Use of Articles in the Pachyonychia Congenita Bibliography

The articles in the PC Bibliography may be restricted by copyright laws. These have been made available to you by PC Project for the exclusive use in teaching, scholarship or research regarding Pachyonychia Congenita.

To the best of our understanding, in supplying this material to you we have followed the guidelines of Sec 107 regarding fair use of copyright materials. That section reads as follows:

Sec. 107. - Limitations on exclusive rights: Fair use
Notwithstanding the provisions of sections 106 and 106A, the fair use of a copyrighted work, including such use by reproduction in copies or phonorecords or by any other means specified by that section, for purposes such as criticism, comment, news reporting, **teaching (including multiple copies for classroom use), scholarship, or research**, is not an infringement of copyright. In determining whether the use made of a work in any particular case is a fair use the factors to be considered shall include - (1) the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use upon the potential market for or value of the copyrighted work. The fact that a work is unpublished shall not itself bar a finding of fair use if such finding is made upon consideration of all the above factors.

We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
What is Pachyonychia Congenita?

Pachyonychia Congenita (PC) is a rare genetic skin disorder.

The name means:
- Pachy - thick
- Onychia - refers to nails
- Congenita - something you are born with.

Symptoms may include some or all of these features:

**Thickened fingernails and/or toe-nails**
Nail infections can be quite painful.

**Hyperkeratosis**
Thickened skin and calluses on palms of hands (palmar) and soles of feet (plantar). The blisters and calluses on the feet are often extremely painful and walking may be difficult or impossible without assistance.

**Follicular hyperkeratosis**
Thickened skin or bumps around hair follicles which are often on arms legs, the waist and/or other areas of friction. This usually lessens with teenage years.

**Leukoplakia**
White growth inside the mouth and on the tongue (mucosa). This may create difficulty in sucking for newborn infants.

**Cysts**
Several different kinds of skin cysts may be a part of PC. Cysts are another cause of pain.

PC may also cause other symptoms such as:
- Pre-natal or natal teeth - teeth present at birth or first months of life.
- Alopecia - hair loss or other hair changes
- Larynx problems - thickening of the vocal chords.
What is role of keratin in skin, hair and nails?

The skin is our largest organ. Our skin protects the network of muscles, bones, nerves, blood vessels, and everything else inside our bodies.

Every square inch or centimetre of skin contains thousands of cells, hundreds of sweat glands, oil glands, nerve endings, hair follicles, and blood vessels. Skin is made up of three layers. The upper layer of our skin, the epidermis, is the tough protective outer layer which is most affected in PC.

The epidermis has several layers of cells called keratinocytes that are constantly flaking off and being renewed. The keratinocytes cells contain lots of keratin.

Keratin is a tough fibrous protein that doesn’t dissolve in fluid. Keratin is one of the structural proteins that supports keratinocyte cells and gives them shape and strength. Nails and hair are almost pure keratin.

You might compare keratin in cells to the framework of a building. When one of the keratin genes has a mistake (mutation), the cells are weakened. This can cause blistering, over production of cells, breakdown of cells and other problems as the cells try to adjust to the lack of strength.

The photographs above show the difference between a cell with normal keratin with a strong network, structure and form within the cell (left photo) and the mutant keratin that does not have any real structure or form within the cell (right photo).

What causes PC

Pachyonychia Congenita is caused by a change in one keratin gene. PC is an autosomal dominant, genetic disorder. What does this mean?

Genes are recipes or sets of instructions in the cells of the body. For example, keratin genes tell the body how to make keratin proteins. If the recipe (gene) is changed (called a mutation) the cells may not make a normal protein.

Images courtesy of www.genome.gov

The basic unit of any living thing is called a cell. It is a small, watery compartment filled with chemicals and contains a complete copy of all the genes for that living thing. Within each cell, there is a nucleus which holds the chromosomes. Humans have 22 pairs of autosomal (non-sex) chromosomes plus one male and one female sex chromosome. These chromosomes hold the DNA or sequence of genes.

During the last few years, it has been possible to decode the entire human genome - all the human genes have been located and named. In 1995 scientists discovered that a mutation in Keratin genes named K6a or K16 or K6b or K17 causes PC. A person has PC if there is one mistake in the code in any one of those four genes.

Out of 30,000 - 40,000 human genes a person has, researchers estimate there are usually about six which have mutations (changes). Most of the time we aren’t even aware of the defective genes we have as there aren’t any harmful effects. This is because we have two copies of nearly all genes (one from our mother and the other from our father) and the healthy gene just carries out the work for the pair.

However, in PC the gene that has the mutation is dominant and won’t allow the other gene in the pair to take over. PC doesn’t hide. If you have a mutation in a PC gene you will have PC and PC symptoms.

How did I get PC?

If your mother or father do not have PC then you have what is called a spontaneous mutation (not an inherited mutation). A mutation is an error in the code in a gene. This is thought to happen when cells are dividing and replicating (copying) in the earliest stages of development. No one knows a specific cause of this. Statements that the PC mutation is caused by a virus or other illness of the mother during pregnancy, or that the mutation is caused by other actions of the parents are not substantiated by any accepted research findings.

If either your mother or father does have PC, then you have what is called inherited of familial PC (meaning it comes through your family).
Health Feature

Whether spontaneous or inherited, if you have PC then you probably have a change or mutation in one keratin gene. The table shows an example of gene pairs with a change in K6a. A change in one partner of the pair in either K6a, K6b, K16 or K17 causes a person to have PC. It seems amazing that one single change in one copy of one gene can cause so many changes in skin, hair and nails!

The example shows a change in keratin gene K6a. However, a mutation (change) in any one of these four keratin genes causes a person to have PC. All of the symptoms associated with PC are from the change in just one gene partner!

![Table showing gene pairs with changes](image)

<table>
<thead>
<tr>
<th>This person doesn't have PC — all 4 pairs of genes are okay</th>
<th>This person has PC — one of the genes in one pair has a change</th>
</tr>
</thead>
<tbody>
<tr>
<td>K6a</td>
<td>K6a</td>
</tr>
<tr>
<td>K6b</td>
<td>K6b</td>
</tr>
<tr>
<td>K16</td>
<td>K16</td>
</tr>
<tr>
<td>K17</td>
<td>K17</td>
</tr>
</tbody>
</table>

What is learned through genetic testing?

Phenotype describes how PC looks and the symptoms that can be seen and felt. Genotype is the specific change (mutation) inside the body which causes PC. Currently medical writings divide PC into two types:

PC-1 Jadassohn - Lewandowsky type

PC-2 Jackson-Lawler type

Generally, Mutations in keratins K6a or K16 are associated with PC-1 and mutations in keratins K6b or K17 are associated with PC-2. However, there are many overlapping features between PC-1 and PC-2.

PC symptoms vary from person to person even among people with exactly the same mutation. The reasons for this variation are not known completely. Some factors which cause individual differences may include (1) the specific gene (2) the type of mutation in that gene (3) the place in the gene where the mutation occurs (4) other genes a person has which may make the change better or worse. Therefore, a diagnosis based only on the physical symptoms will not provide an accurate diagnosis of the specific mutation.

To have any successful gene-based therapy, the specific gene mutation has to be identified. If you have a mutation in the K6a gene, it will do you no good to have a treatment which affects the K16 gene.

Genetic testing is a complex process which may cost from $2,000 US to $3,000 US. Through cooperative funding, PC Project is able to provide genetic testing without cost to those patients who enrol in the International PC Research Registry (IPCRR).

Is there a cure for PC?

There is presently no cure for PC. No successful drug therapy for PC has been reported. The benefits of certain retinoid drugs have been reported. However the side effects appear to be temporary. Patients report the side effects often outweigh the benefits. There are also a few reports of benefits from certain vitamin doses. The main objective of PC Project is to find a cure for PC. Every activity supported by PC Project is based on that goal.

What are the current treatments for PC?

There are no standardized treatments for PC. However, regular care for the feet and nails is required to reduce pain and manage the condition. Each patient manages the symptoms in a variety of ways. Two basic elements of care for the feet and nails are:

1. Soaking to soften calluses and nails, then
2. Removal of excess calluses.

The removal of the calluses (called debridement) may be done at home or with professional care.

Tools include clippers (including wire clippers for thick nails), emery boards, pumice stone, Dremel-type Sanders, razor blades and scalpels. Vaseline is consistently used. Also, ibuprofen or other pain medication is taken in some form by almost all those with PC. Some ‘tips for care’ from patients include:

- Regular (often daily) care and removal of excess calluses
- Keep feet as dry and soft as possible (i.e. use wicking socks and a moisturizing cream or Vaseline)
- Clip or filed nails frequently
- Insoles made of ‘memory’ material are used by some
- Use a shower stool or stand on a soft cushion in the shower.
- Use open shoes or breathable leather shoes that reduce friction. For some, soft shoes such as moccasins are preferred; for others strong supportive lace-up shoes are better.

Chiropody Review
Will my children have PC?

Every person has two copies of the following genes: K6a, K6b, K16, and K17. One copy comes from their mother and one from their father.

A person who does not have PC has two normal genes in each of the keratins and cannot pass PC to their child even if their own mother or father has PC. If you don't have PC symptoms, you don't have PC and cannot pass on a mutation (changed) gene to your children or grandchildren.

A person who has PC has one changed gene (mutation) and one okay gene in one keratin gene pair. Each time a baby is made, a person with PC has a 50/50 chance of either passing on the changed gene or passing on the okay gene.

Misinformation is sometimes provided about genetic inheritance in PC. It may be because with a recessive gene, a disease can 'skip generations' or 'appear again in another child in a 1-in-4 ratio.' Those statements are not true for PC.

Where can I get further information?

The website at www.FC-Prtrject.org provides links to additional information including a complete bibliography of scientific articles published about PC.

Reproduced by kind permission PC Project 2386 East Heritage Way, Suite B Salt Lake City UT 84109 USA.

Disclaimer

This information has been carefully prepared by PC Project as a public service for education purposes. It is provided as general information only. It is not intended as medical advice and is not tailored to the needs of any specific situation.

No diagnosis or decision regarding treatment should be based on the information without consultation with medical professionals.

The information is intended to be accurate and any mistakes are unintentional. No guarantee is made or implied regarding these materials.

Mary Schwartz
Director, PC Project

Men's Shoes for Problem Feet

Sufferers of swollen, bandaged or problem feet resulting from conditions such as diabetes, arthritis or lower leg ulcers can have difficulty finding shoes to fit. If you need extra-roomy footwear for problem feet or ankles, two new styles of men's shoe from Cosyfeet could be the answer. Both styles come in an HH+ fitting and look good while providing supportive comfort.

The Jason shoe is designed to be easily slipped on and off. An elastic panel sits discreetly beneath the tongue, allowing the upper to gently stretch as the foot is inserted.

The Tom style opens wide for easy entry and fastens with an adjustable Velcro strap. Extension pieces are also supplied in case additional strap length is required.

Made with soft leather, both styles have padding inside the upper and around the ankle collar for extra comfort. Shock absorbing polyurethane soles are also included for improved underfoot comfort. In addition, to achieve the best possible fit, both the Jason and Tom have removable insoles.

The Jason shoe comes in brown nubuck, brown leather and black leather while the Tom shoe comes in brown or black leather. Both styles are available in sizes 6 to 13 including half sizes and are priced at £60.00, or £51.06 if you qualify for VAT relief due to a medical condition that affects your feet.

For more information call the Cosyfeet customer care line on 01458 447275. Lines are open Monday to Friday 8.30am to 5.30pm and Saturday 9am to 1pm. Alternatively see www.cosyfeet.com For media enquiries call Marianne Wilson on 0117 944 5226.