KRT6A
- KRT6B
- KRT6C

Inheritance

Pachyonychia congenita is considered an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In about 60 to 70 percent of all cases, an affected person inherits the variant from one affected parent. Thirty to 40 percent of cases result from a new (de novo) variant in the gene that occurs during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- Congenital pachyonychia
- Jackson-Lawler syndrome (PC-2)
- Jadassohn-Lewandowski syndrome (PC-1)
- Pachyonychia congenita syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Pachyonychia congenita 1 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1706595/>)
- Genetic Testing Registry: Pachyonychia congenita 2 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1721007/>)
- Genetic Testing Registry: Pachyonychia congenita 4 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3714949/>)
- Genetic Testing Registry: Pachyonychia congenita syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265334/>)

Genetic and Rare Diseases Information Center

- Pachyonychia congenita (<https://rarediseases.info.nih.gov/diseases/10753/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Pachyonychia congenita%22](https://clinicaltrials.gov/search?cond=%22Pachyonychia%20congenita%22))

Catalog of Genes and Diseases from OMIM

- PACHYONYCHIA CONGENITA 1; PC1 (<https://omim.org/entry/167200>)
- PACHYONYCHIA CONGENITA 2; PC2 (<https://omim.org/entry/167210>)
- PACHYONYCHIA CONGENITA 3; PC3 (<https://omim.org/entry/615726>)
- PACHYONYCHIA CONGENITA 4; PC4 (<https://omim.org/entry/615728>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28pachyonychia+congenita%5BTIAB%5D%29+OR+%28congenital+pachyonychia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>)

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