

Genodermatosis

Is referred to a group of disease which are due to genetically determined disorders

Some of the Genodermatoses

1. Ichthyosis
2. Keratoderma
3. Neurofibromatosis
4. Epidermolysis bullousa
5. Down's syndrome
6. Klinefelter syndrome
7. Tuberous sclerosis



Autosomal dominant

Increased adhesiveness of the stratum corneum cells and failure to separate

Gene: profilaggrin, FLG (filaggrin)

Life-long disorder with exacerbations in dry (winter) weather

يكون طبقات مزقة في بعض الأحيان

العلاج بالمطهرات

Lamellar ichthyosis more severe than vulgaris



1- Ichthyosis اسماك أو لقم

Heterogeneous group of inherited disorders characterized by the accumulation of scale on the skin surface

The word ichthyosis comes from the Greek word for fish, referring to the scaliness of the skin

All types of ichthyosis have dry, thickened, scaly or flaky skin.

Main types of ichthyosis

1. Ichthyosis vulgaris *most common.*
2. Lamellar ichthyosis
3. X-linked ichthyosis *in male*

Incidence: 1 per 300 000 persons

Collodion membrane at birth

Large, dark, plate-like scales generalized with fissuring between scales

Mild erythroderma, Ectropion, Eclabium, Dystrophic nails, Alopecia

No abnormality of mucosa or teeth

Decreased sweating

التم مضموع

للمعول لغوي

Autosomal recessive

Increased cell hyperplasia of the basal cells and increased transit rate through the epidermis

Decreased transit time of epidermal cells with increased mitotic activity

Alteration of scale lipids

Gene defect in transglutaminase 1 (TGM1) that catalyzes cross-linking of proteins in the upper layers of the epidermis

Persistent life-long hyperkeratosis and peeling

Secondary infection common

Ichthyosis vulgaris

Most common form of ichthyosis

Incidence: 1 per 300–2000 persons

Onset 3–12 months of age

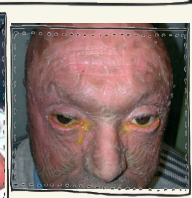
Personal or family history of dry skin or atopy

Extensor surfaces of the extremities and trunk, with extremities more severely affected

Flexural areas spared

القرن الشعري (جلد الخايف)

Hyperlinearity of the palms and keratosis pilaris is common



Management

Babies should be kept in **humidified** incubators to maintain body temperature and prevent dehydration.

Constant monitoring of vital signs

Electrolyte disturbance with intravenous fluid therapy.

Aseptic handling because of risk of **infection**.

Nasogastric tube feeding because of poor sucking.

Aqueous cream to clean skin, use of white soft **paraffin**.

Oral 13-cis retinoic acid reduces scaling. لته الو الحفاض جابنيته لتي

X-linked ichthyosis

Incidence: 1 per 2000–6000 males

Placental steroid sulfatase deficiency syndrome with failure to initiate or progress in labor

Begins in the first year of life

Scales large, thick, adherent and dark (dirty appearance) بشيرة صالغارية

Generalized involvement, milder on face

May involve flexures and neck

Cryptorchidism (20%)

X-linked recessive inheritance (males only)

Pathogenesis

Cholesterol sulfate in epidermis is built up

Increased adhesiveness of the stratum corneum cells and failure of these cells to separate

Gene locus: Xp22.32

Gene: STS (steroid sulfatase)



2- Palmoplantar keratoderma

ichthyosis بقي مع اوبون

Characteristic **thickening of the palms and soles**

Three major patterns: **diffuse**, **focal** or **punctuate**

Can be **inherited** (autosomal or recessive) or **acquired**

Can be associated with ichthyoses or other abnormalities

Abnormalities of keratin 1, 9, 16, others

Persistent, **can be progressive**



Focal ppk

Localized areas of hyperkeratosis located mainly on pressure points & sites of recurrent frictions



Punctuate keratoderma



Multiple small hyperkeratotic papules, spicules, or nodules on the palms & soles



Treatment

Salicylic acid 4–6% in petrolatum

Mechanical debridement

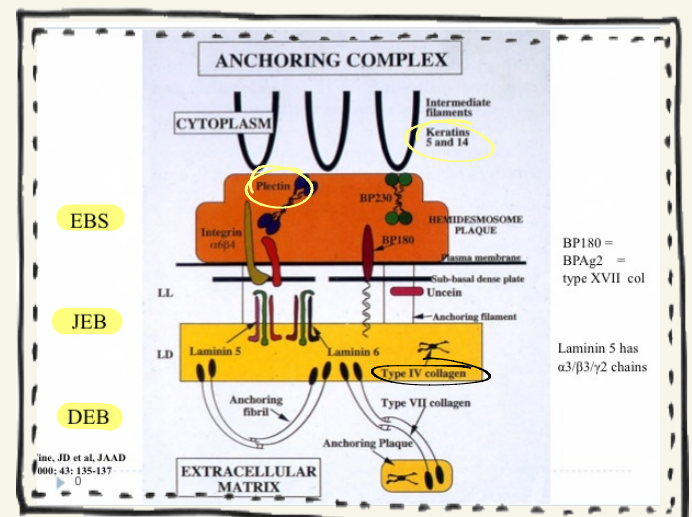
Oral retinoids have variable effect sever case

3- epidermolysis bullosa

أمراض تكل خضاعات ويصير لها لysis

Three major types:

- Simplex (Epidermal)** يجل من اقل خلا muscle و هو يبريخي البقع
Mutations of **keratin 5 / 14** and **plectin**
- Junctional (Basement Membrane)**
Mutations of basement membrane proteins
- Dystrophic (Dermal)** → اصحب نوع
Mutations of type **VII collagen**
- Kindler syndrome**



Diffuse ppk

Uniform involvement of the palmoplantar surface. This pattern is usually evident within the few months of life

EBS

- Mutations in genes for
 - keratins (intermediate filaments)
 - plectin (hemidesmosome plaque)
- Most are autosomal dominant

erosion & necrosis of pressure area
blisters
تقرح في مناطق الضغط
تقرح



Caused by loss of function mutation in the FERMT1 gene encoding kindlin-1 a component of cell adhesive focal contact



قد يحتاجوا الى nephrostomy
وعندهم مشاكل في urogenital

JEB

- Lamina lucida defects of
 - anchoring filaments
 - hemidesmosomes
- Most are autosomal recessive

أغلبهم يولدوا
بصحة تسليخ في الجلد
ملاحظة حول الرقبة
ملاحظة

mucosal membranes



4- neurofibromatosis

- Neurofibromatosis is an autosomal dominant disorder that affects the nervous system, the bone, soft tissue, and the skin.
- Two major subtypes : type 1 neurofibromatosis, and type 2 neurofibromatosis,
- Several other clinical phenotypes of neurofibromatosis have been identified (at least 8)

DEB

- Dominant (DDEB) and Recessive (RDEB)
- Many (>500) mutations identified in collagen VII gene (COL7A1) on 3p21
- Collagen VII is found in the
 - anchoring fibril
 - anchoring plaque

epidermis
dermis

Butterfly children >> children with epidermolysis bullosa



Kindler syndrome

- Autosomal recessive
- Skin fragility and blistering at birth followed by development of photosensitivity and skin poikiloderma
- Skin atrophy, initially localized to hands and feet and then generalized.
- Hand dorsum atrophy and digit webbing results in a characteristic hand aspect.
- Further disease manifestations involve mucous membranes, including oral cavity, esophagus and anus, urogenital tract and eye.

adhesion

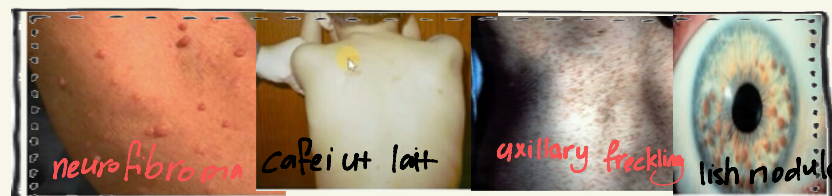
Neurofibromatosis type 1

- Incidence 1 : 4000 of the general population
- Characterized by multiple café au lait macules and neurofibromas in the skin, CNS, bones, muscles and endocrine system

• AD with 50% spontaneous mutation

Diagnostic criteria (at least two)

- ≥6 café au lait macules (during the first 3 years of life)
- Axillary freckling (Crowe sign)
- ≥2 Lisch nodules (iris hamartomas)
- ≥2 neurofibromas or a plexiform neurofibroma (form in late adolescence)
- bone lesions such as sphenoid dysplasia or thinning of long bone cortex with or without pseudarthrosis
- Optic glioma
- First-degree relative with neurofibromatosis type 1



neurofibroma café au lait

axillary freckling lisch node

Neurofibromatosis type 2

Acoustic neuromas of the eighth cranial nerve (90% bilateral)

Multiple CNS tumors (various types)

Few café au lait macules or neurofibromas

No axillary freckling

No iris hamartomas (Lisch nodules)

Autosomal dominant

Pathogenesis

Neurofibromas are caused by **loss of a tumor suppressor gene** with uncontrolled growth of tissues

Neurofibromatosis type 1

Gene: neurofibromin, (tumor suppressor gene)

Neurofibromatosis type 2

Gene: NF2, merlin (Moesin, Ezrin, Radixin-
= schwannomin Like protein) *cytoskeletal protein*

Treatment

Annual visits

Patients should be followed for complications:

optic glioma, neural tumors, developmental disabilities, vascular problems, elevated blood pressure, orthopedic problems, malignancy, psychological problems

Surgical excision of neurofibromas that are rapidly growing or painful

Prognosis

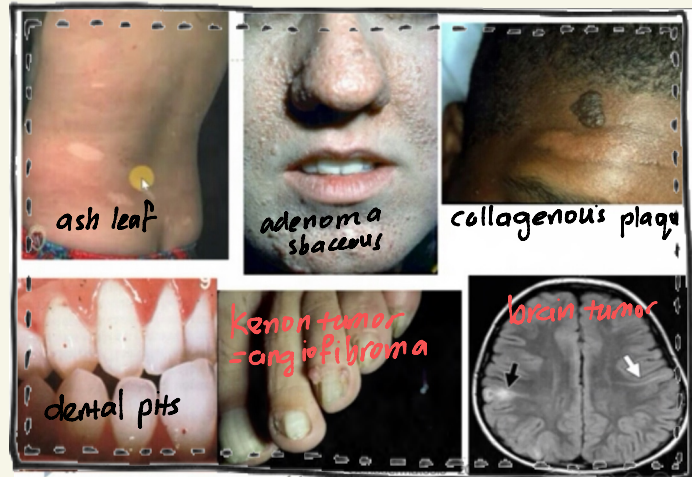
Type 1: progressive and variable; may be an increase in complications around puberty or pregnancy

Type 2: deafness usually in adulthood

5- tuberous sclerosis

Autosomal dominant with mutation in TSC2 gene which produces tuberin (probable tumor suppressor)

- ▶ Ash leaf macule
- ▶ Adenoma sebaceum
- ▶ Collagenous plaques
- ▶ Dental pits
- ▶ Oral fibromas
- ▶ Koenen tumors
- ▶ Cortical tubers (40%)
- ▶ Seizures begin in infancy
- ▶ Retardation (30 to 65%)
- ▶ Rhabdomyoma of heart
- ▶ Angiomyolipoma of kidney



HUDA
AHMED
OTHMAN

IUG