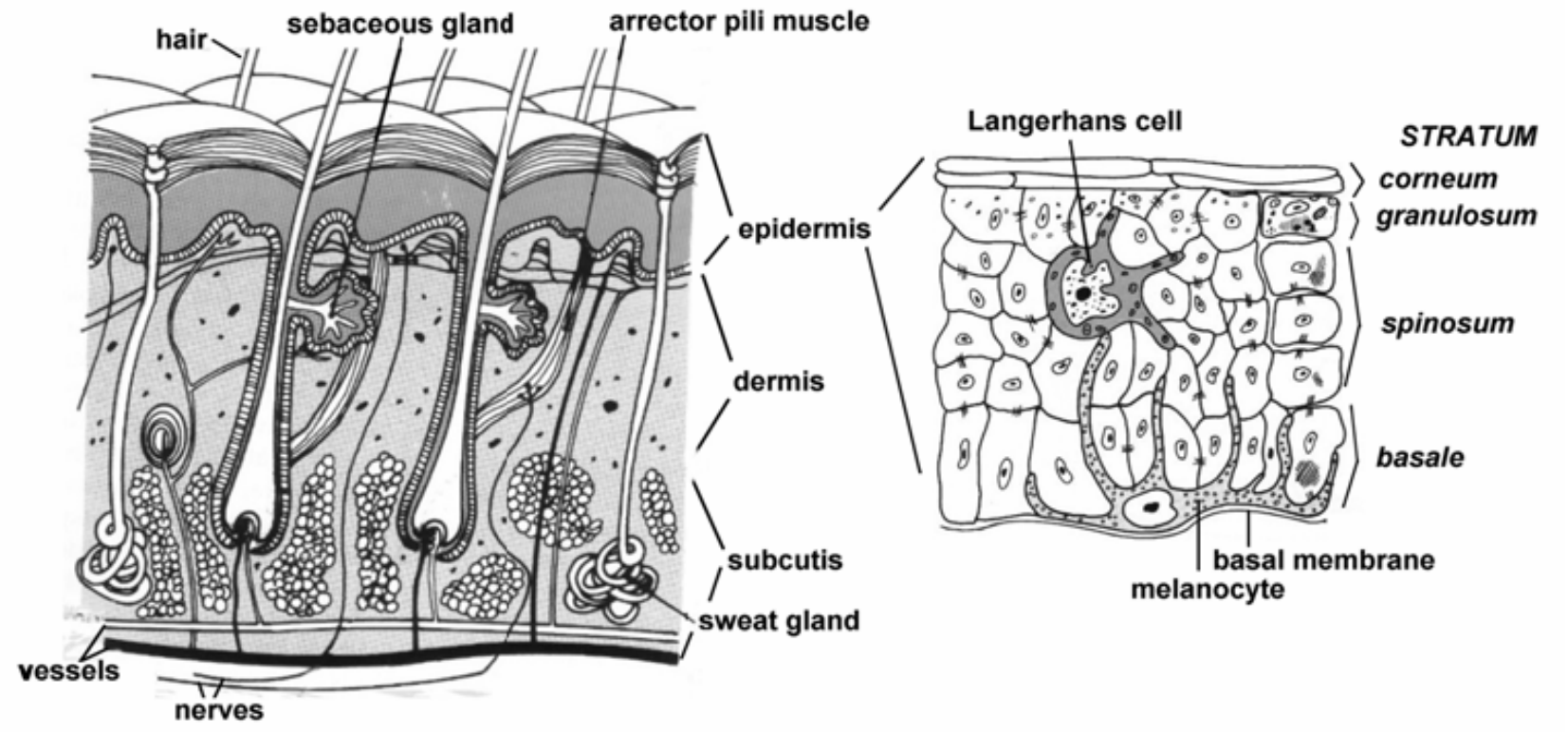
Dermatopathology

A. Histology

Components of the normal integument



Cells of the epidermis

- Keratinocytes: comprises 85% of the cells in the epidermis.
- Melanocytes: 5% of population contains melanosomes responsible for melanogenesis.
- Langerhan’s cells: bone marrow derived antigen presenting cells. 5-8% of the total epidermal cells.

Normal dermis

- Dermal fibres: formed by fibroblasts e.g. collagenous, reticular and elastic and dermal ground substance
- Cellular elements: usually sparsely populated with cells.
  - Fibroblasts,
  - melanocytes,
  - mast cells (mostly around post capillary venules),
  - macrophages,
  - lymphocytes and
  - eosinophil (rare).

B. Immunology

- Langerhan’s cells: antigen presenting cells. They process native antigen, activate memory and effector T cells monitoring the skin surface and migrate to local lymph nodes for the promotion of interactions with unprimed T cells.
- Dermal dendrocytes: antigen presenting cells (APC’s)
- Skin homing lymphocytes: resident lymphocytes on hand to react with APC’s and macrophages.
- Keratinocytes: these produce inflammatory mediators such as IL-1, IL-6, IL-8 and TNF-α.
- Mast cells
- Endothelial cells

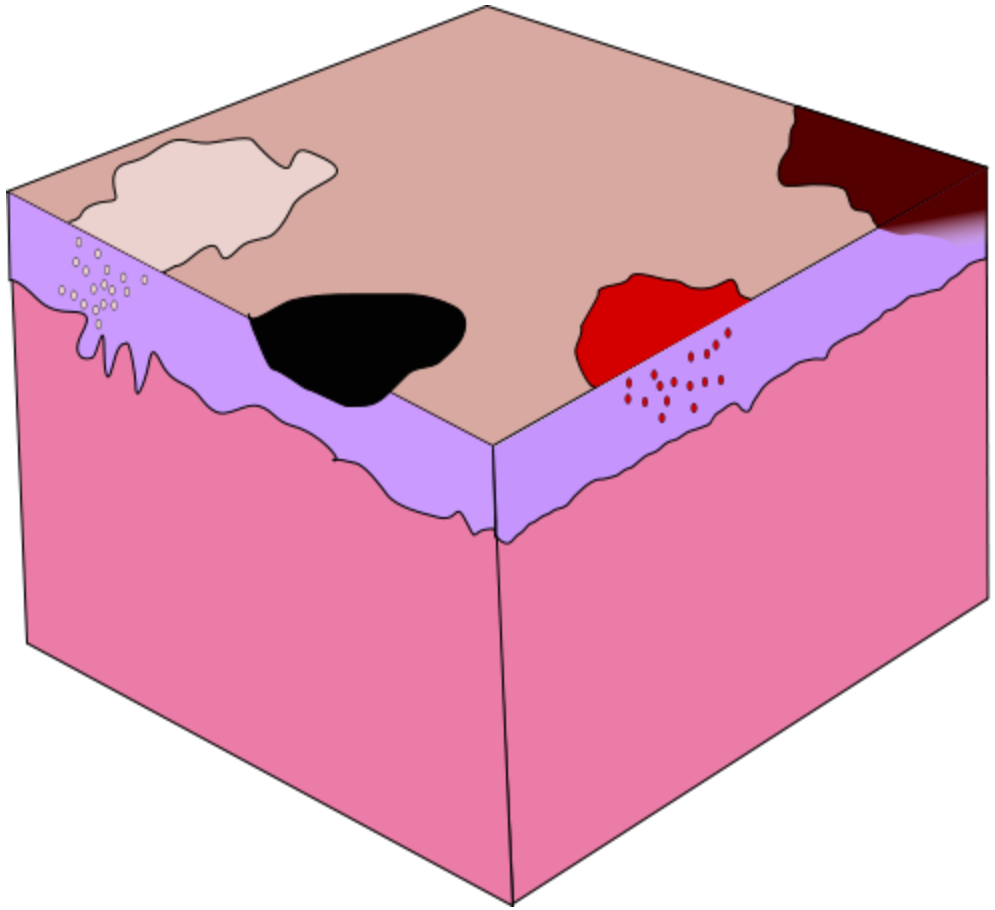
- The skin immune response may be protective and appropriate, as in case of some delayed hypersensitivity reactions and the immunologically-mediated regression of a cutaneous tumour.
- Alternatively, the inappropriate or ill controlled generation of cutaneous immune responses may lead to allergic disease.

C. Gross lesions

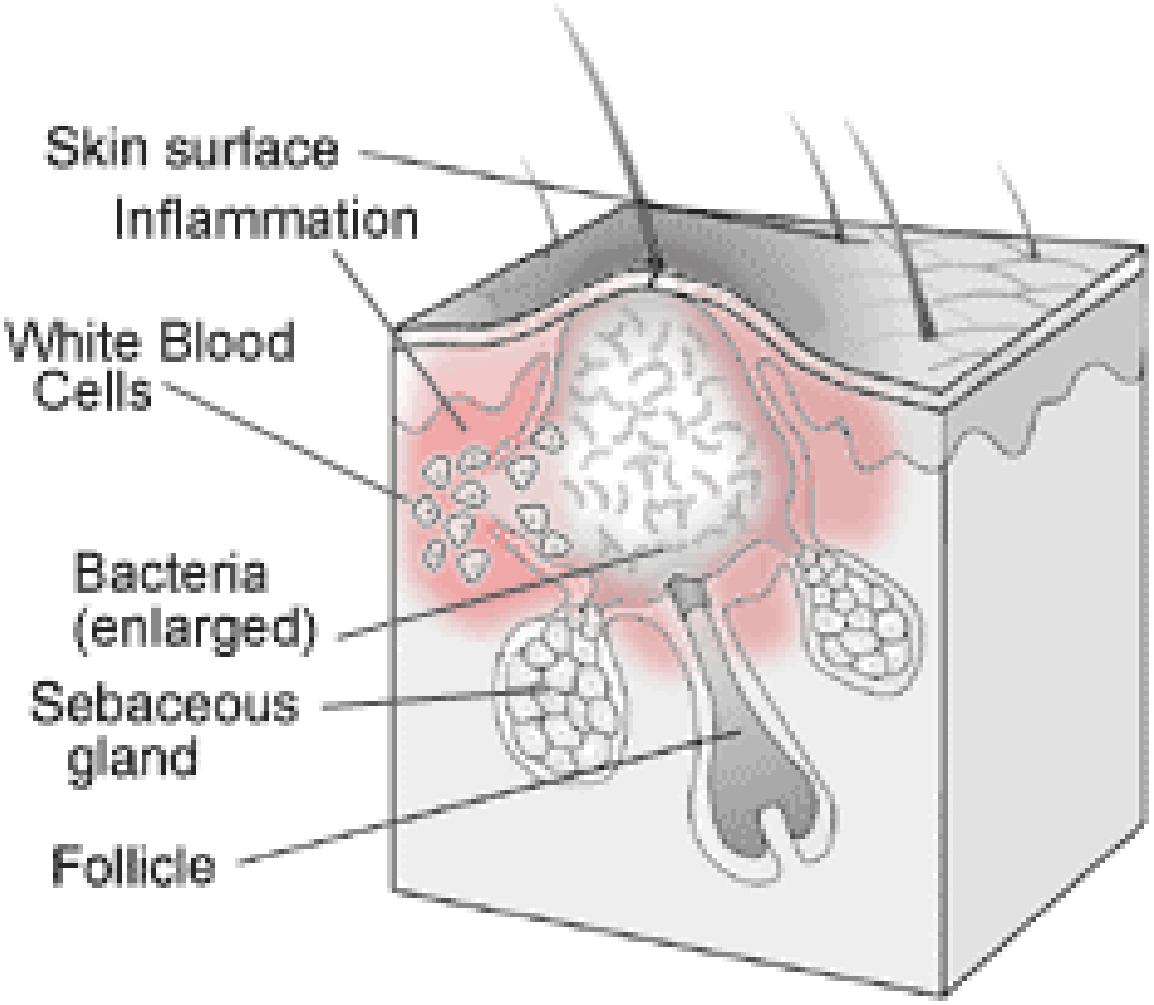
1.Primary gross lesions

- macule or patch
- papule or wheal
- pustule
- vesicle or bulla
- wheal
- nodule
- tumour or cyst

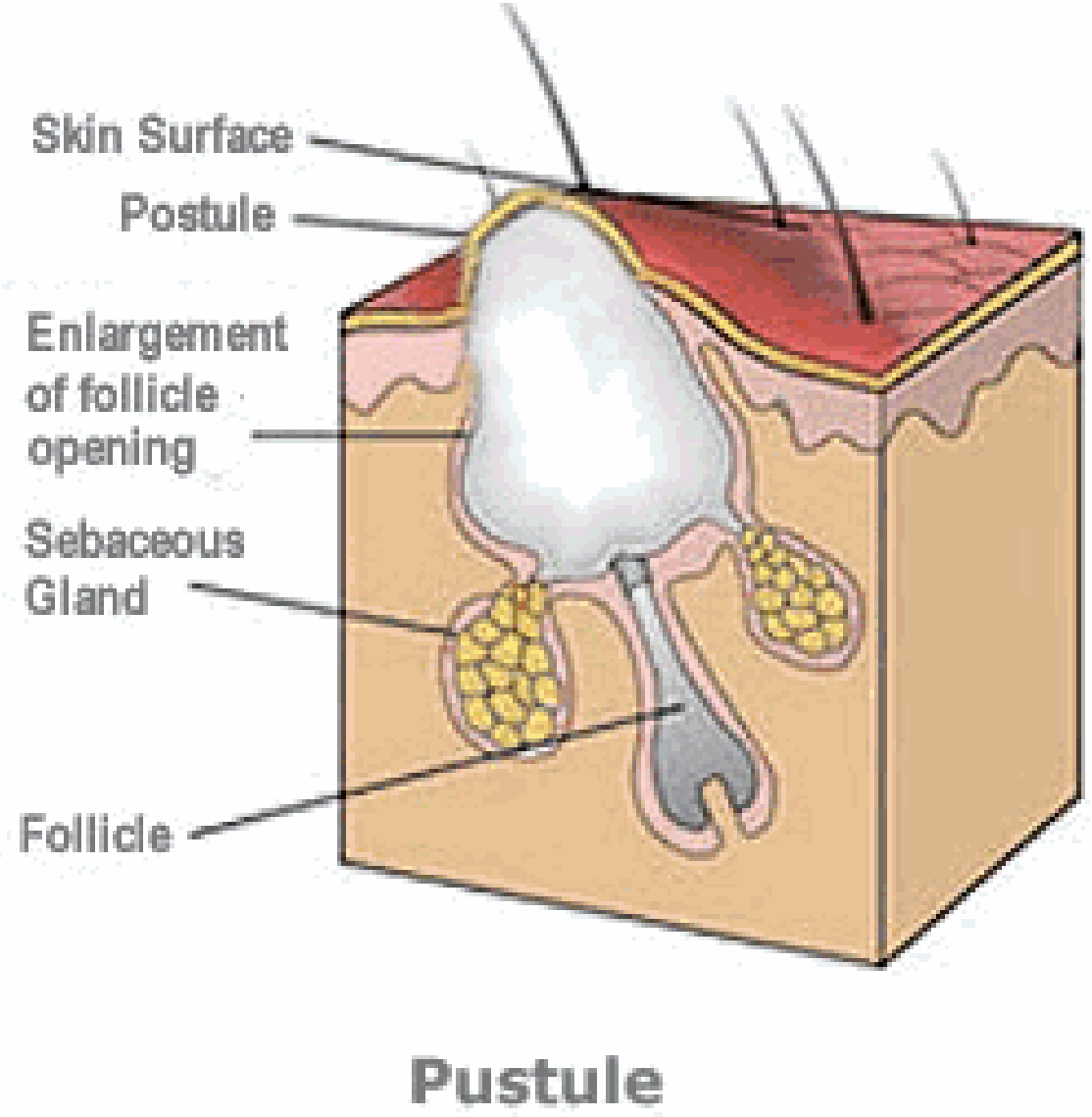
Macule



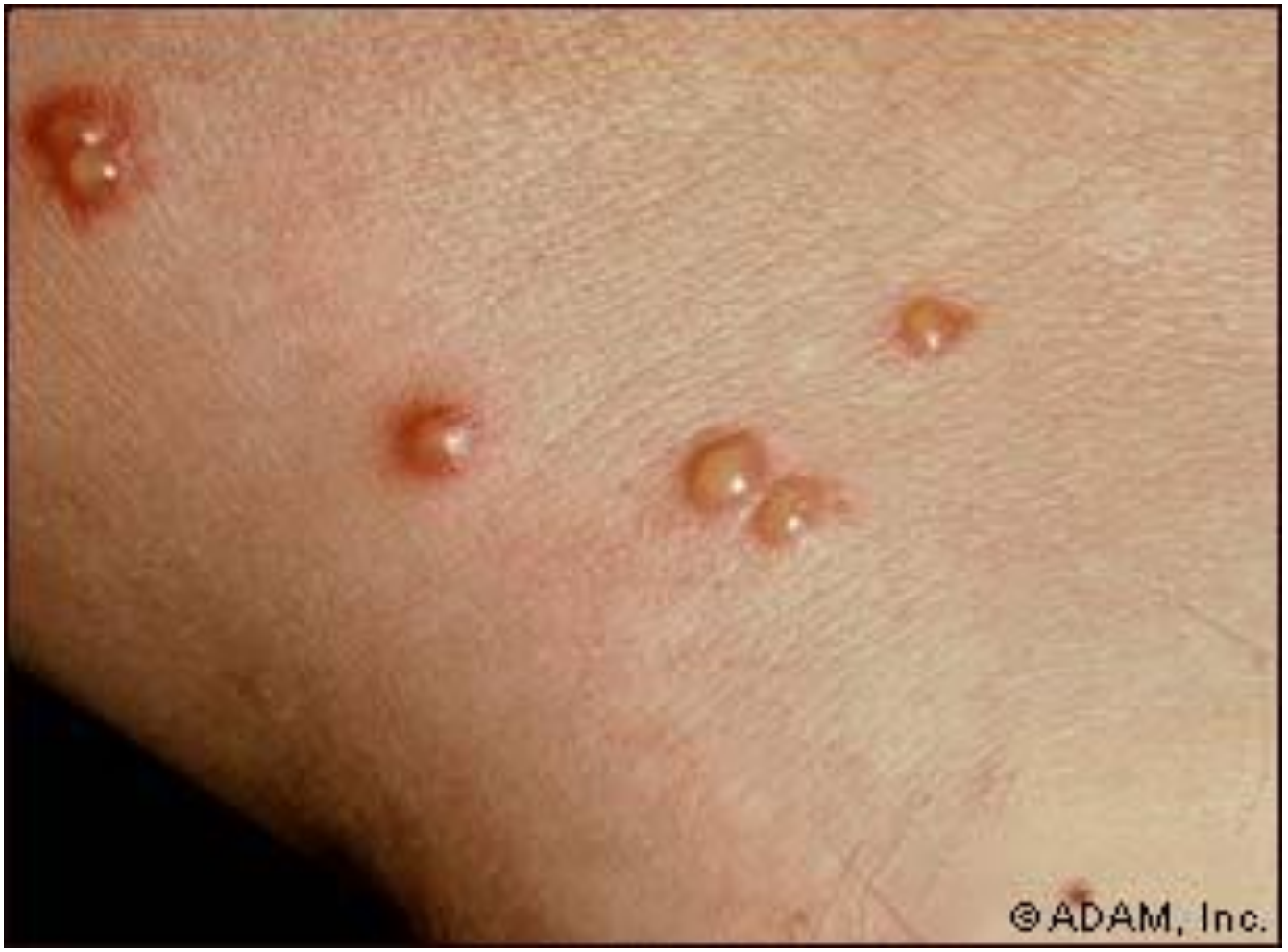
Papule


Skin surface
Inflammation
White Blood Cells
Bacteria (enlarged)
Sebaceous gland
Follicle

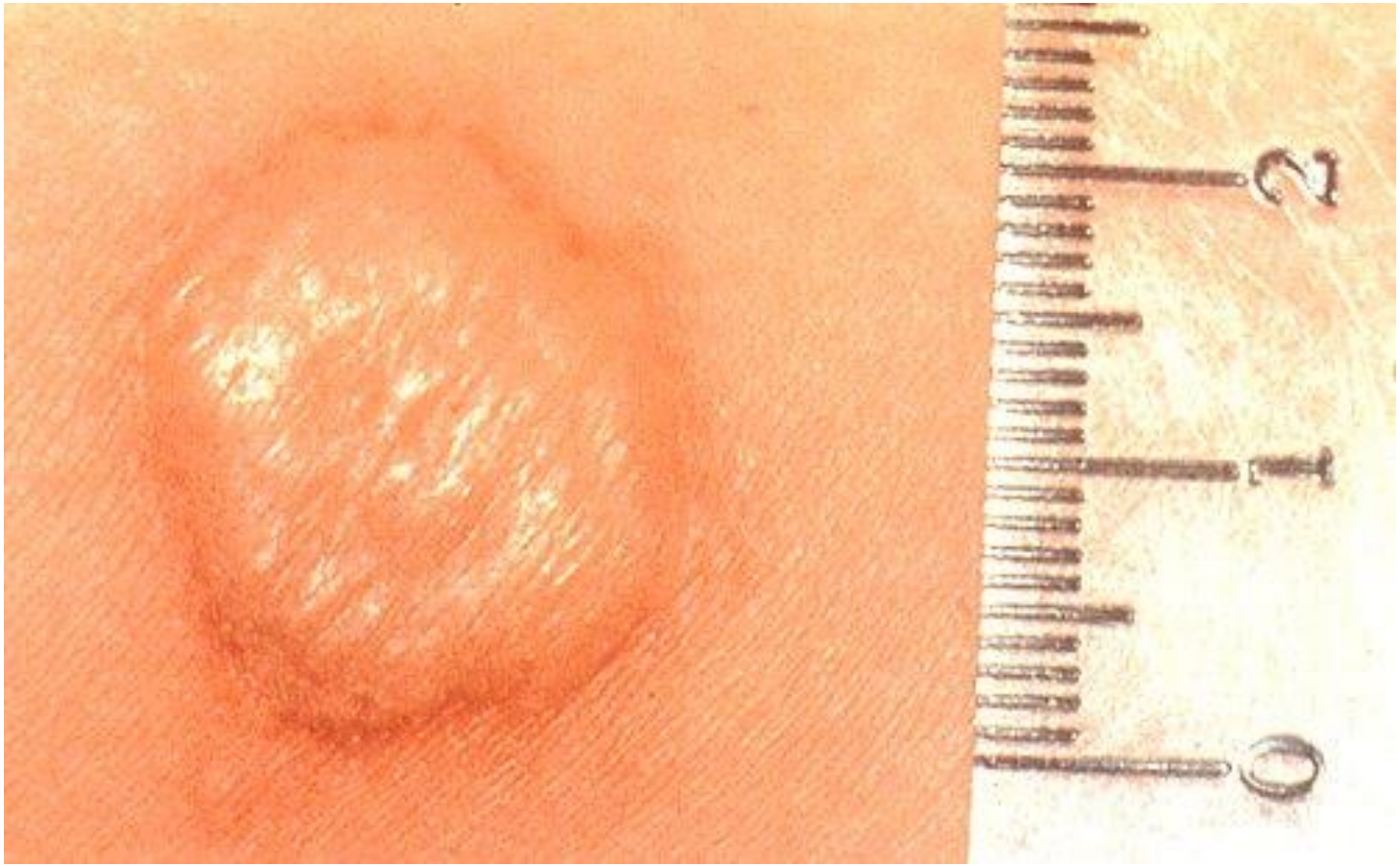
Pustule


Skin Surface
Postule
Enlargement of follicle opening
Sebaceous Gland
Follicle
Pustule

Vesicle

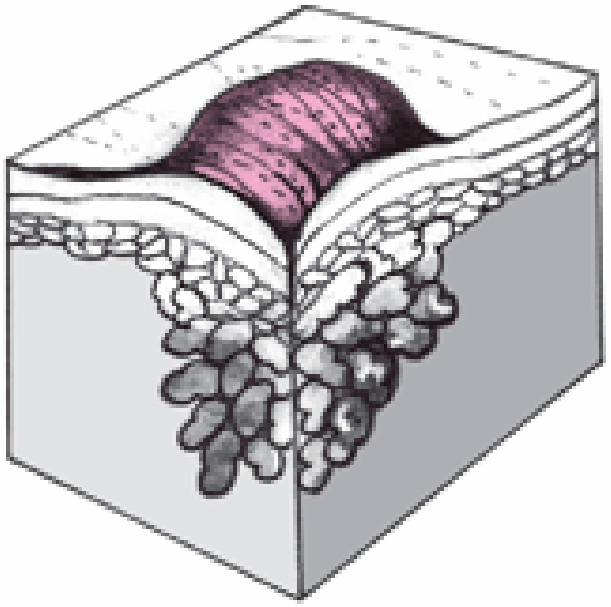


Wheal



Nodule

NODULE

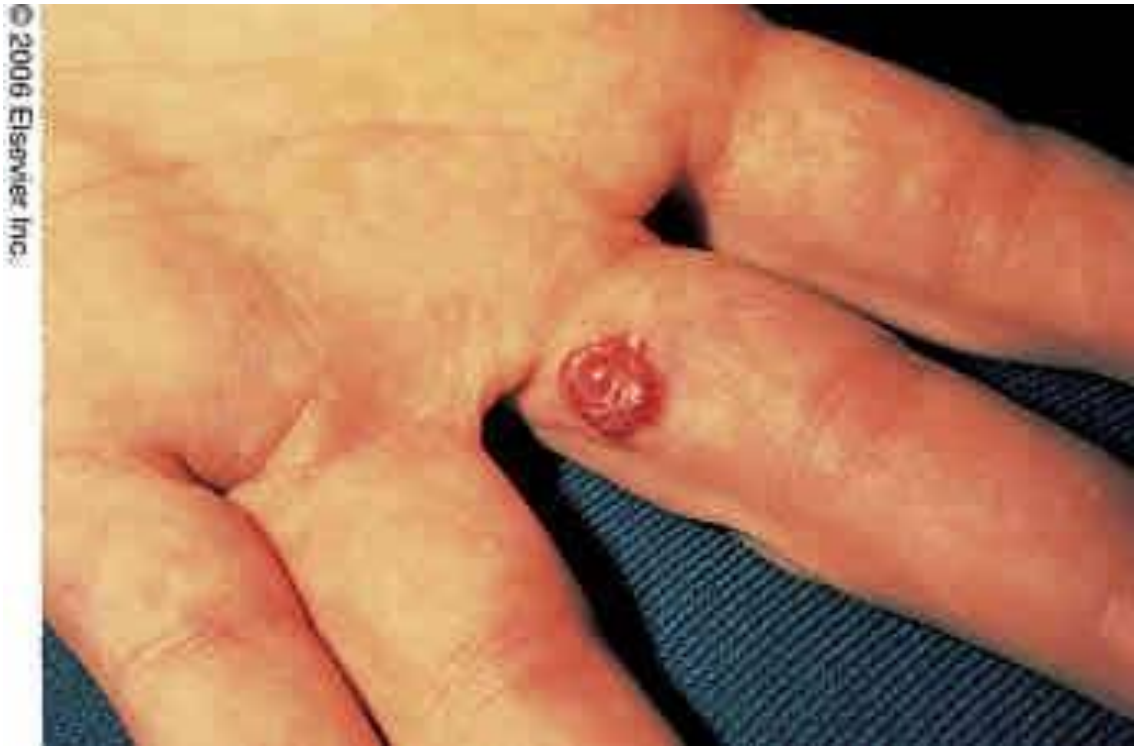


A small, firm, circumscribed, elevated lesion 1 to 2 cm in diameter with possible skin discoloration

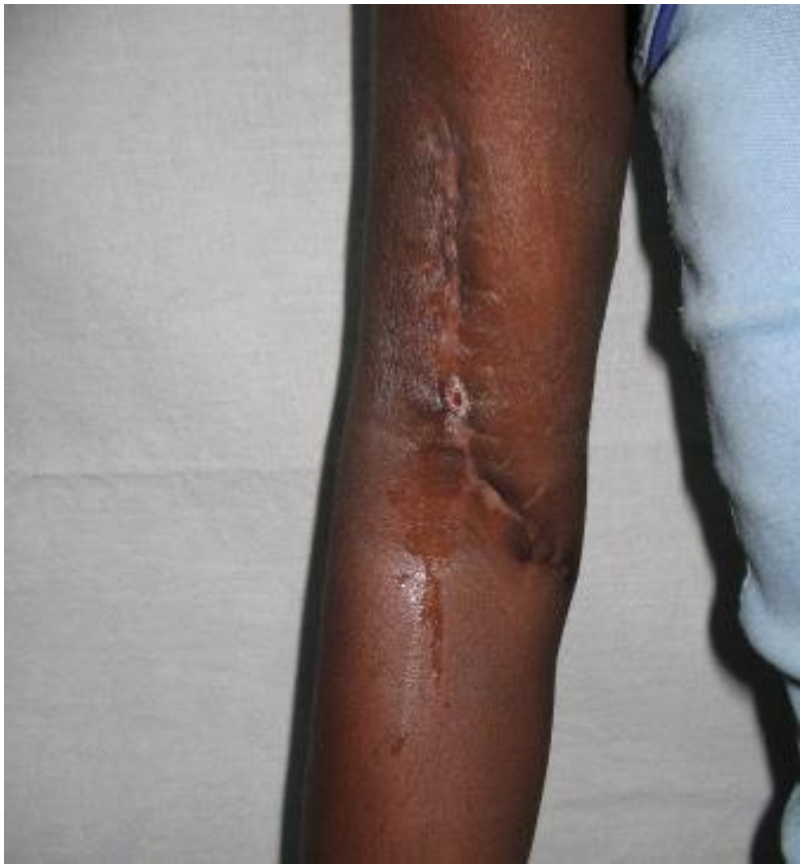
2. Secondary gross lesions

- epidermal collarette
- scar
- erosion or ulcer
- excoriation
- fissure
- lichenification
- callus

epidermal collarette



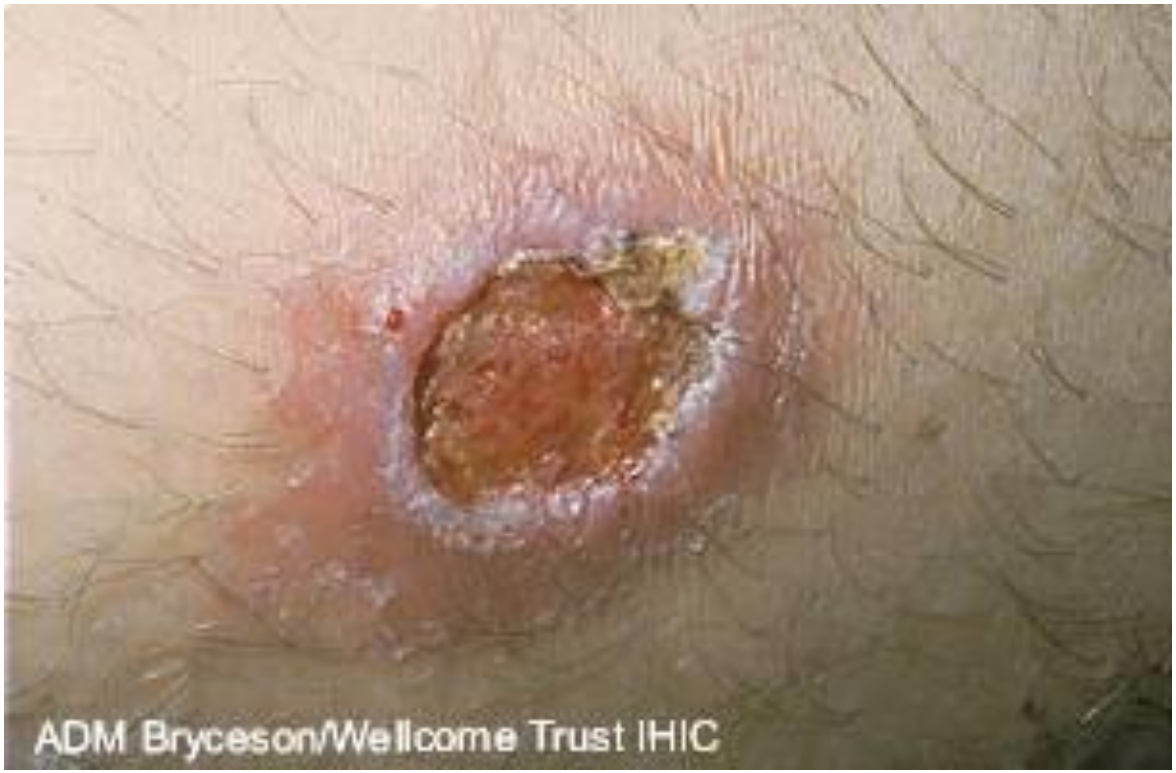
Scar



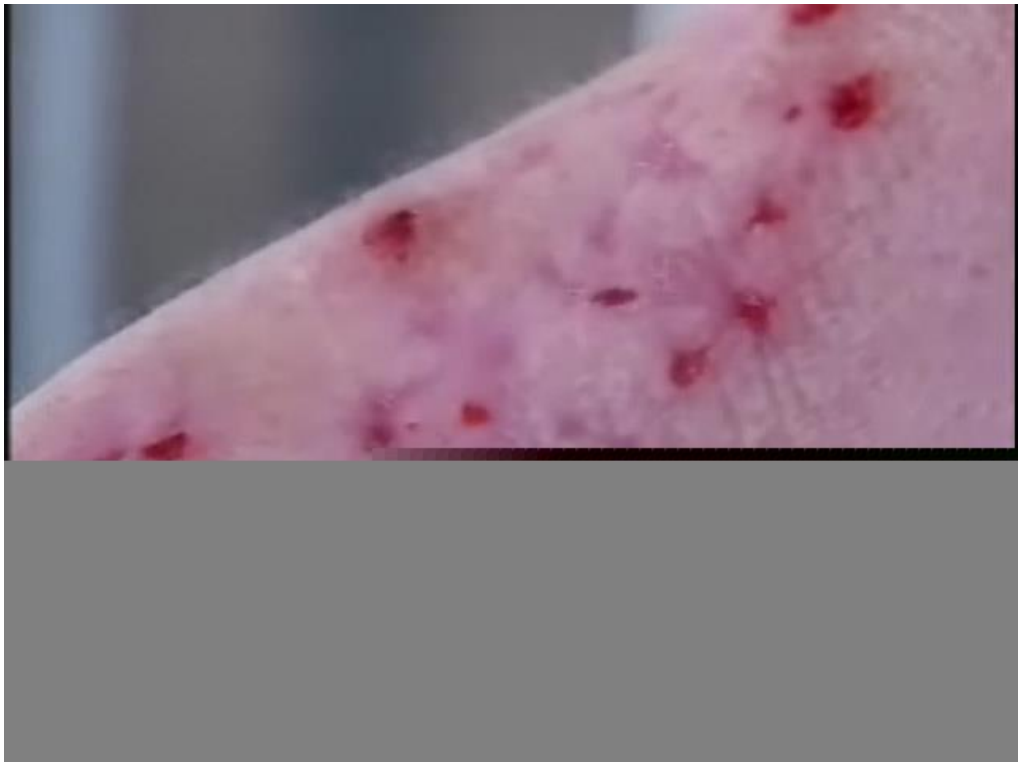
Erosion

- a shallow epidermal defect that does not penetrate the basal laminar zone and consequently heals without scarring;
- it generally results from epidermal disease and self-inflicted trauma.

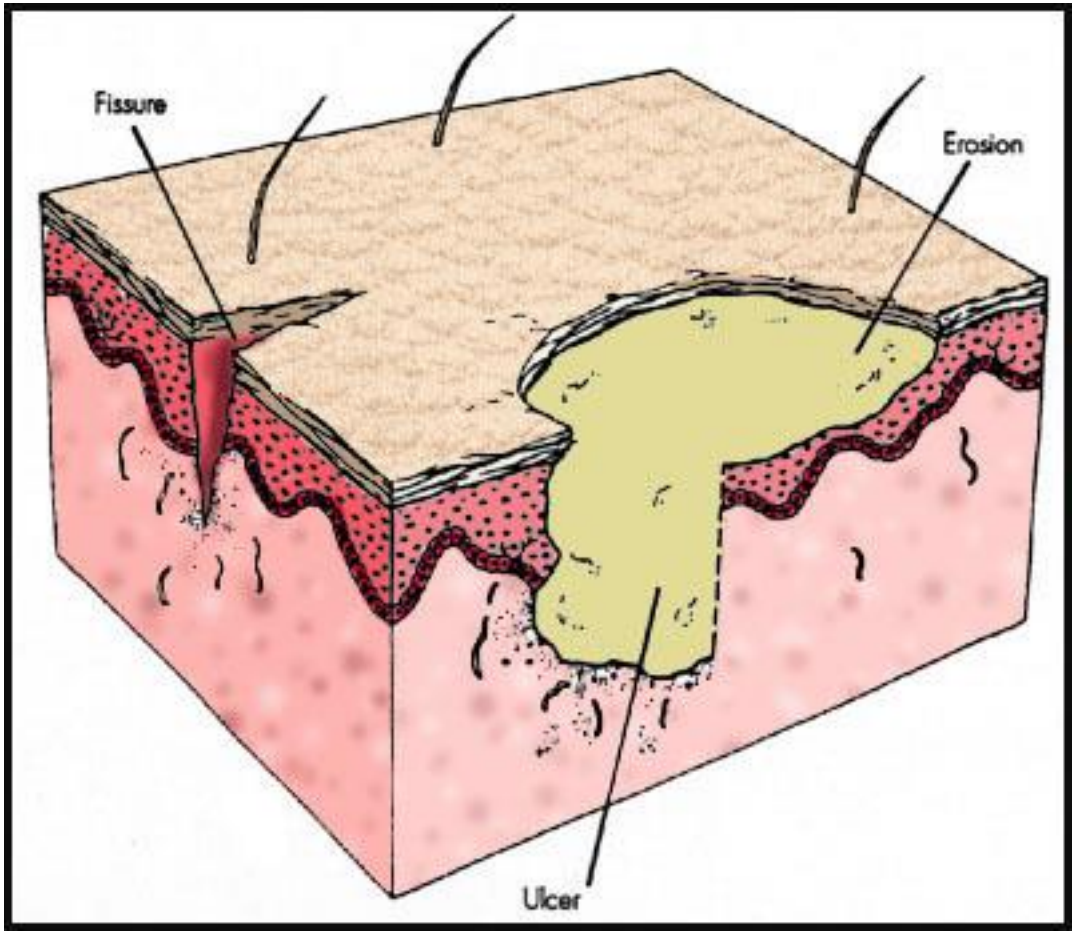
Ulcer



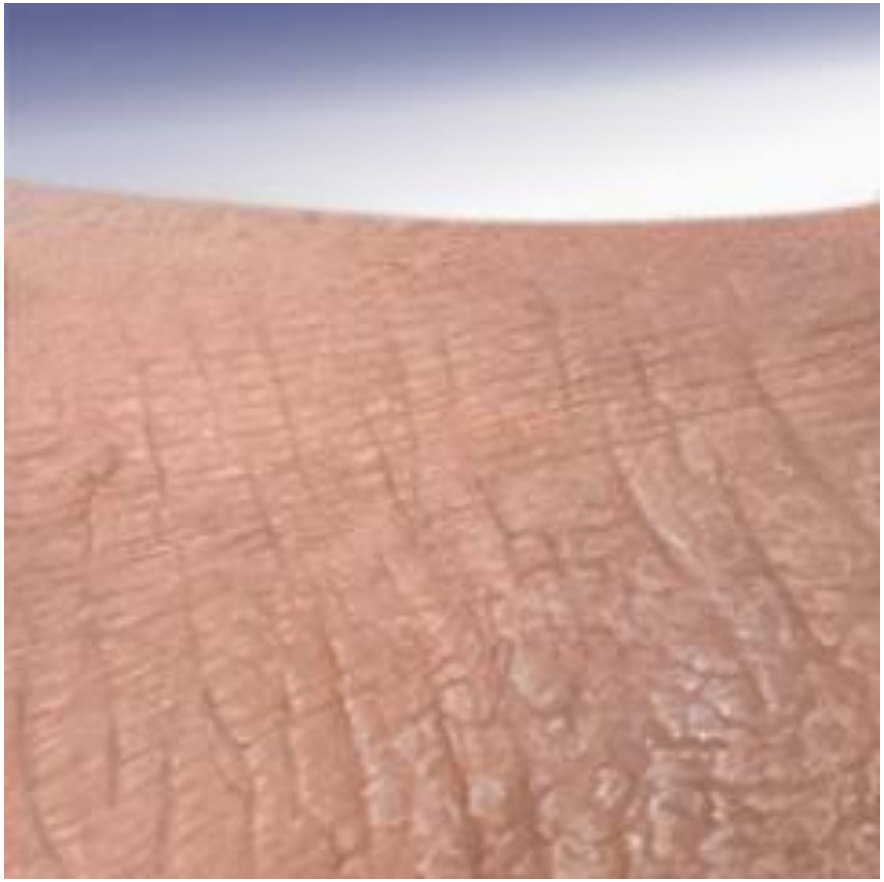
Excoriation



Fissure



Lichenification



Callus

- well-circumscribed, raised, alopecic, grey, keratinous plaque, often over bony prominences

3. Gross lesions that may be primary or secondary

- Alopecia
- Scale
- Crust
- Comedo
- Pigmentary abnormalities

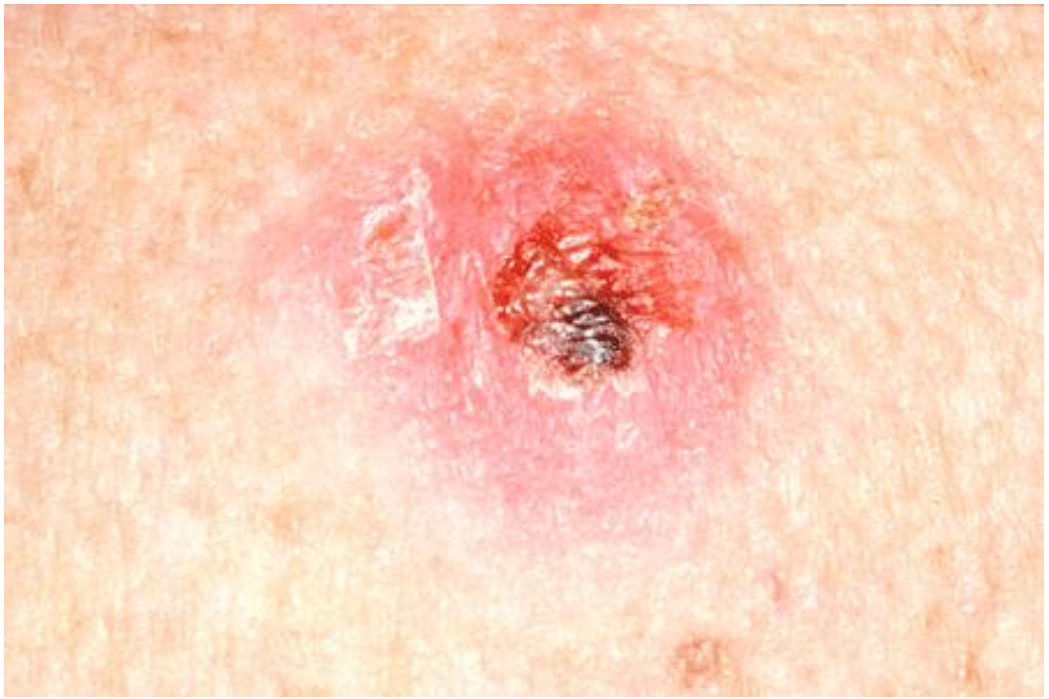
Alopecia

- Loss of hair

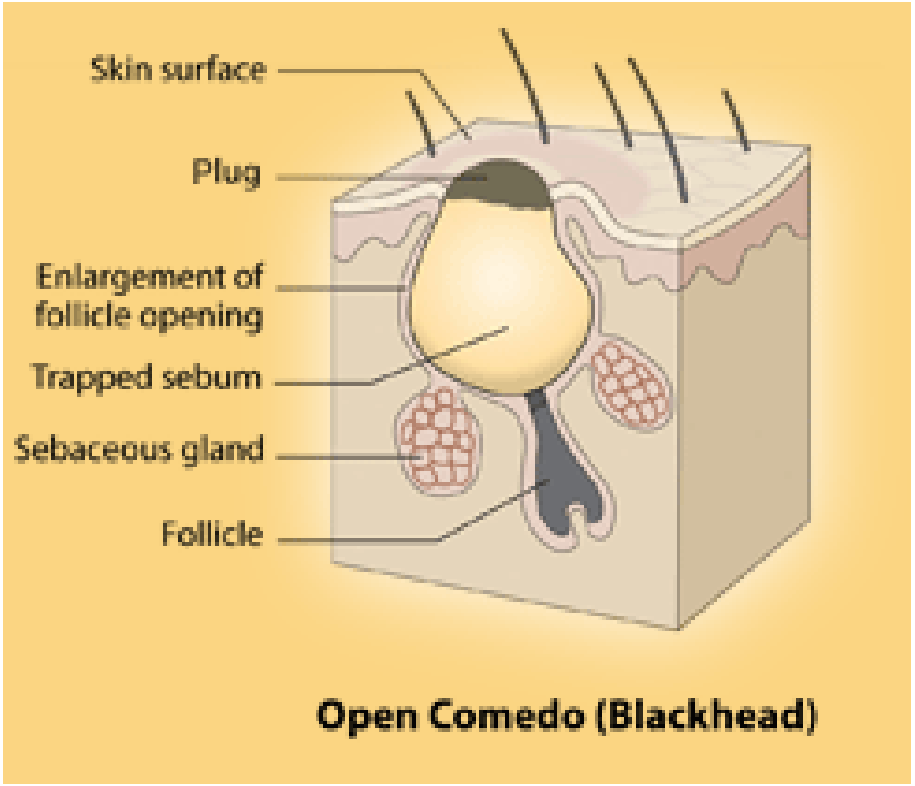
Scale

- accumulation of loose fragments of the horny layer of the skin.
- Loss of cornified cells in epidermal keratinization occurs as individual cells or small clusters not visible to the naked eye.
- Abnormal scaling is the loss in larger flakes.

Crust



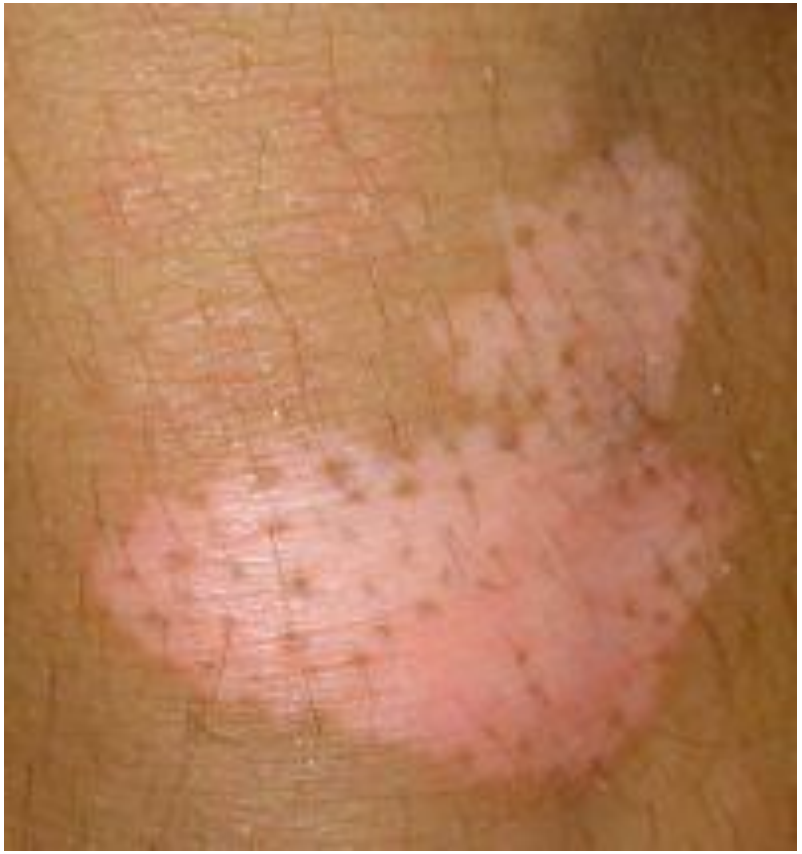
Comedo


Skin surface
Plug
Enlargement of follicle opening
Trapped sebum
Sebaceous gland
Follicle
Open Comedo (Blackhead)

Pigmentary abnormalities

- Hyperpigmentation = increased epidermal and occasionally, dermal melanin. May be associated with post-inflammatory, chronic, traumatic, and endocrine skin lesions.
- Melanotrichia = excess pigment in hair.
- Leukoderma = a general term for white skin, whereas vitiligo refers to a specific disease.
- Leukotrichia = lack of pigment in hair.

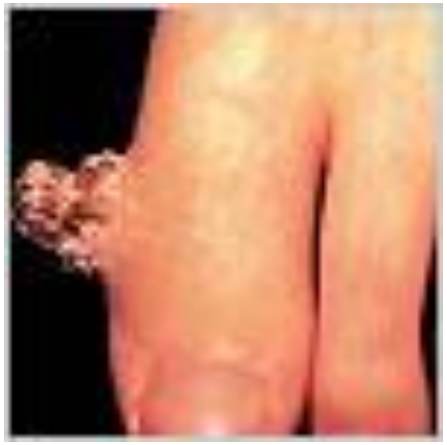
Leukoderma



D. Infections and infestations of the skin

1. Verrucae (warts)

- common lesions of children and adolescents, although they may be encountered at any age.
- caused by human papilloma virus.
- Transmission usually involves direct contact between individuals.
- generally self limited, regressing spontaneously within 6 months to 2 years

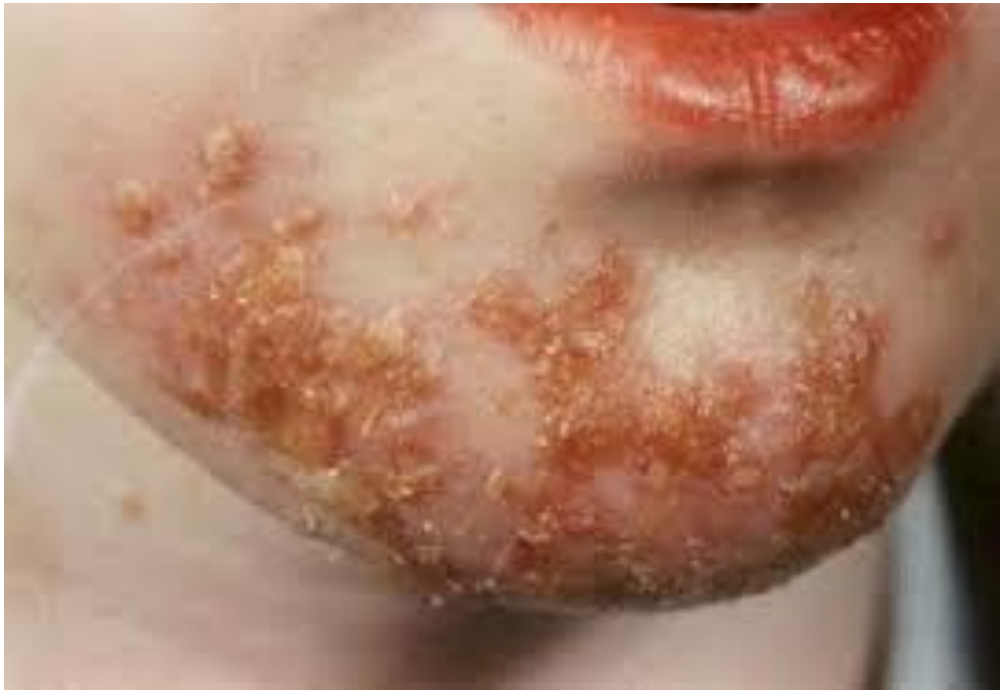


2. Molluscum contagiosum

- A common self limiting viral skin disease caused by pox virus.
- Multiple lesions may occur on the skin and mucous membranes, with predilection for the trunk and anogenital areas.
- Individual lesions are firm and often pruritic

3. Impetigo

- a common superficial infection of the skin caused by staphylococci or streptococci.
- usually involves exposed skin, especially on the hands and face.
- It is initially an erythematosus macule, but multiple small pustules rapidly supervene.
- As pustules break, shallow erosions form, covered with drying serum forming a crust.
- If the crust is not removed, new lesions form about the periphery and extensive epidermal damage may ensue



4. Superficial fungal infections

These are confined to the stratum corneum, where they are caused primarily by dermatophytes.

(i) Tinea capitis

(ii) Tinea barbae

(iii) Tinea corporis

(iv) Tinea cruris

(v) Tinea pedis

5. Arthropod bites, stings and infestations

- Arthropods are ubiquitous. They include:
  - Arachnida - spiders, scorpions, ticks and mites
  - Insecta – lice, bedbugs, bees, wasps, flees, flies and mosquitoes
  - Chilopoda – centipedes
- All these can cause skin lesions, but there is a wide variability in clinical patterns of reaction.

Arthropods can produce lesions in several ways:

(i) Direct irritant effect of insect parts or secretions

(ii) By immediate or delayed hypersensitivity responses (including anaphylactic reaction) to retained or injected body parts or secretions

(iii) By specific effects of venoms

- black widow spider venom → severe cramps and excruciating pain;
- brown recluse spider venom → tissue necrosis

(iv) By serving as vectors for secondary invaders such as bacteria, rickettsia, protozoa and other parasites.

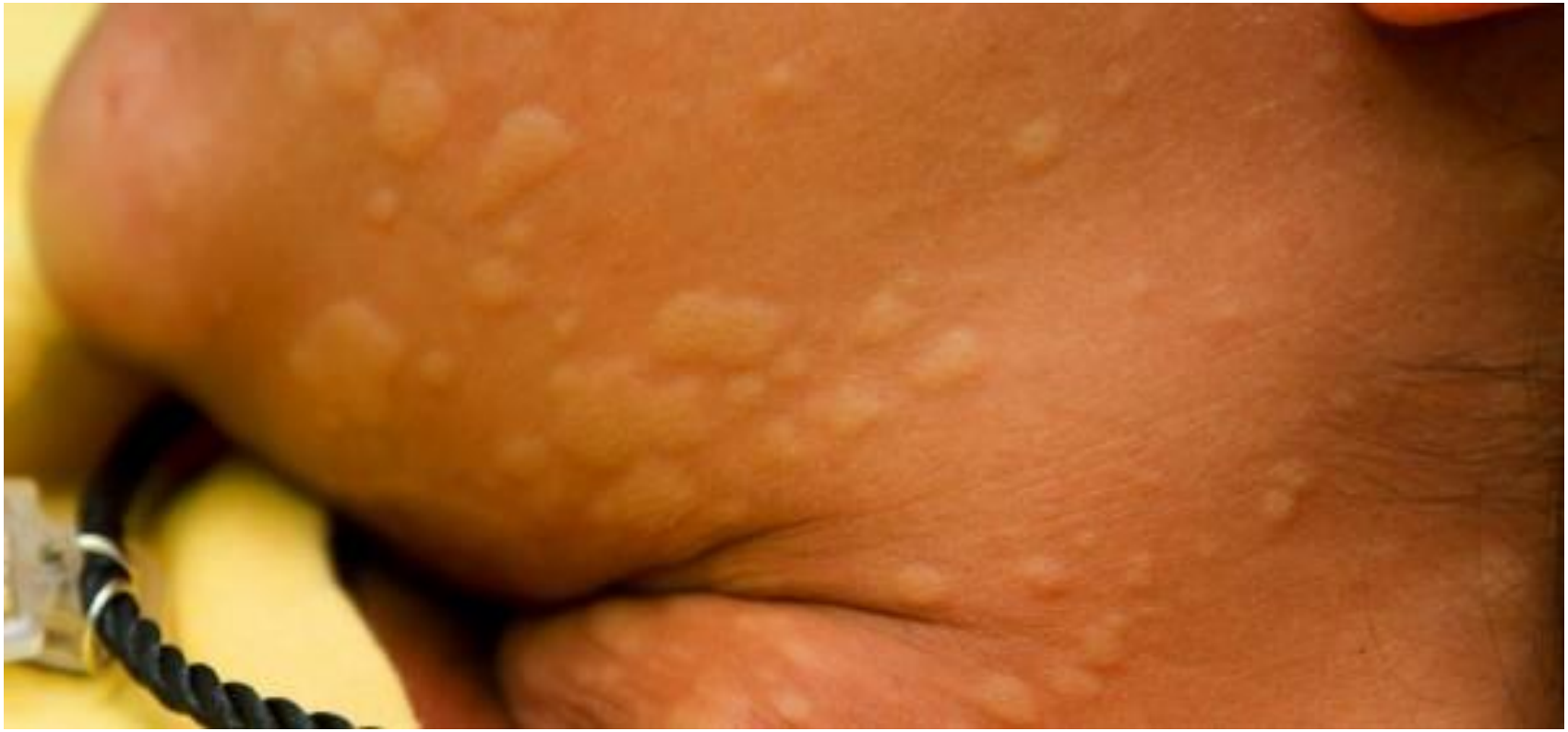
E. Immunological diseases of the skin

1. Acute inflammatory dermatoses

- Inflammatory dermatoses are usually mediated by local or systemic immunologic factors, although causes for many are unknown.

(i) Urticaria (hives)

- characterised by localised mast cell degranulation and resultant dermal microvsacular hyperpermeability, culminating in pruritic oedematous plaques called wheals.
- Individual lesions develop and fade within hours, and episodes may last for days or persist for months.
- Lesions vary from small pruritic papules to large oedematous plaques.
- Persistent urticaria may simply be a result of inability to eliminate the causative antigen or may herald underlying disease e.g. Hodgkin disease.

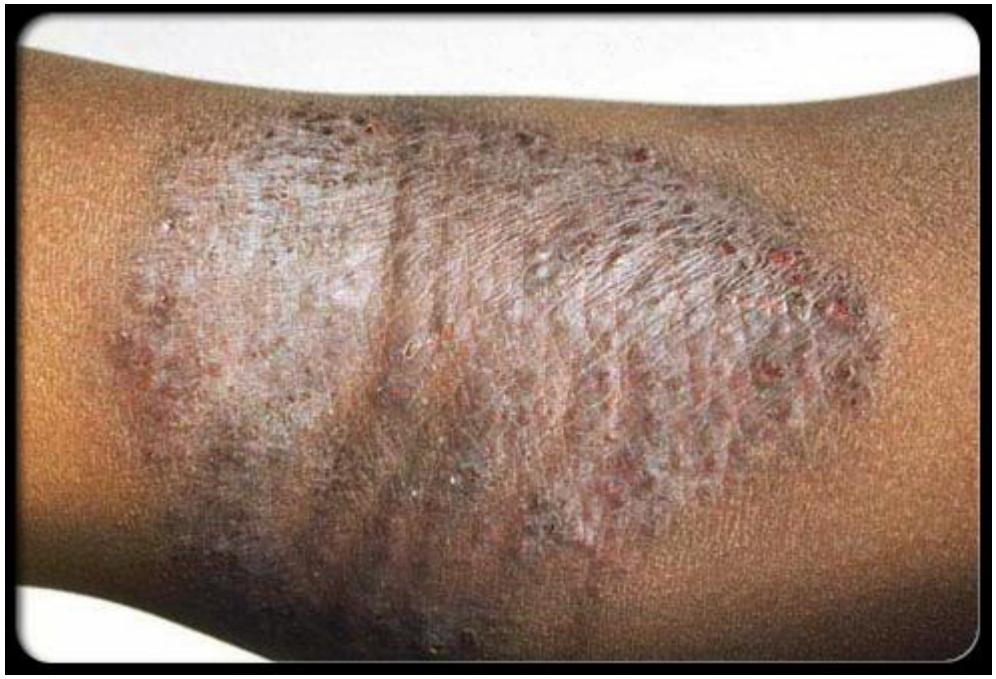


(ii) Acute eczematous dermatitis

- Eczema is a clinical term embracing a number of pathogenetically different conditions all characterised by red, papulo-vesicular, oozing and crusted lesions early on, that with persistence eventually become raised scaling plaques.
- In time it may evolve into a more chronic form with excessive scale, rather than blistering being the dominant clinical feature.

They are classified into the following categories:

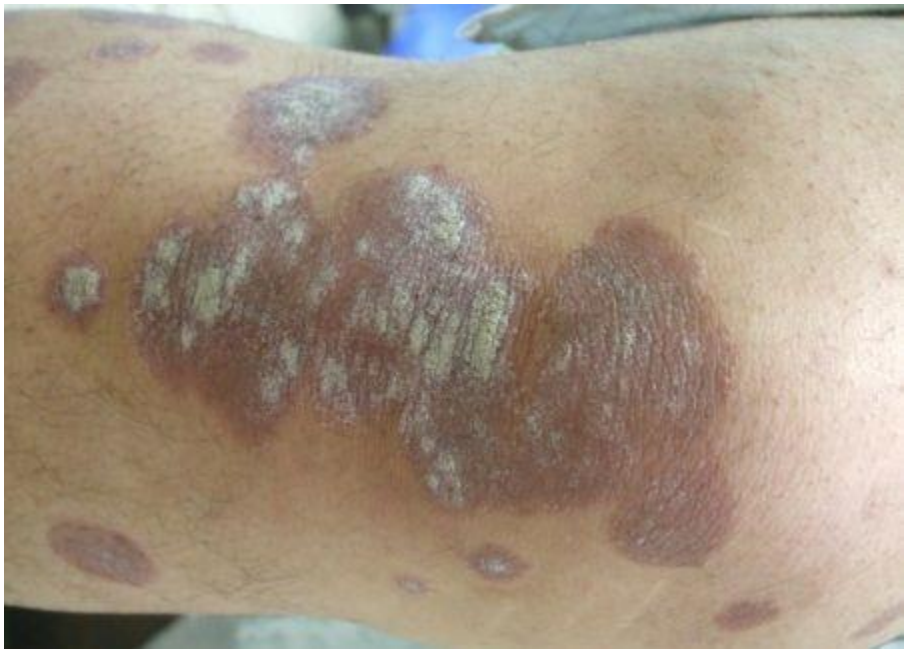
- (a) Allergic contact dermatitis (delayed hypersensisitivity)
- (b) Atopic dermatitis (idiopathic)
- (c) Drug related eczematous dermatitis (penicillin)
- (d) Photoeczematous dermatitis (UV radiation)
- (e) Primary irritant dermatitis (repeated trauma)



2. Chronic inflammatory dermatoses

Psoriasis

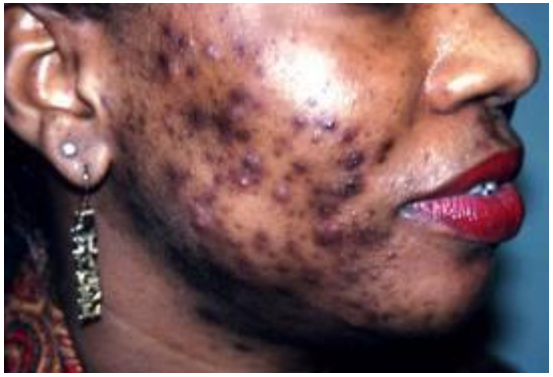
- This is common and can affect persons of all ages.
- It is sometimes associated with arthritis, myopathy, enteropathy, spondylitic heart disease, or AIDS.
- Clinically it most affects the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal cleft and glans penis.
- The most typical lesion is a well demarcated plaque covered by loosely adherent scales.
- The pathogenesis is not yet known



G. Disorders of epidermal appendages

Acne vulgaris

- it affects both males and females in middle to late teenage years
- milder in people of Asian descent.
- Acne vulgaris in adolescents is believed to occur as a result of physiological hormonal variations and alterations in hair follicle maturation.
- Inflammatory acne is characterised by erythematosus papules, nodules and pustules.



H. Disorders of pigmentation and melanocytes

1. Vitiligo

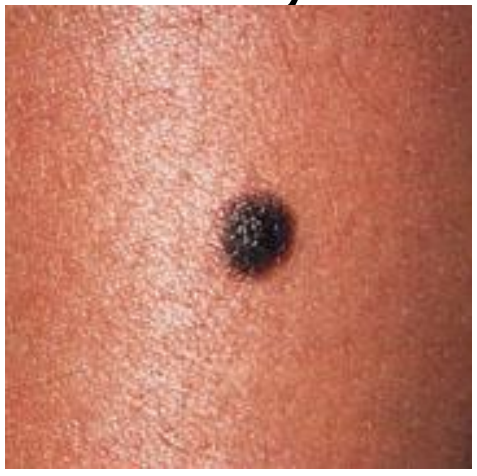
- partial or complete loss of pigment producing melanocytes within the epidermis.
- Clinical lesions are asymptomatic, flat, well demarcated zones (macules) of pigment loss.
- The size varies from few to many centimetres.
- There are several theories of pathogenesis of destruction/loss of melanocytes.
- Most evidence supports autoimmune causation

2. Melasma

- This is a mask like zone of facial hyper pigmentation commonly seen in association with pregnancy.
- It presents as poorly defined, blotchy macules involving the cheeks, temples and forehead bilaterally.
- It often resolves spontaneously after the end of pregnancy.
- It may also occur during administration of oral contraceptives or hydantoins or may be idiopathic.

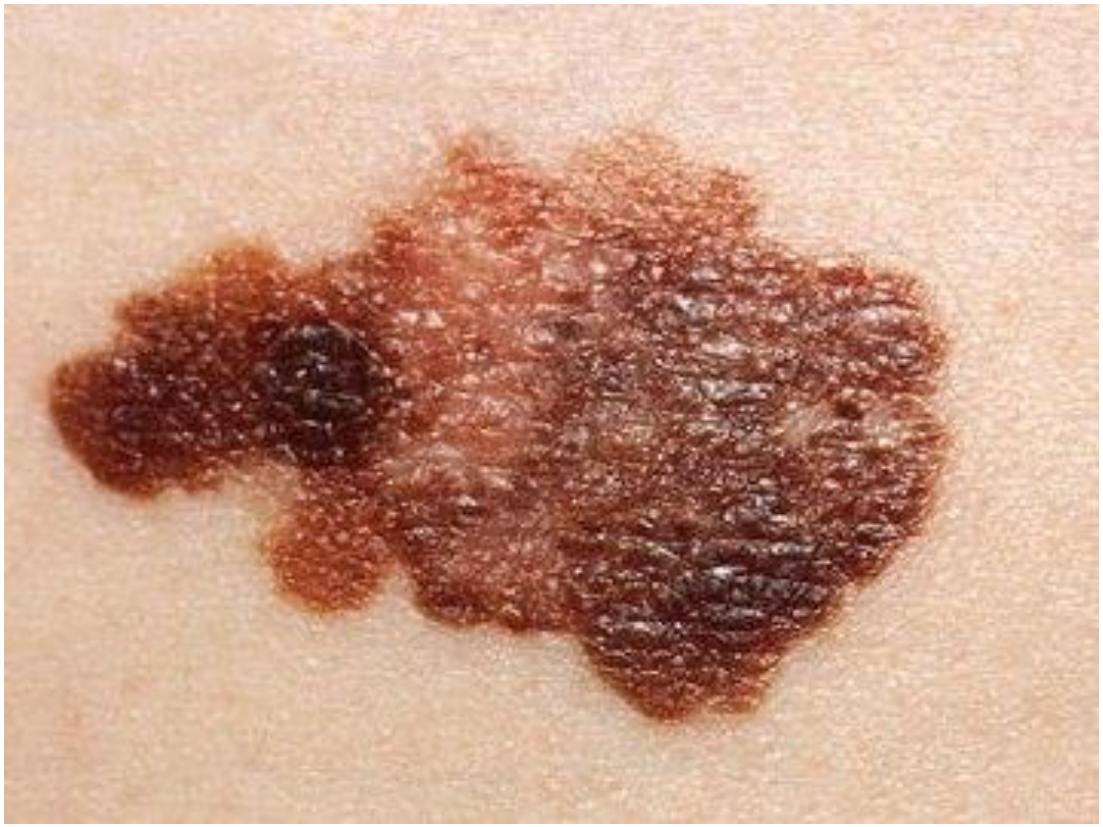
3. Nevocellular nevus (mole)

- This is a congenital or acquired neoplasm of melanocytes.
- Common acquired nevocellular nevi are uniformly pigmented, small (less than 6mm across), solid regions of macules to papules with well defined borders.
- They are biologically important as a model of tumour progression into dysplastic nevi and the heritable melanoma syndrome.



4. Dysplastic nevi

- These are larger than most acquired nevi and may occur as hundreds of lesions o the body surface.
- They are flat macules, slightly raised plaques or target like lesions with a darker raised centre and irregular flat periphery.
- They usually show variability in pigmentation (variegation) and borders that are irregular in contour.
- Unlike ordinary moles, they have a tendency to occur on non-sun exposed as well as sun-exposed body surfaces.
- Transition from these lesions to early melanoma can occur within a period as short as several weeks.

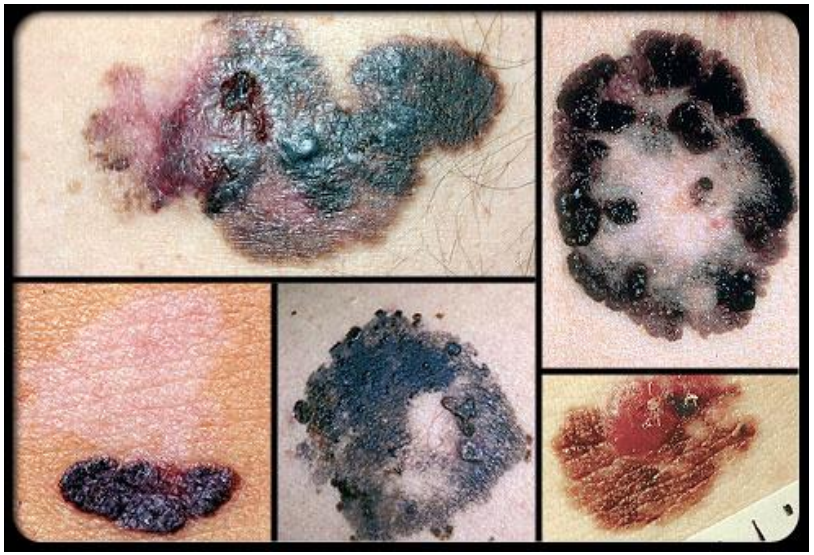


I. Skin neoplasms

1. Malignant melanoma

- The majority arise in the skin
- Sunlight plays an important role in the development of skin malignant melanoma.
- Lightly pigmented individuals are at a higher risk
- Sunlight is not the only predisposing factor.
- The presence of a pre-existing nevus (e.g. dysplastic nevus), hereditary factors and exposure to carcinogens may play a role in development and evolution of the lesion.

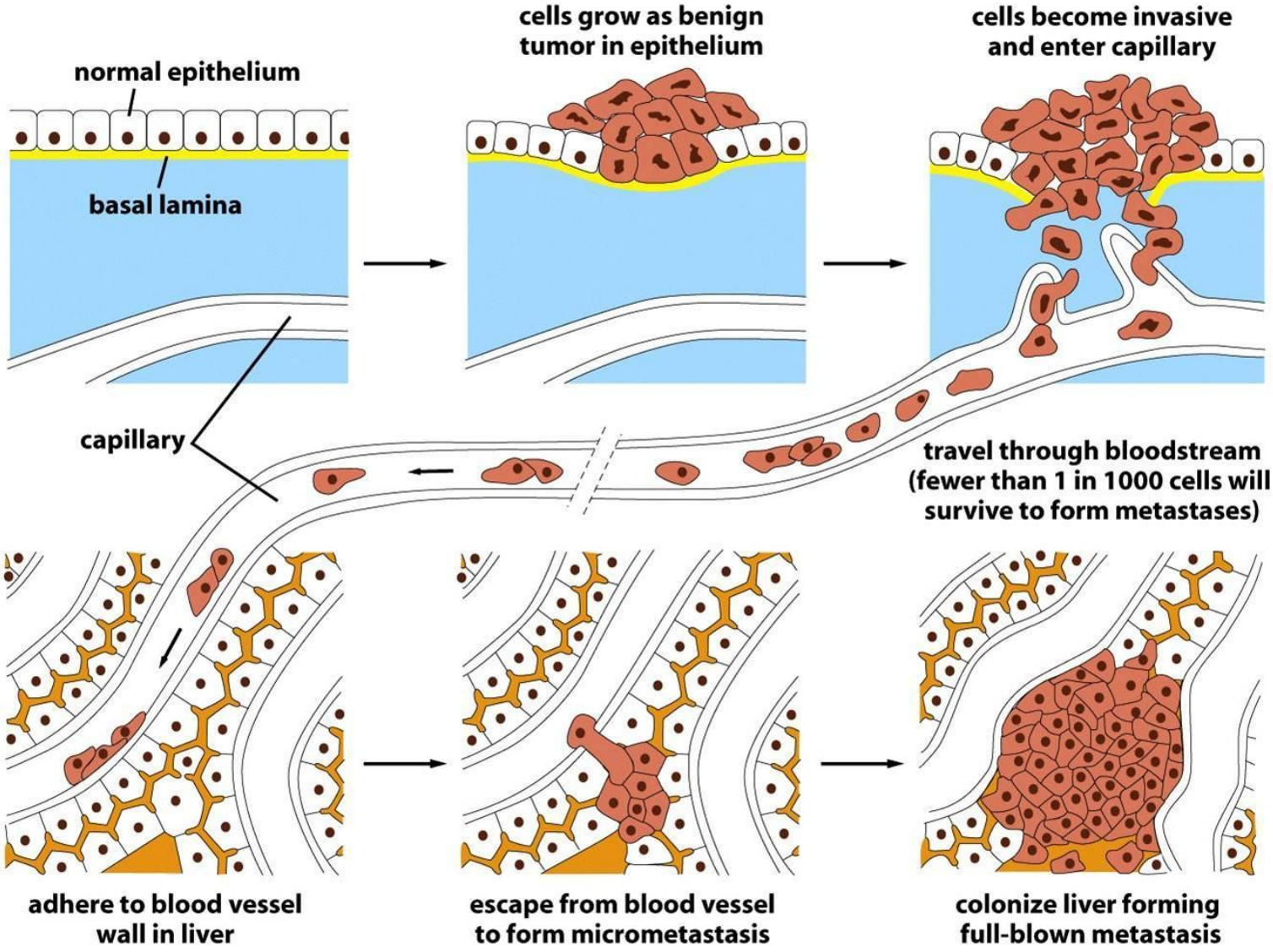
- Malignant melanoma of the skin is usually asymptomatic, although itching may be an early manifestation.
- The most important clinical sign of the disease is change in colour in a pigmented lesion.
- Unlike nevocellular nevi, melanomas exhibit striking variations in pigmentation.
- The borders of melanomas are not smooth round and uniform as in nevocellular nevi but are irregular.



- The clinical warning signs of melanoma are:
  - Enlargement of a pre-existing mole
  - Itching or pain in a pre-existing mole
  - Development of a new pigmented lesion during adult life
  - Irregularity of borders of a pigmented lesion
  - Variegation of colour within a pigmented lesion

2. Benign epithelial tumours

- These are common and are usually biologically inconsequential.
- They are derived from the keratinizing stratified squamous epithelium of the epidermis and hair follicles (keratinocytes) and the ductular epithelium of cutaneous glands.

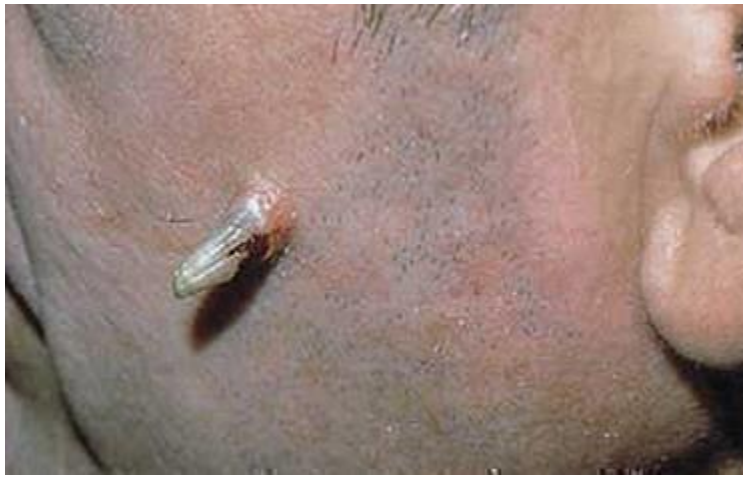

normal epithelium
basal lamina
cells grow as benign tumor in epithelium
cells become invasive and enter capillary
capillary
travel through bloodstream (fewer than 1 in 1000 cells will survive to form metastases)
adhere to blood vessel wall in liver
escape from blood vessel to form micrometastasis
colonize liver forming full-blown metastasis

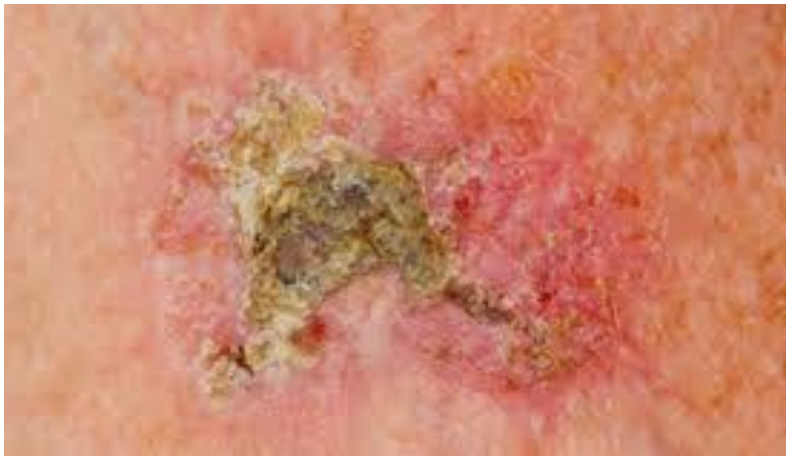
3. Premalignant and malignant dermal tumours

(i) Actinic keratosis

- Before the development of overt malignancy of the epidermis, a series of progressively dysplastic changes occur.
- Because this dysplasia is usually the result of chronic exposure to sunlight and is associated with the build up of excess keratin, these lesions are called actinic keratosis.
- They occur in a particularly high incidence in light skinned individuals.
- Exposure to ionizing radiation, hydrocarbons and arsenicals may induce similar lesions.

- They are usually less than a centimetre in diameter and have a rough sandpaper-like consistency.
- Some lesions may produce so much keratin that a “cutaneous horn” may develop. Such horns may become so prominent that they actually resemble horns of animals.
- Skin sites commonly exposed to the sun are most frequently affected. The lips may also develop similar lesions (actinic cheilitis).
- A large number of actinic keratosis eventuate into skin cancer.

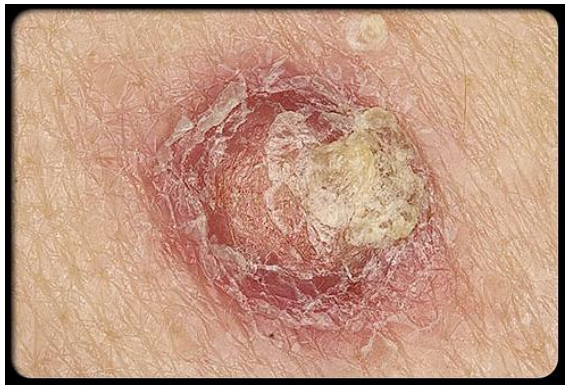


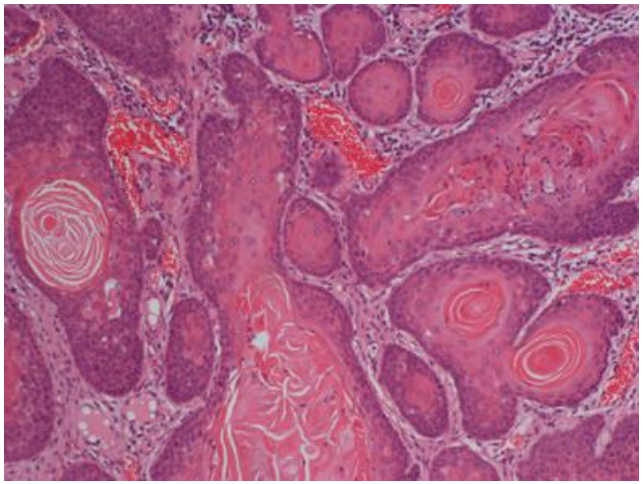


(ii) Squamous cell carcinoma

- This is the most common tumour arising on sun-exposed sites in older people.
- These tumours have a higher incidence in men than women except for lesions on the lower legs.
- Predisposing factors:
  - sunlight,
  - industrial carcinogens (tars and oils),
  - chronic ulcers
  - draining osteomyelitis,
  - old burn scars,
  - ingestion of arsenicals,
  - ionizing radiation

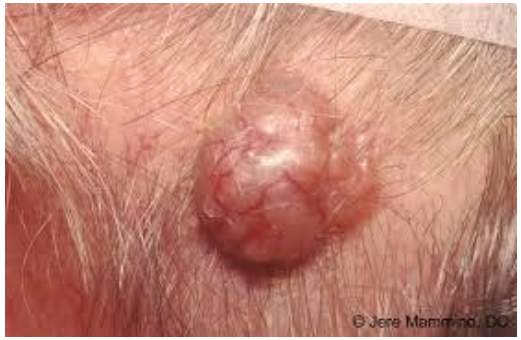
- The most common exogenous cause of squamous cell carcinoma (SCC) is exposure to UV light with subsequent DNA damage and associated mutagenicity.
- Individuals who are immunosuppressed as a result of chemotherapy or organ transplantation, or who have **xeroderma pigmentosum** (inherited defects in DNA replication and repair) are at higher risk of developing neoplasms especially SCC.



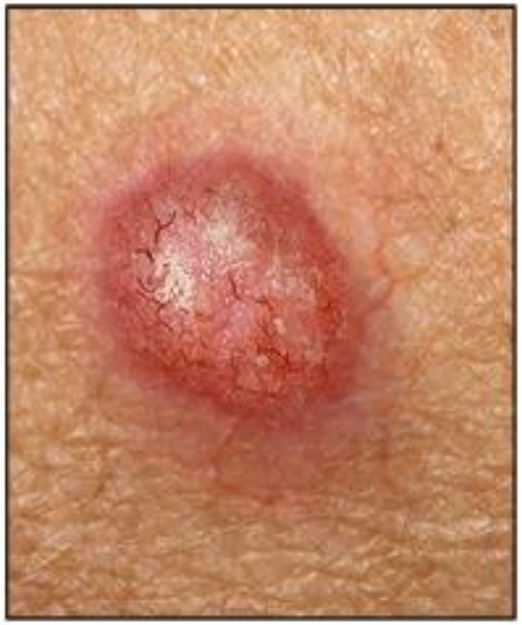


(iii) Basal cell carcinoma

- sites subject to chronic sun exposure and in lightly pigmented people.
- incidence rises sharply with immunosuppression and in patients with xeroderma pigmentosum
- present clinically as pearly papules, often containing prominent, dilated, subdermal blood vessels (telangiectasis).
- Some tumours contain melanin pigment and thus appear similar to nevocellular nevi or melanoms.
- Advanced lesions may ulcerate, and extensive local invasion of bone or facial sinuses may occur after many years of neglect or in unusually aggressive tumours.



Basal cell carcinoma



Squamous cell carcinoma