

### Definitions:

#### DEFINITIONS OF MICROSCOPIC TERMS

<b>Acantholysis</b>	Loss of intercellular cohesion between keratinocytes
<b>Acanthosis</b>	Diffuse epidermal hyperplasia
<b>Dyskeratosis</b>	Abnormal, premature keratinization within cells below the stratum granulosum
<b>Erosion</b>	Discontinuity of the skin showing incomplete loss of the epidermis
<b>Exocytosis</b>	Infiltration of the epidermis by inflammatory cells
<b>Hydroptic swelling (ballooning)</b>	Intracellular edema of keratinocytes, often seen in viral infections
<b>Hypergranulosis</b>	Hyperplasia of the stratum granulosum, often due to intense rubbing
<b>Hyperkeratosis</b>	Thickening of the stratum corneum, often associated with a qualitative abnormality of the keratin
<b>Lentiginous</b>	A linear pattern of melanocyte proliferation within the epidermal basal cell layer
<b>Papillomatosis</b>	Surface elevation caused by hyperplasia and enlargement of contiguous dermal papillae
<b>Parakeratosis</b>	Keratinization with retained nuclei in the stratum corneum. On mucous membranes, parakeratosis is normal.

### Major Skin Cells:

- 1) Keratinocytes
- 2) Melanocytes: anchor to basement membrane and pump out pigment for protection from sunlight damage
- 3) Langerhans' cells: antigen-presenting system

### Normal Skin Structure and Function:

Function: Barrier between the individual and the external environment

### Burn victims:

Loss of barrier leading to loss of fluid and secondary bacterial infections.

### Eczema/Dermatitis:

Damage to the skin resulting in inflammation and spongiosis with edema of the epidermis. Hypersensitive reaction to certain chemicals or drugs. Atopic eczema patients are predisposed to allergic rhinitis and asthma.

### Immersion:

Prolonged immersion in water may overwhelm the barrier (ie. occlusal dressing of burns or under surgical dressings) - can be an advantage in topical therapy.

### Incidences of Skin Diseases:

**Common:** acne, psoriasis, eczema, seborrheic warts and viral warts, actinic raitosis, basal cell carcinoma, squamous cell carcinoma.

**Uncommon:** pemphigoid, pemphigus, melanoma and scabies.

**Rare:** xeroderma pigmentosum, mycosis fungoides.

**Age, Sex, Anatomical Site, Rare, Exposure and Geography.**

### Disorders: Inflammatory&Hematopoietic cells

**Polymorphonuclear leucocytes (polymorphs)** - accumulate in the skin due to response to infections e.g Staphylococcus aureus in impetigo.

**Psoriasis:** neutrophilic infiltrate with intra-epithelial migration forming sterile abscesses. Others are Sweet's disease and pyoderma gangrenosum show a heavy dermal neutrophilic infiltrate - 2nd to chronic inflammatory bowel disease.

**Autoimmune conditions:** e.g dermatitis herpetiformis show neutrophilic infiltrate where as bullous pemphigoid shows an eosinophilic infiltrate.

### Disorders: Inflammatory&Hematopoietic cells (cont)

**Lymphocytic infiltrate:** seen in most chronic inflammatory skin diseases and comprises mostly T-lymphocytes (CD4/Helper T-cells)

**Eczema:** lymphocytic infiltrate and spongiosis

**Lupus erythematosus and lichen planus**

**Cutaneous lymphomas:** primary (mycosis fungoides) or secondary ( peripheral T-cell lymphoma, anaplastic large cell lymphoma etc.)

**Mycosis fungoides:** T-cell lymphoma - Sézary syndrome

**Histiocytic infiltrates:** seen in granulomatous skin diseases e.g. bacterial (mycobacteria), fungal (candidiasis) or protozoal infections.

**Systemic diseases:** e.g. Sarcoidosis.

**Primary granulomatous skin diseases:** granuloma annulare or necrobiosis lipoidica.

### Infections:

Clinical appearance depends on:

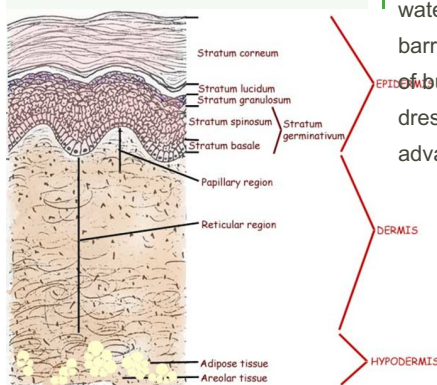
1. Site
2. Nature of organism
3. Nature of the body's response to the infection.

**Routes of transmission:** hematogenous or penetration of the skin barrier

### Definitions (cont.):

<b>Spongiosis</b>	Intercellular edema of the epidermis
<b>Ulceration</b>	Discontinuity of the skin showing complete loss of the epidermis revealing dermis or subcutis
<b>Vacuolization</b>	Formation of vacuoles within or adjacent to cells; often referred to as basal cell-basement membrane zone area

### Skin Diagram:



By AlbertEinstein

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### Viral Infections:

Viruses are obligate intracellular organisms – metabolic basal cells.

#### Human Papilloma Virus (HPV):

DNA virus with numerous subtypes.

Skin and oral mucosa causes squamous papillomas, verrucae vulgaris, verruca plantaris, verruca plana, condyloma acuminatum (genital warts)

**Molluscum contagiosum:** DNA pox virus – umbilicated self-limiting lesion in children.

**Herpes virus:** HVS1 and HPV2 (blistering vesicles), herpes zoster (chickenpox) and shingles.

**Human herpes virus 8 (HHV8):** Kaposi's sarcoma (HIV)

### Bacterial Infections:

**Impetigo:** Staph.aureus in children but Strep. in elderly

**Cellulitis:** Streptococcus pyogenes

**Tuberculosis of the skin (lupus vulgaris):** Mycobacterium tuberculosis or Mycobacterium bovis the cause of scrofuloderma.

### Bacterial Infections: (cont)

#### Leprosy (Hansen's disease):

Mycobacterium leprae (lepromatous and tuberculoid). Lepromatous form fatal while tuberculoid form destroy tissue and nerves resulting in mutilated leonine facies and auto-amputations of digits.

### Fungal and Protozoa Infections:

#### Fungal:

Common ringworm (tinea)  
Tinea pedis (athletes foot)  
Candida, Blastomyces and Nocardia

#### Protozoal:

Leishmaniasis infections transmitted by sandflies, organism infiltrates the macrophages

### Uticaria:

Hives or wheals (reaction pattern), itching and swelling. Sudden marked increase in the permeability of the dermal blood vessels resulting in edema of the dermis – erythematous or edematous lesions.

**Histology:** shows marked infiltrate of eosinophils and mast cells

### Uticaria: (cont)

**Causes:** Plant and animal toxins, physical stimuli e.g. heat, cold or stress, various drugs (aspirin and antibiotics)

Histamine is the mediator and increase in IgE.

### Lupus erythematosus (SLE or LE)

-Autoimmune disease affecting connective tissue with antibodies directed against DNA.  
-Multisystem disease involving almost any organ, most common is skin and kidneys.

-Epidermis and adnexa involved.  
-Skin only: Discoid lupus – erythematous, scaly and older lesions show hyperpigmentation.

-Often symmetrical on the face with a butterfly rash over nose and cheeks, and on scalp it may cause scarring alopecia.

-Immunofluorescence show IgG and IgM at the epidermal basement membrane – “lupus band test”

### Psoriasis:

Genetically determined – HLA haplotypes (HLA Cw6, B13 and B17).

Disease of epidermal proliferation and excess keratin production, driven by cytokines released from activated T-cells in the dermis

Silver-grey scales of parakeratosis on extensor surfaces such as knees and elbows.

First appearance may be at site of trauma e.g. surgical wound – “Koebner effect”.

Result in destructive arthropathy (psoriatic arthritis)

Small bleeding points – Auspitz's sign.

**Histology:** rete ridges becomes acanthotic with the dermal papillae covered by thin epidermis two or three layers thick.

Loss of the granular cell layer.



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### Psoriasis: (cont)

Erythematous lesions - caused by dilated vessels in upper dermis.  
Numerous polymorphs that migrate from the vessels into the epidermis forming pustules (micro-abscesses)- pustular psoriasis.  
May also involves the sole of feet and palms of hands.  
**Treatment:** Coal tar, Methotrexate and arsenic.  
**Current therapy:** Retinoid (Vit A analogues).

### Panniculitis:

Inflammation of the subcutaneous fat.  
Most common type is **Erythema nodosum** which occurs as painful red nodules on the shins.  
Follow a streptococcal infection or in association with inflammatory bowel disease or tuberculosis.

### Lichen Planus:

- Characterized by destruction of keratinocytes, probably mediated by interferon-gamma and tumour necrosis factor from T-cell in the dermis.
- Affects the skin, most commonly the inner surface of the wrist.
- Appears as white lacy lesion – presents as itchy, polygonal, violaceous papules that may form blisters.
- May be caused by certain drugs or medications.
- Mucosal surface white striae – Wickham's striae.
- Histology shows a lymphohistiocytic infiltrate in a band-like fashion at the dermo-epidermal junction- classical lichenoid reaction pattern.
- Basal cell vacuolar degeneration, apoptosis, keratinocyte necrosis.
- In contrast to psoriasis, LP show an increase in the granular cell layer.
- Rete ridges show "sawtooth" morphology.
- Treatment: Steroids

### Benign epidermal neoplasms & tumour-like:

**Skin tags or fibro-epithelial polyps:** seen frequently in the elderly and common in the axilla. Due to friction rather than a true neoplasm.

**Seborrheic keratosis (basal cell papillomas):** common in the elderly, dark greasy looking nodules with an irregular surface. Rarely turn malignant. Stuck-on appearance.

**Histology:** Convoluted surface with keratin tunnels (horn cysts). The may become inflamed. Often remove for cosmetic purposes and to exclude melanoma.

**Squamous papilloma:** Benign neoplasm of squamous epithelium, HPV induced lesion.

**Cyst:** Epidermal (infundibular) cyst and pilar (tricholemmal) cyst are the most common.

### Pre-malignant lesions:

**Actinic keratosis:** In sun-exposed areas , show dermal solar elastosis, need to evaluate for keratinocyte intra-epithelial neoplasia (KIN I-III)

**Bowen's disease:** Squamous cell carcinoma in-situ.

### Basal cell carcinoma (BCC):

Very common skin malignancy, most commonly on the face of elderly people.  
Related to chronic sun exposure.  
Locally very aggressive and destructive, however metastasis are extremely rare.  
Nodular or superficial BCC has a better prognosis while micro-nodular and morpheic are more aggressive and recurrence is high.

Associated with mutations in the Drosophila gene patched-PTCH1 (tumour suppressor gene)which is a member of the sonic hedge-hog pathway.

**Clinically:** ulcerated irregular lesions – rodent ulcers with raised pearly borders and blood vessels visible on the border.

**Histology:**cells look like normal basal epithelial cells, islands of basaloid cells with peripheral palisading.

May develop from the basal cell layer or hair follicles.



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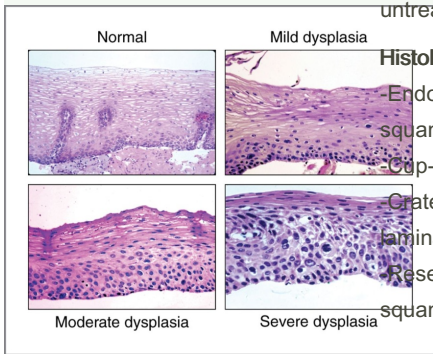
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### Squamous cell carcinoma (SCC):



### Keratoacanthoma: (cont)

Regresses spontaneously if left untreated

#### Histology:

- Endophytic-endophytic squamous proliferation,
- Cup-shaped lesion
- Crater-like center filled with laminated keratotic material
- Resembles a well differentiated squamous cell carcinoma

-Are common and usually caused by chronic UV exposure.

-Other: immunosuppression, irradiation, chemical carcinogens, HPV infections and chronic infections.

-More common in the elderly .

-Rarely SCC arises at the edge of a chronic skin ulcer (Majolin's ulcer).

-Very aggressive and invasive however metastasize late.

-Excision can be curative and SCC are more sensitive to radiation than BCC's.

### Keratoacanthoma:

Rapidly growing, cup-shaped squamous epidermal lesion

Involves sun-exposed skin of elderly - face

### Melanocyte Derived Lesions:

- > Melanocytes are pigmented cells
- > Found in basal layer of epidermis
- > Melanin is synthesized by melanosomes
- > Found on skin and mucosal surfaces – oral cavity, vagina, conjunctiva etc.

### Types of Benign Lesions:

#### Lentigos:

Increase in single melanocytes in basal areas. Small, pigmented macule.

#### Naevi:

Increase in groups of melanocytes. Melanocytes form nests.

### Types of Benign Lesions: (cont)

#### Freckle:

Increase in melanin production by normal melanocytes which are taken up by adjacent keratinocytes. UV stimulation.

#### Naevus:

Common in light-skinned individuals. Absent at birth and appear in early childhood.

Increase in number through early adulthood. Found mainly on sun-exposed areas. Different stages

#### STAGE 1 - JUNCTIONAL:

At dermo-epidermal junction –intraepidermal nests. Tan or brown pin-point macules (1-2mm). Gradually enlarge. Increase in number of individual melanocytes at dermo-epidermal junction.

#### STAGE 2 – COMPOUND:

Nevus is elevated above skin surface. Childhood \ adolescence. Slightly raised due to nests of melanocytes

### Naevus: (cont)

#### STAGE 3- INTRADERMAL:

Middle to old age. Nevus cells detach from dermo-epidermal junction. Smaller, more mature and less metabolically active. Cannot divide. Two components Junctional and intradermal. Pink due to lack loss of melanin

#### Histology of Stage 2:

- Nests of melanocytes at dermo-epidermal junction and infiltrating dermis
- Pigmented
- Dendrites lost
- Nuclei become round, inconspicuous nucleoli

#### Blue Naevus:

- Occurs in deep dermis
- Bluish tinge
- Any area of skin
- Less than 5mm in diameter
- Solitary
- Malignant transformation is rare

### MALIGNANT LESIONS:

#### Melanoma

- Common skin cancer
- Can arise from any melanocyte, composed of malignant melanocytes.
- Usually pigmented but may be unpigmented.



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### MALIGNANT LESIONS:

#### Melanoma (cont)

- Etiology associated with fair skin and sunburn
- Asymmetrical (ABCDE)
- Irregular borders
- Varying colours: blue, black--brown, ulcerated
- >6mm
- Evolution
- Prognosis depends on thickness of lesion and presence of surface ulceration – Breslow thickness
- > 1 mm depth indicates significant risk for metastasis
- Cure rate for completely excised non-ulcerated melanomas below 1mm is 100%

#### Main Variants:

- 1. Lentigo maligna melanoma:** - sun damaged skin of the elderly, develops from a pre-existing in situ lesion termed a lentigo maligna (Hutchinson's melanotic freckle).
- 2. Acral lentiginous melanoma:** - palms and soles, most common type in Non-Caucasians.
- 3. Superficial spreading melanoma:** - most common type in people from European descent
- 4. Nodular melanoma:** - retain no features to identify a pre-existing in situ lesion

### Vesiculo-Bullous Conditions:

Fluid –filled cavities

Within the skin

Caused by the separation of two layers of tissue and leakage of plasma into the space

Bullae: > 5mm

Vesicles: < 5mm

### DISTINCT MECHANISMS OF BLISTER FORMATION:

Direct destruction of bonds between epithelium e.g. pemphigus

Cells forced apart by edematous fluid e.g. eczema

Cellular destruction leaving gaps e.g. herpes infection

Basement membrane or its attachments to epidermis or dermis altered e.g. bullous pemphigoid

### Pemphigus:

BONDS BETWEEN EPITHELIUM IS BROKEN

Common in middle-aged to elderly

Mortality rate of approximately 40%

Autoantibodies directed against desmosomes

### Pemphigus: (cont)

Bridges lysed and epidermis falls apart

- Blister formed containing epithelial cells within cavity (acantholysis)

- Various forms:  
Pemphigus vulgaris  
Pemphigus foliaceus  
Pemphigus vegetans

- Skin very fragile  
- Firm pressure on normal-looking skin will cause blister formation (Nikolsky's sign)

### Bullous Pemphigoid (BP):

More common than pemphigus

Usually over 60 years of age

Self-limiting

Associated with periods of pruritis

Blister forms at dermo-epidermal junction

### Etiology:

- > Circulating antibodies against lamina lucida of the BM.
- > Linear deposition of antibodies along basement membrane (IgG)
- > Causes antigen-antibody complexes and release of complement factors as well as degranulation of mast cells
- > Blisters are more persistent

### DERMATITIS HERPETIFORME:

- Characterized by small, itchy blisters
- On extensor surfaces of knees and elbows
- Young adults
- May be associated with Coeliac disease
- Pruritic lesions
- Bullous forms at dermo-epidermal junction
- **Immunofluorescence:** Granular deposits of IgA
- Therapy: Response to dapsone

### Bullous and Acantholytic Dermatitis:

#### Intra-epidermal/Suprabasal Cleft:

1. Pemphigus Vulgaris: IgG (intercellular)
2. Pemphigus Foliaceus: IgG (subcorneal)
3. Pemphigus Erythematous: IgG

#### Sub-epidermal Cleft:

1. Bullous Pemphigoid: linear IgG and C3 at basement membrane.
2. Dermatitis Herpetiformis: granular IgA papillary dermis.
3. bullous Systemic Lupus Erythematosus: IgG, IgA and C3.



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