



Foundation for Ichthyosis & Related Skin Types

Foundation for Ichthyosis & Related Skin Types, Inc.[®] **Netherton Syndrome**

What is Netherton Syndrome?

Netherton syndrome is a less common form of ichthyosis. In older children and adults the scaling may have a distinctive circular pattern (ichthyosis linearis circumflexa). But in infants and younger children, the skin is more commonly red and scaly all over, lacking the distinctive circular pattern. Hair shafts are fragile and break easily due to trichorrhexis invaginata, or “bamboo hair,” resulting in short sparse hair. Another characteristic of Netherton syndrome is a predisposition to allergies, asthma, and eczema. Adults and children with Netherton syndrome are also predisposed viral skin infections with herpes and human papilloma virus, in addition to bacterial skin and systemic infections.

What are the signs & symptoms?

Newborns with Netherton syndrome have reddened skin (erythroderma), and, less commonly, a thick shell-like covering of the skin (collodion membrane). Babies with Netherton syndrome may be born prematurely. Trouble gaining weight during infancy and childhood is common, and can be severe. Infants may also have recurrent skin infections and septicemia (infection in the blood). They may develop hypernatremia (elevated sodium levels in the blood) due to excessive loss of fluid from the skin surface. Because hairs may not be affected at birth, and then may be sparse in all babies during the first months of life, the characteristic hair defect that is diagnostic of Netherton syndrome may not be detected initially. Infants with Netherton syndrome may be misdiagnosed as having ARCI-CIE type (congenital ichthyosiform erythroderma), atopic dermatitis, or psoriasis. Atopic dermatitis (red, itchy patches of skin) may be present, and a cradle cap-like scale and redness may appear on the face, scalp and eyebrows.

Autosomal recessive mutations in SPINK5 have been shown to cause Netherton syndrome. Individuals must inherit two mutant copies of SPINK5 in order to have the disease, with each parent contributing one mutated gene; the parents (“carriers”) show no evidence of Netherton syndrome. (For more information on the genetics of Netherton syndrome, request FIRST’s publication, *Ichthyosis: The Genetics of Inheritance*)

This gene encodes a protein that limits the activity of certain proteases (enzymes that digest proteins) in the skin protein. In Netherton syndrome increased protease action in the skin results in too few layers of the outer skin (stratum corneum), and reduced activity of antimicrobial peptides. Therefore agents that remove scale (keratolytics), such as the alpha-hydroxy acids (lactic acid, glycolic acid), salicylic acid and oral retinoids are not helpful in the management of this disorder, and may aggravate the symptoms.

How is it diagnosed?

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 you 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 Gene Discovery Study with Dr. Keith Choate or for more information about genetic tests performed you can visit GeneDx, www.genedx.com.

What is the treatment?

Current treatment options are limited to topical treatment with mild moisturizers containing petrolatum or lanolin and/or a skin barrier repair formula containing ceramides or cholesterol. Topical calcineurin inhibitors (pimecrolimus and tacrolimus) have been shown to be helpful for individuals with Netherton, must be used sparingly because they are absorbed easily through the abnormal stratum corneum, and widespread use can lead to dangerously high blood levels. Topical steroids are also readily absorbed, and should be used in low potency forms to limited areas of the body for short periods of time. Recently a few reports of treatment of Netherton syndrome with systemic immunomodulatory medications have been published. The potentially limited benefits of these medications must be weighed against the risks of systemic medications.

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.

February 2021