



## Dyskeratosis Congenita

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### What is Dyskeratosis Congenita (DC)?

- DC is a rare genetic disorder that can impact your bone marrow's ability to make blood cells normally. All of your blood cells (red blood cells, white blood cells and platelets) are made in the bone marrow. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help form a clot when we bleed.
- DC also affects many organs, including the skin, liver, and lungs.
- Not all patients will have symptoms of the disease.

### What causes Dyskeratosis Congenita?

- DC is part of a large group of diseases called telomere disorders.
- Telomeres are part of the end of the DNA in our chromosomes.
- Every cell in your body has DNA. When cells divide, the ends of the chromosomes (telomeres) get shorter and shorter. Once these telomeres get too short, it causes damage to the cell and prevents it from working and dividing the right way.
- Doctors at Children's of Alabama have been involved in discovering new genes that can cause DC and helping understand the reason why cells from DC patients become damaged early in life.

### How is Dyskeratosis Congenita inherited?

DC can be passed on, or inherited, in several ways.

- **Autosomal dominant** - DC is passed on to a child from an adult who has the condition. There is a 50% chance that the disease will be passed to the child. Many times there are very few signs or symptoms of DC, so the parent may have this condition and not know it. The disease may be more severe in children than the parents.
  - **X linked** - This type is due to a mutation of the dyskerin gene, which is located on the X chromosome. Only males get this type, while moms (females) are carriers of the disease. A mom who carries a dyskerin mutation has a 50% chance of passing the disease to her male children. Symptoms usually occur early in life, before 10 years of age. Most will also have other signs and symptoms of the disease.
  - **Autosomal recessive** - In autosomal recessive disease, there is often no family history of the condition. Each parent is a carrier and they do not have DC or any symptoms. However, they can pass on the abnormal gene to their children. 1 in 4 children from a family where both parents are carriers have a chance to get this disease.
- It is important to remember that many people may have the gene for DC, but not have any symptoms.
  - In certain forms of DC, symptoms may not appear for many years. People as old as 70 have been diagnosed with this condition.
  - In other types, symptoms may appear in the first few years of life.

### How rare is Dyskeratosis Congenita?

- DC is not as rare as first thought.
- Many patients may have the condition and do not know it.
- DC affects about 1 in 20,000 people.

### What are the symptoms of Dyskeratosis Congenita?

- Defects in fingernails and toenails, including ridges, breaking, and loss of nails
  - Skin pigment changes, often patchy and on the neck and upper chest or areas of sun exposure
  - Whitish plaques in the mouth, called leukoplakia
- Some patients may have:
- Bone marrow failure, which could include low white blood cells, red blood cells, or platelets
  - Lung disease or pulmonary fibrosis
  - Skin and blood cancers
  - Liver disease

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## **How is Dyskeratosis Congenita diagnosed?**

- Your physician will obtain a detailed patient and family history, perform a careful physical examination, and may order the following tests:
  1. Complete blood count- This test may show that your blood has low numbers of red blood cells, white blood cells and platelets. Many times the red blood cells are abnormally large.
  2. Bone marrow aspiration and biopsy- This is needed to help your doctor learn if your bone marrow is making normal numbers of blood cells. This test will also show if leukemia, a type of cancer, is present. It is performed at Children's of Alabama under sedation.
  3. Telomere length test - Your physician can send a blood to a specialized lab to measure the length of telomeres in the DNA of your blood cells, and compare that result to people that do not have that disease. Dyskeratosis congenita may be suspected if your blood cell telomere length is very short.
  4. Genetic testing- Testing can be done on over 13 genes that have been shown to cause DC. Blood is sent to a specialized lab outside of UAB, and it can take several months to get this result back.

## **How is Dyskeratosis Congenital treated?**

- Treatment depends on symptoms and blood counts.
- Many different types of doctors may work together to treat the disease, including hematologists, GI specialists, pulmonary doctors, and bone marrow transplant physicians.
- Your doctors at Children's of Alabama are very trained to treat DC and are members of a large organization (Clinical Care Consortium for Telomere Associated Ailments, or CCCTAA) of centers that have experience with this condition. The following are treatment options:
  1. Transfusion- Some patients may need transfusions with platelets or red blood cells if they are not making enough of these cells. If this treatment is needed, care is taken to reduce the chance of having to repeat blood transfusions.
  2. Androgen therapy- Androgens are hormones that patients can take by mouth to improve blood counts. Danazol is type of androgen therapy. This drug elevates blood counts in about 50% of patients, decreasing the need for a transfusion. Side effects may include oily or pimply skin, deepening of the voice, hair growth or loss, behavioral changes, hot flashes, breast enlargement in males and females, loss of menstruation, and liver toxicity. There is an increased risk of developing liver tumors when the drug is taken for a long time.
  3. Bone marrow transplantation- Bone marrow transplant (BMT) can cure the blood problems that occur with DC. Special precautions need to be taken when a patient with DC has a bone marrow transplant. The UAB Pediatric Bone Marrow Transplant team has expertise in performing bone marrow transplants in children with DC. Special preparations before treatment will be used to reduce the chance of having side effects.

## **What are other problems experienced by patients with Dyskeratosis Congenita?**

- Children with DC are at increased risk of illnesses compared with other patients with bone marrow failure. They require individualized, multi-disciplinary care.
  - Pulmonary problems- many patients with DC will develop asthma early. As they get older, there can be problems with the lungs getting stiff (fibrosis). Pulmonary function testing will be performed and a doctor specializing in lung disorders would be consulted.
  - Liver problems- There is an increased risk of developing scarring (fibrosis) in the liver as DC patients get older. A biopsy is needed to confirm this diagnosis. It is rare to occur in children.
  - Cancer- There is an increased risk of developing leukemia (AML) as well as solid tumors. Your doctors can advise you on ways to best prevent these, including monitoring for cancer during routine follow up appointments.

## **Is there any research being done on Dyskeratosis Congenita?**

- There are several research studies on DC being done at Children's Hospital and UAB hospital. Some of these studies are looking at ways to correct the bone marrow failure by correcting the genetic mutation (gene therapy). Other studies are looking at the role of oxidative stress in this disease, and the potential for intervention with anti-oxidants.