# *HOMO SAPIENS* DISEASES - CUTANEOUS APPARATUS AND SUBCUTANEOUS TISSUE

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**Diseases of skin** (see also physiology of skin)

Pathogenetic processes :

- with regard to the stratum corneum and stratum granulosum
  - **parakeratosis** : process of keratinization in which the keratinocytes in stratum corneum retain their nuclei; abnormal in skin, normal in mucous membranes. It occurs in ...
    - psoriasis
  - **hyperkeratosis / lichenification / lichenoid dermatosis** : hypertrophy of the stratum corneum layer of the skin, whether by normal or abnormal keratinocytes. It occurs in ...
    - lichen planus
    - **Kyrle's disease / hyperkeratosis penetrans** : a rare chronic disorder of keratinization characterized by a papular eruption with hyperkeratotic cone-shaped plugs in the hair follicles and eccrine ducts, which project through the epidermis into the dermis, producing a foreign body giant cell reaction and pain. The usually discrete lesions leave a depression on removal; they may coalesce to form patches, and coalescing plaques are often seen
    - **keratosis pilaris** : a condition in which hyperkeratosis is limited to the hair follicles, usually on the extensor surfaces of the thighs and arms, but occurring anywhere, with discrete follicular papules which re-form after removal
    - **keratosis punctata** : a form of hyperkeratosis in which the lesions are localized in multiple points on the palms and soles; it is transmitted as an autosomal dominant trait.
  - **hypergranulosis** : increase in thickness of the granular layer. It occurs in ...
    - lichen planus
  - **keratolysis** : softening and dissolution or peeling of the horny layer of the epidermis.
    - **pitted keratolysis / keratolysis plantare sulcatum / cracked heels** : a superficial bacterial infection of the skin of worldwide distribution usually involving the weight-bearing portions of the soles of the feet, and characterized by the formation of shallow asymptomatic discrete round pits, some of which become confluent and form fissures; the specific etiologic agent is unknown
    - **ulcus interdigitale** : keratolysis of the horny layer of the skin between the toes, a disease similar to cracked heel.
- with regard to the stratum spinosum and stratum basale
  - **acanthosis** : keratinocyte (acanthocyte / spur cell) hyperplasia in stratum spinosum with thickening of the epidermis
    - **papillomatosis** : increase in keratinocytes with formation of projections from the surface of the skin, i.e. papillae. It occurs in ...
      - wart
      - acanthosis nigricans
      - confluent and reticulate papillomatosis / Gougerot-Carteaud syndrome : a progressive, pruritic papillomatosis, probably a genodermatosis, seen chiefly in girls, especially those at or near puberty, beginning in the intramammary and midback areas as slightly keratotic pigmented papules that increase in size and spread over the trunk and other body areas; centrally located lesions tend to become confluent and peripherally located ones to become reticulate
    - **psoriasiform epidermal hyperplasia** : increase in keratinocytes with elongation of rete ridges and elongation of dermal papillae. It occurs in ...
      - psoriasis
    - **acanthosis nigricans (AN)** : a skin disease characterized by diffuse velvety acanthosis with gray-black warty patches usually situated in back of the neck, the axillae or groin or on elbows or knees

      Aetiology :
      - endocrinopathy
        - multiple endocrine neoplasia (MEN) IIA / Sipple's syndrome
        - insulin resistance => hyperinsulinemia (most commonly) => insulin acts as an agonist also on IGF-1R
      - paraneoplastic (more rarely) in patients with carcinoma of abdominal viscera (**malignant acanthosis nigricans**)
      - benign, nevoid form, more or less generalized
      - benign juvenile form associated with obesity (**pseudoacanthosis nigricans**) (post-receptorial insulin-resistance)
  - **dyskeratosis** : cell death associated with premature keratinization below the level of the stratum granulosum
  - **spongiosis** : widening of the interspaces between keratinocytes due to edema fluid without detachment of cells from each other. It occurs in ...
    - allergic contact dermatitis (ACD) / type IV hypersensitivity
    - Gilbert pytiriasis rosea
  - **acantholysis** : detachment of keratinocytes from each other due to loss of intercellular contacts. This often is associated with the cell assuming a spherical shape, i.e., a round profile in sections
  - **vacuolization** : the formation of vacuoles within cells. This term is used often in reference to changes in the basal keratinocytes
  - **ballooning degeneration** : intracellular edema with cellular swelling. This is often secondary to viral injury or nutritional deficiency
- with regard to dermis
  - **necrobiosis** : swelling, basophilia, and distortion of collagen bundles in the dermis, sometimes with obliteration of normal structure, but without actual necrosis, seen especially in granuloma annulare and necrobiosis lipoidica

Symptoms :

- **pruritis / pruritis / itching** : an unpleasant cutaneous sensation that provokes the desire to rub or scratch the skin to obtain relief.

  Aetiology (prurigos) :
  - cutaneous diseases

- systemic arterial hypertension
- psychogenic factors
- microorganisms
    - higher density of the commensal *Demodex folliculorum* (>= 5 live parasites/cm$^2$ of skin), triggering inflammatory or specific immune reactions, mechanically blocking the follicles, or acting as a vector for bacteria. Immunohistochemical findings suggest that a delayed hypersensitivity reaction, possibly triggered by antigens of follicular origin, probably related to *D. folliculorum*, may occur, stimulating progression of the affection to the papulopustular stage[ref]. Ongoing research has shown that bacteria from patients with rosacea may behave differently at the higher skin temperature that may be present in patients with rosacea. Another group has isolated bacteria from the *Demodex* mites; these bacteria may play a pathogenic role in papulopustular rosacea by facilitating follicular-based inflammatory changes[ref]. In rosacea patients (ages 11-50 years old) 44% were infested with *D. folliculorum* as compared to normal controls (23.0%). The difference was significant. The mean +/-SD of mite density ranged between 13.2+/-0.9 to 18.2+/-1.2 as compared to normal controls with mite density ranged between 1.4+/-0.25 to 2.4+/-0.3. *Demodex* infestation in rosacea patients was 66.1% in squamous, 66.7% in erythemato-telangiectate and 83.3% in papulo-pustular rosacea. The highly infested site was check (27.3%) with mean mite density of 25.3+/-1.3, followed by the area around the orbit (23.4%) with a density of 19.0+/-1.2, the area around the nose (19.5%) with mite density of 7.1+/-1.5, then chin (15.6%) with a density of 8.2+/-1.4 and lastly the area around the mouth (14.1%) with a mite density of 14.2+/-1.3. Undoubtedly, infestation with *D. folliculorum* particularly in large number causes rosacea[ref]. The mite prevalence in the rosacea group (51%) was significantly higher than in the rest of the study population (eczema 28% and lupus discoides 31%). Demodex mites were found on all facial sites. The most infested areas in the whole study group were the forehead (49%) and the cheeks (44%). Males were more frequently infested (59%) than females (30%). We did not find any significant difference in mite counts of infested follicles between rosacea and the control group. A lympho-histiocytic cell infiltration was seen around the infested hair follicles[ref].
    - *Helicobacter pylori*

Classification : 4 subtypes of rosacea:

- erythematotelangiectatic
- papulopustular
- phymatous
- ocular

Recently, a standard grading system for assessing gradations of the severity of rosacea has been reported. Little is known about the cause of rosacea.

Symptoms & signs : transient or persistent facial erythema, telangiectasia, edema, papules and pustules that are usually confined to the central portion of the face; chronic inflammation that may begin as a tendency to flush or blush easily, and progress to persistent redness in the center of the face that may gradually involve the cheeks, forehead, chin and nose. It also may involve the ears, chest and back. As the disease progresses, small blood vessels, tiny pimples and pustules begin to appear on and around the reddened area; however, unlike acne, there are no blackheads. In more advanced cases of rosacea pimples and pustules may cause enlargement of the sebaceous glands of the nose resulting in puffy cheeks and enlarged red nose (**rhinophyme**).

**Rosacea fulminans** is a rare disease of unknown cause which occurs exclusively in women years after adolescence. Although the etiology is unknown, immunologic, hormonal, and vascular factors have been suggested. When rosacea fulminans occurs during pregnancy and in women taking oral contraceptive pills, hormonal factors may be a trigger. Rosacea fulminans is localized specifically to the face, with the chin, cheeks, and forehead bearing the brunt of the attack. A dull red, cyanotic erythema of all involved facial areas, extending beyond the inflammatory nodules, is typical[ref]

Laboratory examinations : standardised skin surface biopsy (SSSB)

Therapy[ref] :

- flushing is better prevented rather than treated, and its etiology investigated. β-blockers, atenolol in particular, are worthy of prophylactic trials examining their efficacy in treating the flushing associated with rosacea. Currently, clonidine is the only drug available for the treatment of flushing
- treatment for erythrosis includes topical and systemic therapies. Metronidazole 1% cream and azelaic acid 20% cream have been reported to reduce the severity score of erythema. The systemic treatment of erythrosis is based on the association of *Helicobacter pylori* with rosacea. However, this role is still being debated.

  Eradication of *H. pylori* can be achieved using a triple therapy regimen lasting 1 to 2 weeks [omeprazole and a combination of 2 antibacterials (a choice from clarithromycin, metronidazole or amoxicillin)]
- treatment of facial telangiectases : flashlamp-pumped long-pulse dye laser and the potassium-titanyl-phosphate laser
- treat the papulopustules of rosacea :
    - systemic treatment includes metronidazole, doxycycline, minocycline, clarithromycin and isotretinoin
        - benzoyl peroxide-erythromycin gel was superior to metronidazole gel in decreasing *Demodex folliculorum* by the first examination, but the effect of the two drugs on *Demodex folliculorum* was similar by the second examination[ref]
        - severe or persistent cases may be treated with oral metronidazole, tetracyclines or isotretinoin[ref]
        - 5% permethrin cream[ref] is superior to metronidazole 0.75% gel and placebo in decreasing *Demodex folliculorum*, and is as effective as metronidazole 0.75% gel in treating erythema and papules[ref1, ref2].
        - daily topical application of >50% diluted *Eucalyptus globulus* (camphor oil)[ref] with glycerol and 500 mg metronidazole orally[ref]
        - oral ivermectin, in combination with topical permethrin[ref]
    - topical treatment is based on metronidazole cream and gel. Crotamiton 10% cream or permethrin 5% cream may be useful medications for papulopustular rosacea, although they are rarely successful in eradicating *D. folliculorum*. Oral or topical ivermectin may also be useful in such cases. Ocular involvement is common in patients with cutaneous rosacea and can be treated with orally administered or topical antibacterials.
- once rhinophyma starts to be evident, the only way to correct it is by aggressive dermatosurgical procedures. Decortication and various types of lasers can also be used. Associated conditions, such as seborrheic dermatitis and possible contact sensitizations, deserve attention.

- drugs
    - **bromide button** : a verrucous cutaneous lesion occurring as a result of sensitivity to bromides (bromoderma)
    - **iodide button** : a verrucous cutaneous lesion occurring as a result of sensitivity to iodides
- systemic diseases
    - increased androgen incretion
        - adrenal incretion
            - Cushing disease
            - congenital adrenal hyperplasia (CAH)
        - ovarian incretion
            - polycystic ovary syndrome (PCOS)
    - disseminated cryptococcosis
    - dimorphic fungi
    - Behçet disease (pseudofolliculitis)

- **hair color alterations**
    - **canities** : diffuse grayness or whiteness of the scalp hair, especially as associated with aging.
        - **hemicanities** : grayness of the hair on one side of the body.

      Pathogenesis : defective self-maintenance of melanocyte stem-cells. This process is accelerated dramatically (gray a few weeks after birth) with Bcl2-deficiency, which causes selective apoptosis of melanocyte stem-cells within the niche at their entry into the dormant state, but not of differentiated melanocytes. Furthermore, physiologic aging of melanocyte stem-cells was associated with "ectopic pigmentation or differentiation" within the niche, a process accelerated by mutation of the melanocyte master transcriptional regulator Mitf (mice goes white in 6 to 10 months)[ref]
    - **achromotrichia / hypochromotrichia** : loss of pigment in the hair
    - **leukotrichia** : whiteness of the hair in a circumscribed area
    - **melanotrichia** : abnormal hyperpigmentation of the hair.
    - **heterotrichosis** : growth of hair of different colors on the body.
        - **heterotrichosis superciliorum**
    - **poliosis** : circumscribed depigmentation of the hair, particularly of the scalp, in association with a pathologic condition
        - **autoimmune poliosis**