National Institute of Arthritis and Musculoskeletal and Skin Diseases

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Understanding Pachyonychia Congenita

What Is Pachyonychia Congenita?

Pachyonychia congenita (PC) is a very rare genetic disorder affecting primarily the skin and nails. Its effects, which are evident at birth or early in life, include overgrowth of the nails, and thick, painful calluses on the soles of the feet.

Who Gets It?

PC affects people of both sexes and all racial and ethnic groups. It occurs when a single copy of the gene responsible for the disorder is altered. In about half of the cases of PC, the disorder is inherited from a parent. In the other half, the disorder occurs spontaneously, meaning there is no family history of the disorder.

What Are the Symptoms?

The most common symptom of PC is the presence of thickened nails, which can occur on all or just some of the fingers and toes. Painful blisters and thick calluses on the soles of the feet are usually evident when a child begins to walk. Less commonly, blisters and calluses can form on the palms of the hands.

Depending on the specific form of PC, other features may include thick white patches on the tongue and inside the cheeks; bumps around the hair follicles on the elbows, knees, and waistline; and cysts all over the body. In one type of PC, babies are born with teeth that crumble and fall out soon after birth.

Some symptoms tend to persist over time, but others may change, depending on a person's weight, activity level, and exposure to environmental stressors. Cysts may worsen during puberty, but bumps around the hair follicles may improve with age.

What Causes PC?

PC is caused by mutations in one of at least five genes involved in the production of keratins, which are tough, fibrous proteins that make up the skin, nails, and hair.

These mutations alter the structure of the keratin in such a way that leaves skin cells more vulnerable to minor stress, such as walking. Painful blisters form and then are covered by thick calluses on the soles of the feet and, in some cases, on the palms of the hands as well.

Keratin defects are also responsible for nail thickening and other features of the disorder.

What Are the Different Forms of PC?

PC types are classified based on the gene that is altered. Scientists have identified mutations in five responsible genes, *KRT6A, KRT6B, KRT6C, KRT16,* and *KRT17*. When mutations occur in the *KRT6A* gene, the disease is classified as PC-K6a. Similarly, mutations in the *KRT6B* gene cause PC-K6b, in the *KRT6C* gene cause PC-K6c, in the *KRT16* gene cause PC-K16, and in the *KRT17* gene cause PC-K17.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

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Thickened nails and calluses occur in all forms of PC, but their severity, as well as other symptoms, depends largely on the specific genetic mutation.

How Is It Diagnosed?

PC cannot be diagnosed by symptoms alone, because many of the symptoms are similar to those of other conditions. For example, thickened nails also can be caused by psoriasis, and white patches inside the mouth may be confused with thrush, a yeast infection common in infants. The only definitive way to diagnose PC is with a genetic test, which can be completed using a saliva sample with a special kit.

Effective Treatments for PC

The most effective treatments are mechanical ones. These include:

- Grinding or shaving down thickened nails and skin (while taking care not to get them too thin, which could lead to increased pain and infection).
- Wearing gloves to protect the hands during activities like riding a bicycle or using hand tools.
- Wearing comfortable shoes and wicking socks that reduce moisture and minimize the friction that can aggravate painful calluses.

How Is It Treated?

At present, there is no cure or effective medical treatment for PC. Urea and salicylic acid preparations are often recommended to thin the calluses, but typically patients report them to be ineffective. Over-the-counter medications are commonly used to treat the pain associated with PC symptoms.

What Types of Doctors Treat PC?

Because PC is extremely rare, few doctors have experience treating it. A dermatologist may be the best choice. Your own primary care doctor may also be the best person to treat you because she or he knows your medical history, your lifestyle, and your special needs. It is important to have a good relationship with your doctor to have help when infections occur or other special needs arise.

What Research Is Being Conducted on PC?

Research on PC is focusing on “shutting down” the responsible gene and reducing the pain caused by PC. Potential therapies in development include:

Topical rapamycin. A small trial showed that treatment with rapamycin—a drug that suppresses the immune system and is used to prevent the rejection in organ transplantation—was effective at reducing painful PC symptoms. However, side effects, including infection and cancer risk, limit the use of the oral medication. Scientists are investigating a topical form of rapamycin that can be absorbed through the skin, in hopes that applying it directly over calluses can relieve symptoms while avoiding the systemic side effects of oral rapamycin.

siRNA. Another line of research involves a genetic therapy called small interfering RNA (siRNA) to shut down the faulty genes responsible for PC without interfering with healthy ones. Early research suggests that injecting siRNA into callused, blistered skin may effectively target the cause of the blistering with minimal side effects.

Shoe inserts. Painful calluses on the soles of the feet can make walking difficult or impossible for people with PC. Scientists are working to develop special shoe insoles that cushion and cool the foot to reduce pain.

Statins. Early research suggests that the cholesterol-lowering drugs known as statins may affect the *K6a* gene—one of the genes responsible for PC. However, data from several patient studies have not yet confirmed the effectiveness of statins for PC treatment.

Neuropathic pain medicines. A study done in 2011 on PC patients found that many have neuropathic pain, and some studies are underway using drugs targeted at this type of pain.

Resources

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Website: www.niams.nih.gov

National Institutes of Health's Office of Rare Diseases Research Genetic and Rare Diseases Information Center
Website: http://rarediseases.info.nih.gov

National Library of Medicine's Genetics Home Reference
Website: http://ghr.nlm.nih.gov/condition/pachyonychia-congenita

Pachyonychia Congenita Project
Website: www.pachyonychia.org

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FOR YOUR INFORMATION

This publication contains information about medications used to treat the health condition discussed here. When this publication was printed, we included the most up-to-date (accurate) information available. Occasionally, new information on medication is released.

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