Foundation for Ichthyosis & Related Skin Types, Inc.®

Harlequin Ichthyosis

What is Harlequin Ichthyosis?

Harlequin ichthyosis is a recessively inherited disorder. Individuals must inherit two recessive genes in order to show the disease, one from each parent, but the parents ("carrier") show no signs of the ichthyosis. (For more information on the genetics of harlequin ichthyosis refer to FIRST's publication, *Ichthyosis: The Genetics of Its Inheritance.*) Recently the cause of harlequin ichthyosis was traced to the ABCA12 gene. The ABCA 12 gene is believed to encode a transporter protein involved in the transport of epidermal lipids across cell membranes. Identification of this gene will make DNA-based prenatal diagnosis possible.

What are the Signs and Symptoms?

Harlequin ichthyosis is an extremely rare form of ichthyosis and the most severe. The newborn child is covered with plates of thick skin that crack and split apart. The thick skin plates can pull at and distort facial features. The tightness of the skin pulls around the eyes and the mouth, forcing the eyelids and lips to turn inside out, revealing the red inner linings. The chest and abdomen of the infant may be severely restricted by the tightness of the skin, making eating and breathing difficult. The hands and feet may be small, swollen, and partially flexed. The ears may appear to be misshapen or missing, but are really fused to the head by the thick skin. Harlequin infants need to be cared for in the neonatal intensive care unit immediately

Premature birth is typical, leaving infants at risk for complications from early delivery. These infants are also at high risk for difficulty breathing, infection, low body temperature, and dehydration. Constriction and swelling of the mouth may interfere with the suck response and infants may need tube feeding. Medical monitoring is difficult because of the abnormal skin; electrodes cannot be placed effectively and blood vessels cannot be seen under the skin. Placing lines in the artery and vein of the umbilical cord can aid in monitoring the infant and delivering fluids and nutrition. These infants may have problems maintaining normal levels of electrolytes, especially sodium in their blood. They are particularly prone to develop hypernatremia (high sodium levels in the blood). The baby's corneas need to be lubricated and protected if the eyelids are forced open by the tightness of the skin. A high humidity environment in a heated incubator is necessary to help maintain body temperature and to prevent the skin from cracking.

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 Disorders of Keratinization study with Dr. Keith Choate or for more information about genetic tests performed you can visit GeneDx, www.genedx.com.

What is the Treatment?

The thick plate-like skin will gradually split and peel off. Antibiotic treatment may be necessary to prevent infection at this time. Administration of oral etretinate (1 mg./kg. body weight) may accelerate shedding of the thick scales. Most harlequin infants will need one-on-one nursing care for the first several weeks of life.

In the past, these infants rarely survived the first few days of life. However, with recent advances in neonatal care and perhaps with the administration of etretinate[1], 1 mg./kg. body weight, harlequin infants can survive. Several surviving children are now in their teenage years, with several in their twenties. The surviving children display dry, reddened skin, which may be covered by large thin scales, and sparse hair. Physical development may be delayed by the enormous calorie needs their skin function demands, but mental and intellectual developments are expected to be normal. Harlequin ichthyosis demands a meticulous skin care regimen to keep the skin moisturized and pliable and to prevent cracking and fissuring that may lead to infection.

[1] It takes a week or two for etretinate to work loosening the scales. Because most of the fatalities from this condition occur in the first few days of life, many of the successes attributed to etretinate use in the medical literature may be equally due to the high quality of care in the immediate newborn period and to a less severely affected newborn. Some newborns with harlequin ichthyosis will not survive, even with the best of care, because of the severity of their condition.

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

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