



## Foundation for Ichthyosis & Related Skin Types, Inc.® Autosomal Recessive Congenital Ichthyosis – Congenital Ichthyosiform Erythroderma (ARCI\_CIE) type

### What is Autosomal Recessive Congenital Ichthyosis (ARCI) - Congenital Ichthyosiform Erythroderma type (CIE, Non-bullous CIE, nb-CIE)?

Autosomal recessive congenital ichthyosis (ARCI) is a recently adopted term referring to a heterogeneous group of disorders that share an autosomal recessive pattern of inheritance, collodion membrane presentation at birth, and overlap in causative gene mutations.<sup>1</sup> After shedding of the collodion membrane, skin of individuals with ARCI can show a variety of appearances. These different phenotypes have been termed lamellar ichthyosis (LI), congenital ichthyosiform erythroderma (CIE), and harlequin ichthyosis (HI). While significant overlap can occur between phenotypes and individual patients may manifest different phenotypes across their lifetime, these descriptors remain useful in classifying individuals with ARCI and often in predicting the underlying gene mutation. ARCI is a rare disorder, estimated to occur in approximately 1 in 200,000 births.<sup>2</sup>

### What are the Signs & Symptoms?

At birth, most individuals have a “collodion” presentation, so called because a clear membrane (the collodion) covers their bodies. Sometimes described as having a shellacked appearance, these newborns have skin that is taut, dark and split. Often the eyelids (ectropion) and lips (eclabium) can be forced open by the tightness of the skin, and there may be contractures around the fingers. The collodion membrane is gradually shed over the first few days to weeks of life, after which the skin can take a number of appearances. Such cases usually go on to develop either the LI or CIE phenotypes, with HI being comparatively rare.

In those with the CIE phenotype, shedding of the collodion membrane reveals diffuse redness and fine white scaling of the entire skin surface (termed erythroderma). These symptoms are due to overproduction of skin cells in the epidermis that reach the stratum corneum (the outermost layer of skin) in as few as four days, compared to the normal fourteen. Since cells are produced faster than they are shed, the stratum corneum and underlying layers expand. The severity and type of scaling varies within CIE. While scale is usually fine and white on the face, scalp, and torso in CIE, scale on the legs can be large and plate-like (more like that of lamellar ichthyosis). People with CIE also may have thickened nails, or thickened skin on the palms of the hands and soles of the feet. Hair may be sparse but its structure is normal. People with CIE have an increased susceptibility to skin infection, and heat intolerance is common. Internal organs are not affected.

### How is it diagnosed?

Many genes are now known to cause CIE, including *transglutaminase 1 (TGM1)*, *12R-lipoxygenase (ALOX12B)*, *lipoxygenase-3 (ALOXE3)*, *ATP-binding cassette sub-family A member 12 (ABCA12)*, *cytochrome P450 4F22 (CYP4F22)*, *ichthyin (NIPAL4)* and *patatin-like phospholipase (PNPLA1)*.<sup>3</sup> These encode for various proteins involved in production and integrity of the stratum corneum. Mutations in CIE usually (but not always) are transmitted via autosomal recessive inheritance. Individuals must inherit two recessive genes in order to show the disease, one from each parent, but the parents (“carrier”) show no signs of CIE. (For more information on the genetics of CIE refer to FIRST’s publication, *Ichthyosis: The Genetics of its Inheritance*.) CIE is sometimes referred to by the term non-bullous congenital ichthyosiform erythroderma (n-CIE) to distinguish it from bullous congenital ichthyosiform erythroderma, which shows additional features of skin fragility and is due to dominantly inherited mutations in keratin proteins.

Doctors frequently use genetic testing to help define which ichthyosis a person actually has. This may help them to treat and manage the patient. Another reason to have a genetic test is if you or a family member wants to have children. Genetic testing, which would ideally be performed first on the person with ichthyosis, is often helpful in determining a person's, and their relative's, chances to have a baby with ichthyosis. Genetic testing may be recommended if the inheritance pattern is unclear or if you or a family member is interested in reproductive options such as genetic diagnosis before implantation or prenatal diagnosis.

Results of genetic tests, even when they identify a specific mutation, can rarely tell how mild or how severe a condition will be in any particular individual. There may be a general presentation in a family or consistent findings for a particular diagnosis, but it's important to know that every individual is different. The result of a genetic test may be "negative," meaning no mutation was identified. This may help the doctor exclude certain diagnoses, although sometimes it can be unsatisfying to the patient. "Inconclusive" results occur occasionally, and this reflects the limitation in our knowledge and techniques for doing the test. But we can be optimistic about understanding more in the future, as science moves quickly and new discoveries are being made all the time. You can receive genetic testing through the [Yale University's Disorders of Keratinization study](#) with Dr. Keith Choate or for more information about genetic tests performed you can visit GeneDx, [www.genedx.com](http://www.genedx.com).

## What is the treatment?

CIE is treated topically with skin barrier repair formulas containing ceramides or cholesterol, moisturizers with petrolatum or lanolin, and mild keratolytics (products containing alpha-hydroxy acids). (For more information on which products contain these ingredients, [ask for FIRST's Skin Care Product Listing](#).) Additionally, CIE can be treated systemically with oral synthetic retinoids (for example, acitretin or isotretinoin). Retinoids are only used in severe cases of ichthyosis due to potential for effects on bones, tendons, and ligaments, and other complications.<sup>4,5</sup> Careful monitoring and early treatment should be initiated for skin infections that can exacerbate the condition.

## References:

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*This information is provided as a service to patients and parents of patients who have ichthyosis. It is not intended to supplement appropriate medical care, but instead to complement that care with guidance in practical issues facing patients and parents. Neither FIRST, its Board of Directors, Medical & Scientific Advisory Board, Board of Medical Editors, nor Foundation staff and officials endorse any treatments or products reported here. All issues pertaining to the care of patients with ichthyosis should be discussed with a dermatologist experienced in the treatment of their skin disorder.*



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***Improve lives and seek cures for those affected by ichthyosis and related skin types.***

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