Non-syndromic Ichthyoses

Non-syndromic ichthyoses are a group of genetic skin disorders that manifest with dry, scaly skin but without associated systemic symptoms or syndromes. They are caused by mutations in keratin proteins that affect the barrier function of the skin. There are several subtypes, each with distinct clinical features and genetic causes.

### Inheritance Pattern

- **Autosomal Semi-dominant**
  - 1. Ichthyosis vulgaris

- **Autosomal Dominant Keratinopathic**
  - 2. Steroid sulfatase deficiency

- **Autosomal Recessive Colloidal membrane**
  - 3. Superficial epidermolytic ichthyosis (KRT 2e)

- **XLR**
  - 4. Congenital self-healing collodion baby

### Skin Layer

- **Suberficial Epidermis**
  - 1. Ichthyosis vulgaris
  - 3. Superficial epidermolytic ichthyosis (KRT 2e)
  - 5. Ichthyosis hystrix of Curth Macklin

- **Suprabasal Layers**
  - 2. Steroid sulfatase deficiency
  - 6. Ichthyosis en confetti

### Resolving?

- **Resolving**
  - 4. Congenital self-healing collodion baby
  - 8. Harlequin ichthyosis
  - 9. Congenital ichthyosiform erythroderma (non-bullous)
  - 10. Lamellar ichthyosis

### Disease  |  Gene/Onset  |  Unique Qualities
--- | --- | ---
1. Ichthyosis vulgaris  | Gene: FLG  
Onset: Infancy or childhood  | Spares flexures  
Hyperlinearity of palms/soles  
Keratosis pilaris/Atopic diathesis  
Fine adherent scale on extremities and trunk
2. Steroid sulfatase deficiency  | Gene: STS or arylsulfatase C deficiency  
Onset: Infancy  | If continuous gene deletion of STS occurs = Kalman syndrome  
“Dirty” brown scale  
Spares flexures  
Comma-shaped corneas [only finding found in female carriers]  
Prolonged labor secondary to placental sulfatase deficiency  
Decreased serum estriol in pregnancy  
Increased risk of testicular cancer  
cryptorchidism
3. Superficial epidermolytic ichthyosis  | Gene: KRT2E  
Onset: Birth  | Erythroderma + superficial blisters at birth  
Mauserung phenomenon – German for molting; superficial shedding of skin with palms/soles spared
Onset: Birth  | After resolution, skin appears normal
Non-syndromic ichthyoses (continued)
by Parin Pearl Rimtepathip, MD, Janna Mieko Vassantachart, MD, and Maria A. McGowan, MD

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene/Onset</th>
<th>Unique Qualities</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Ichthyosis hystrix of Curth Macklin&lt;br&gt;Aka Ichthyosis hystrix</td>
<td>Gene: KRT1&lt;br&gt;Onset: Early childhood</td>
<td>• Diffuse or striate PPK&lt;br&gt;• “porcupine quill”-like verrucous yellow-brown scaling, esp on hand and feet&lt;br&gt;• Digital constriction/pseudoainhum PPK</td>
</tr>
<tr>
<td>6. Ichthyosis en confetti&lt;br&gt;Aka Congenital reticular ichthyosiform erythroderma or Ichthyosis variegata</td>
<td>Gene: KRT10&lt;br&gt;Onset: Birth</td>
<td>• At birth, erythroderma&lt;br&gt;• After birth, confetti-like areas of scaling&lt;br&gt;• Joint contractures&lt;br&gt;• Hypoplasia of mammillae&lt;br&gt;• Dorsal acral hypertrichosis</td>
</tr>
<tr>
<td>7. Epidermolytic ichthyosis&lt;br&gt;Aka Bullous congenital ichthyosiform erythroderma</td>
<td>Gene: KRT1, KRT10&lt;br&gt;Onset: Birth</td>
<td>• Erythroderma with blisters and erosions at birth&lt;br&gt;• After birth, hyperkeratosis + cobblestone appearance with predominance over joints&lt;br&gt;• Retinol exacerbates skin fragility&lt;br&gt;• Malodorous with frequent skin infections&lt;br&gt;• Gait and posture abnormalities&lt;br&gt;• Somatic mosaicism [extensive epidermal nevus aka ichthyosis hystrix] vs gonadal mosaicism [offspring with full expression of disease]</td>
</tr>
<tr>
<td>8. Harlequin ichthyosis</td>
<td>Gene: ABCA12&lt;br&gt;Onset: Birth</td>
<td>• Extreme eclabium and ectropion&lt;br&gt;• Early initiation of systemic retinoids reduces mortality&lt;br&gt;• Death is secondary to sepsis and respiratory insufficiency&lt;br&gt;• Ear deformities</td>
</tr>
<tr>
<td>9. Congenital ichthyosis-form erythroderma (non-bullous)</td>
<td>Gene: ALOXE3, ALOX12B&lt;br&gt;Onset: Birth</td>
<td>• After collodion membrane resolves, develop white fine scale in generalized distribution [Flexures involved] - like “snow flakes”&lt;br&gt;• Erythroderma as background [hence not bullous]&lt;br&gt;• +/- palm/soles&lt;br&gt;• Heat intolerance and hypohydrosis&lt;br&gt;• +/- scarring alopecia and ectropion</td>
</tr>
<tr>
<td>10. Lamellar ichthyosis</td>
<td>Gene: TGM1&lt;br&gt;Onset: Birth</td>
<td>• Thick plate-like brown scale with significant flexure involvement&lt;br&gt;• Ectropion/eclabium&lt;br&gt;• Heat intolerance&lt;br&gt;• Scarring alopecia</td>
</tr>
</tbody>
</table>

References: