Ichthyosis vulgaris is a skin disease in which patients present with scaly skin. Although there is no ultimate cure for this disease, many therapies have been used successfully to limit it. In this article, readers will learn more about the etiology, pathophysiology, clinical features, diagnostic techniques, and common treatment modalities for this condition.

Definition of Ichthyosis Vulgaris

Ichthyosis vulgaris is a cutaneous dermatologic disease of abnormal keratinization characterized by scaling of the skin that usually subsides during summer. It is the most common inherited ichthyosis, and it is inherited in an autosomal dominant fashion with variable penetrance. Atopic disease has been associated with this condition; 37-50% of those with ichthyosis vulgaris exhibit signs of atopic disease.

Epidemiology of Ichthyosis Vulgaris

Among keratinization disorders, ichthyosis vulgaris is the most common with an incidence of 1 in 250. It is commonly seen in Caucasians living in temperate climates. Males and females are equally affected with no racial predisposition. The typical age of onset is 3-12 years.

Hereditary ichthyosis, the most common variety, accounts for 95% of ichthyosis cases. It
is present at birth and presents within the first year in most cases.

Etiology of Ichthyosis Vulgaris

Ichthyosis vulgaris can be hereditary or acquired:

**Hereditary ichthyosis vulgaris**

Hereditary ichthyosis vulgaris is inherited in an **autosomal dominant** fashion with variable penetrance. There is a mutation in the genes that encode skin barrier formation. Ichthyosis vulgaris is caused by **loss-of-function mutations** of the *filaggrin gene* (the gene that codes for filaggrin protein).

In loss-of-function mutations, the function for which the gene encodes is lost. Filaggrin (filament-aggregating protein) is a 37-kD peptide that forms the main part of the **keratohyalin granule** present in the granular layer.

Normally, it binds to keratin filaments, resulting in their aggregation, thus causing flattening of the **stratum corneum corneocytes** (keratinocytes). The normal function of this gene has a crucial role in the integumentary **barrier function**. Filaggrin gene has been mapped to **chromosome 1q21**. Mutations of this gene predispose the affected individual to **atopic eczema**, **atopic asthma**, and even **psoriasis**.

Other factors that determine the severity of scaling include deficiency of amino acid breakdown products of filaggrin that are water-retentive and defects in **serine proteases**. A mutation in the **steroid sulfatase gene** can also lead to more severe ichthyosis.

**Acquired ichthyosis**

Acquired ichthyosis is a disease of adulthood that is seen following an internal pathology, such as malignancy or medication use.

Pathology and Pathophysiology of Ichthyosis Vulgaris

**Filaggrin mutations** result in disorganized lamellar bilayers and impaired lamellar bilayer maturation. Filaggrin proteolysis is important for skin homeostasis. It is usually fully degraded into constituent amino acids, namely, glutamine, arginine, and histidine, and subsequently hydrolyzed further into acidic, polycarboxylic acid osmolytes that are responsible for maintaining the **stratum corneum** hydration (the “natural moisturizing factors”).

Filaggrin metabolites are reduced in patients with ichthyosis vulgaris. This causes reduced levels of “natural moisturizing factors” that in turn results in a reduction in skin hydration, an elevated skin surface pH, and increased **transepidermal water loss** (TEWL). These changes are responsible for the xerotic skin seen in ichthyosis vulgaris.

Reduction in filaggrin also decreases the ability of the squames to maintain their hydration as they move up progressively through the **stratum corneum**; this results in the characteristic excessive scale.

The abnormal barrier function leads to compensatory repair mechanisms, including **epidermal hyperplasia**; this results in **hyperkeratosis**. Lower levels of filaggrin
proteins are also associated with reduced epidermal **urocanic acid** (a major ultraviolet- absorbing **chromophore**) levels and increased sensitivity to ultraviolet light. This may be the reason for the higher prevalence of **non-melanoma skin cancer** seen in patients with atopic dermatitis.

**Symptoms and Signs of Ichthyosis Vulgaris**

At birth, the skin *feels and looks normal*; however, in the neonatal period, the skin may present a **dry and scaly appearance**. Scaling of the skin usually is obvious from two months onwards. The scale is typically white or grey; small, flaky, or branny in texture; and semi-adherent with edges that are turned up. The **typical location of scaling is on the extensor aspects** of the arms as well as the lower legs; flexural creases are usually spared. The **nappy or diaper area is often spared**.

Regarding the trunk involvement, the back may be more affected than the abdominal wall. Mild **dandruff** and involvement of the **pinnae** may be seen in some patients. **Palmoplantar hyperlinearity** (linear grooves that cross perpendicularly to the **thenar** and **hypothenar eminences**), which is a reflection of mild **hyperkeratosis**, is a helpful feature in many ichthyosis vulgaris patients, though the soles and palms are usually free of scaling.

**Keratosis pilaris** (keratotic elevations located around **hair follicle orifices**) is seen in both **atopic eczema** and **ichthyosis vulgaris**, and is usually seen on the extensor aspects of the arms and thighs.

Symptoms include mainly dryness or roughness of the skin and cosmetic blemishes. Pruritus is not present in isolated ichthyosis vulgaris; however, it may be present in those who have coexistent eczema. Marked seasonal variation is seen in most patients, with amelioration of symptoms in warm and sunny weather. A significant proportion of patients (38%) report gradual improvement during adolescence; however, in some patients, the condition worsens with age.

**Bathing suit ichthyosis** is an entity typically present in congenital ichthyosis that is inherited in an **autosomal recessive** fashion. The main feature of this condition is substantial scaling present along with the bathing suit areas. The extremities and the center of the face are typically spared. **Transglutaminase-1 deficiency** is responsible for this condition.
Diagnosis of Ichthyosis Vulgaris

Both light microscopy, as well as electron microscopy, may be employed to examine skin biopsy samples. It is recommended that samples for biopsy be procured from areas that have maximal hyperkeratosis. Areas that have minimal scaling are best not taken for histopathologic examination. The preferred site for biopsy is the lower leg (anterior surface) because the thickest scales/stratum corneum are found here.

Histological similarity exists between acquired and hereditary ichthyosis. Compact hyperkeratosis is usually present in the stratum corneum although some involved regions may have a laminated appearance. Follicular plugging, if present, may represent coexistent keratosis pilaris. Another characteristic histologic finding is the presence of granular layer that is single-layered or absent altogether. Sarcoïdosis may present with features of ichthyosis, called ichthyosiform sarcoïdosis, which characteristically has multiple noncaseating dermal granulomas.

Differential diagnoses

The other diagnoses to be considered are

1. Xerosis
2. Ichthyosiform sarcoïd.
3. Allergic contact dermatitis
4. Asteatotic eczema
5. Drug eruptions
6. Harlequin ichthyosis
7. Impetigo
8. Irritant contact dermatitis
9. Lamellar ichthyosis
10. Pediatric atopic dermatitis
11. X-linked ichthyosis.

Therapy of Ichthyosis Vulgaris

There is no definitive treatment for ichthyosis. Reduction of morbidity and prevention of complications are the goals of pharmacotherapy in this condition. The defective integumentary barrier allows allergens access beyond the epidermis to come into contact with the antigen-presenting cells. Hence, an important prophylactic approach is to restore the barrier function of the skin using emollients and moisturizers.

Moisturizers are very beneficial for patients suffering from ichthyosis vulgaris and atopic dermatitis.

Management of ichthyosis vulgaris involves hydration of the skin and application of an ointment to prevent evaporation, which causes disaggregation of corneocytes by the loss of adhesion between cells and leads to the formation of a new stratum corneum.

Topical retinoids, such as tretinoin are useful skin-hydrating medications. However, they are irritating or cause stinging to the skin following topical application. They are contraindicated in pregnant women due to teratogenicity. A topical retinoid that is receptor-selective, tazarotene, is beneficial especially in patients who find tretinoin irritating.

Over-the-counter products available for the treatment of ichthyosis vulgaris usually
contain propylene glycol or urea as their main constituent. Both urea and propylene glycol are called humectants. These agents retain the moisture/hydration level in the skin. Urea maintains hydration levels by forming water inclusions in the skin. It may also help in epidermal gene regulation, thus improving the barrier function of the skin. In contrast, propylene glycol acts by withdrawing water via stratum corneum due to the presence of a water gradient. Shedding of thick skin is seen in the following hydration.

A humectant lotion, ammonium lactate (12%), is the commercially available form of lactic acid. This agent may be applied twice daily and has been very beneficial in the control of ichthyosis vulgaris. It has superior action compared to creams that are petrolatum-based. It reduces the excessive keratinization in the skin afflicted by ichthyosis vulgaris. Its exact mechanism of action is not known.

Other useful methods of management

Salicylic acid may be used for scale removal. It is a keratolytic agent that acts by promoting the shedding or peeling of corneocytes. Also, it induces disaggregation of the corneocytes situated in the upper layers. However, excessive use should be avoided due to risk of systemic toxicity following topical administration over a large surface area, especially in pediatric patients.

Steroids are not indicated as a mainstay of treatment for ichthyosis vulgaris; however, pruritus may be alleviated by the use of a mild topical steroid.

The coexistent systemic disease should be treated in cases of acquired ichthyosis vulgaris.

Prognosis

Ichthyosis vulgaris improves during summer and in humid climates. The hereditary variety improves during adulthood. Thus, the disease runs a predictable course.

However, the most common causes of morbidity and mortality include:

- Cosmetic blemish among adolescents.
- Secondary infections of skin lesions.
- An underlying disease in the acquired variety.

Review Questions on Ichthyosis Vulgaris

The correct answers can be found below the references.

1. Which of the following areas is spared in ichthyosis vulgaris?

   A. Forearm  
   B. Lower limbs  
   C. Back  
   D. Diaper area  
   E. Extensor surfaces

2. Regarding the inheritance pattern of hereditary ichthyosis vulgaris, which of the following is true?

   A. Autosomal dominant with variable penetrance  
   B. Autosomal dominant with fixed penetrance
3. Which of the following is a treatment modality for ichthyosis vulgaris?

A. Moisturizers
B. Local heat
C. Three doses of methylprednisolone
D. Systemic retinoids
E. Plasmapheresis

References


Hereditary and Acquired Ichthyosis Vulgaris via medscape.com

Laclotion (Ammonium Lactate) lotion via nih.gov

Correct answers: 1D, 2A, 3A

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