Skin Pathology

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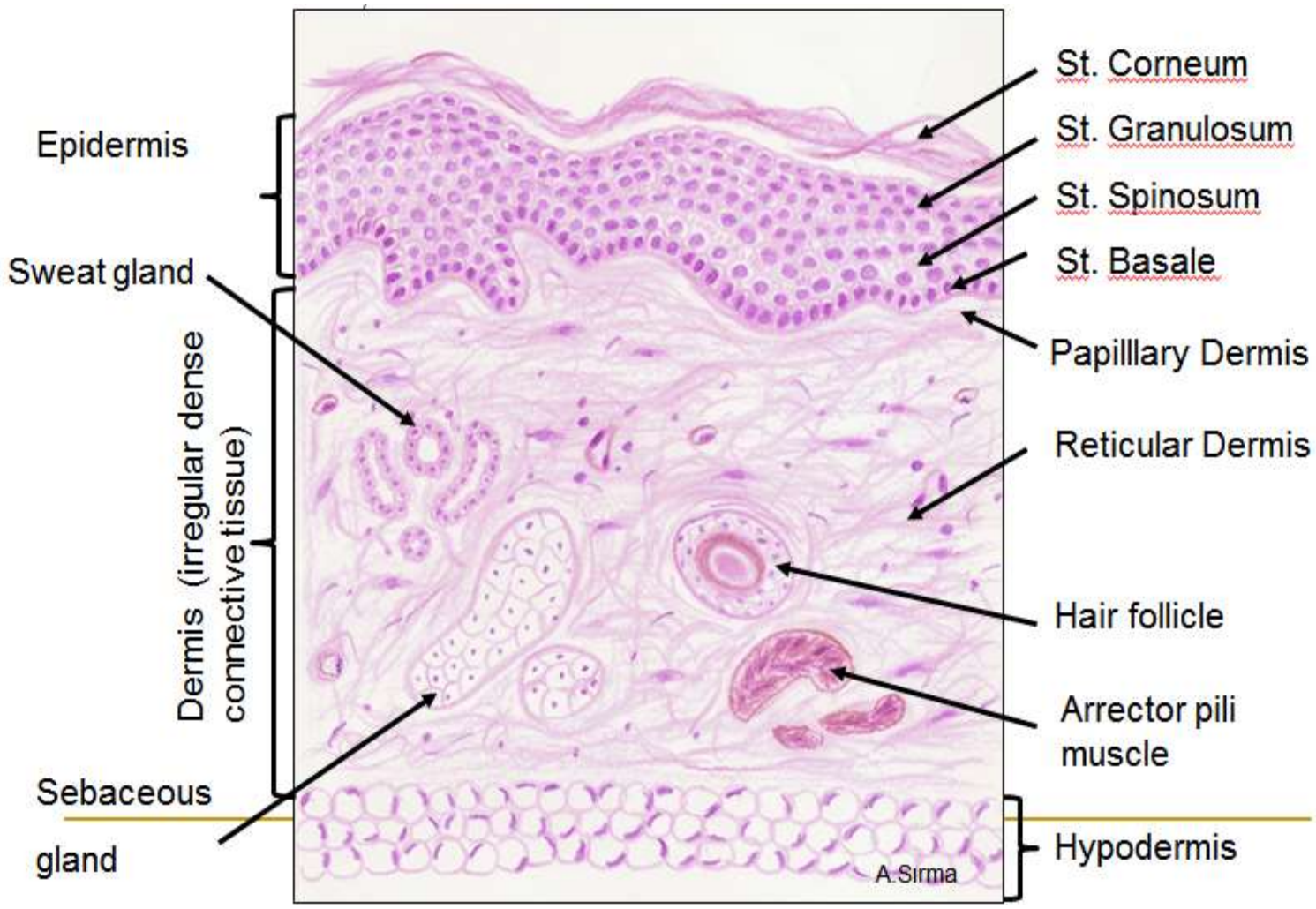
Normal histology

Skin consists of 3 layers:

- Epidermis (keratinized, squamous).
- Dermis (connective tissue, skin adnexae).
- Subcutaneous fatty tissue.



Macroscopical terms in dermatopathology

- ***Macule***: any flat, colored lesion of skin 5 mm in diameter or less
- ***Patch***: any flat colored lesion more than 5 mm
- ***Papule***: elevated, solid lesion, equal or less than 5mm in diameter.
- ***Nodule:*** elevated, solid lesion, more than 5mm in diameter.
- ***Plaque:*** elevated flat-topped area, usually more than 5 mm in diameter
- ***Vesicle***: elevated, fluid filled lesion, equal or less than 5mm in diameter
- ***Bullae***: elevated, fluid filled lesion, more than 5mm in diameter.
- ***Pustule***: pus filled elevated area.
- ***Scale***: dry, horny, plate-like skin area (due to imperfect cornification).
- ***Wheal:*** erythematous, edematous and pruritic plaques

Macroscopical terms in dermatopathology

Microscopical terms in dermatopathology

- ***Hyperkeratosis***: hyperplasia of stratum corneum with abnormal keratin.
- ***Parakeratosis:*** a mode of keratinization characterized by retention of nuclei in the stratum corneum.
- ***Acanthosis***: epidermal hyperplasia.
- ***Dyskeratosis***: abnormal keratinization occurring mainly within individual cells.
- ***Acantholysis***: loss of cohesion between keratinocytes (due to loss intercellular connections).
- ***Papillomatosis***: elongation &/or widening of dermal papillae.
- ***Spongiosis:*** intercellular edema of epidermis.

Inflammatory disorders of skin

1. Acute inflammatory dermatoses: characterized by

- Duration of days to weeks
- Inflammatory cells infiltration mononuclear cells rather than neutrophils.
- Edema, vascular, epidermal & subcutaneous injury.
- Examples: like URTICARIA, & ECZEMA.

❖ Urticaria:

➢Often between 20- 40 yrs.

➢**Characterized by:**

- Localized mast cell degranulation.
- Dermal microvascular hyperpermeability that result in formation of erythematous, edematous and pruritic plaques (Wheals).
- The lesions may develop & fade within hours, & may persist for more than months.
- ***Sites***: any areas exposed to pressure such as the trunk, distal limbs & ears.

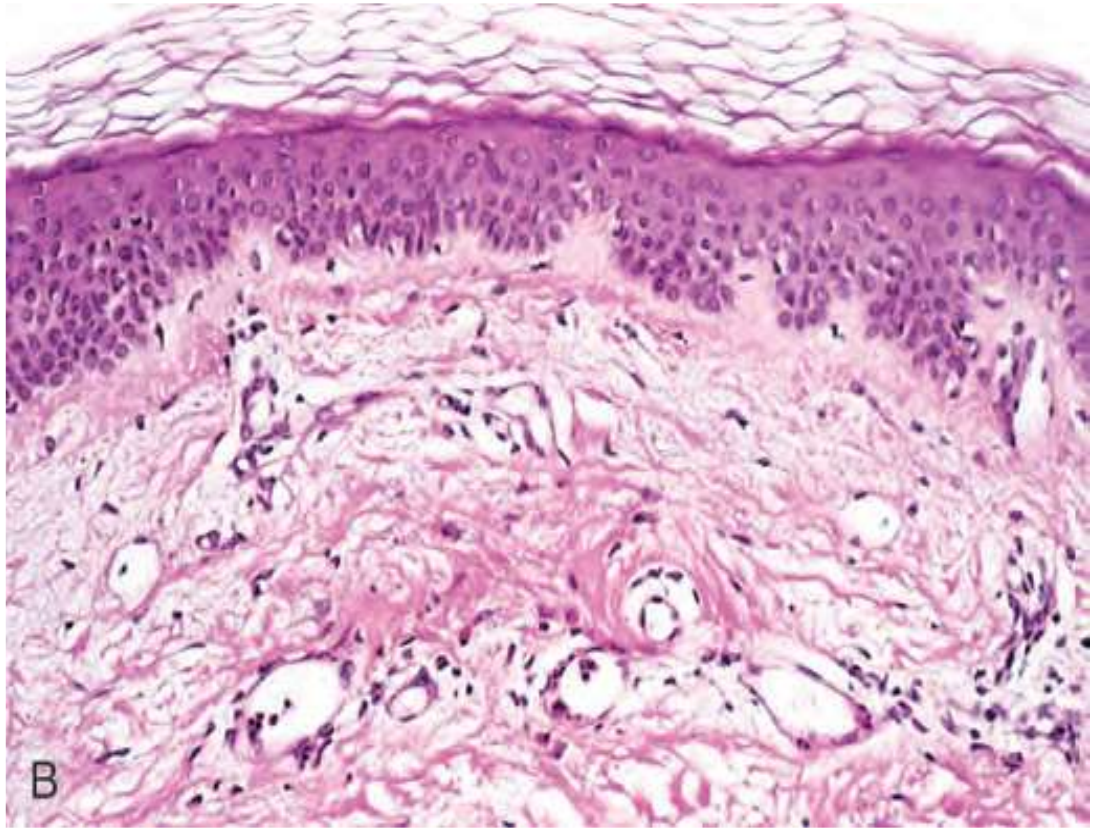
➢***Mic:*** characterized by:

1. Perivenular infiltrate

consisting of mononuclear cells, admixed with neutrophils or eosinophils

2. Superficial dermal edema

result in widely spaced collagen bundles than in normal skin.



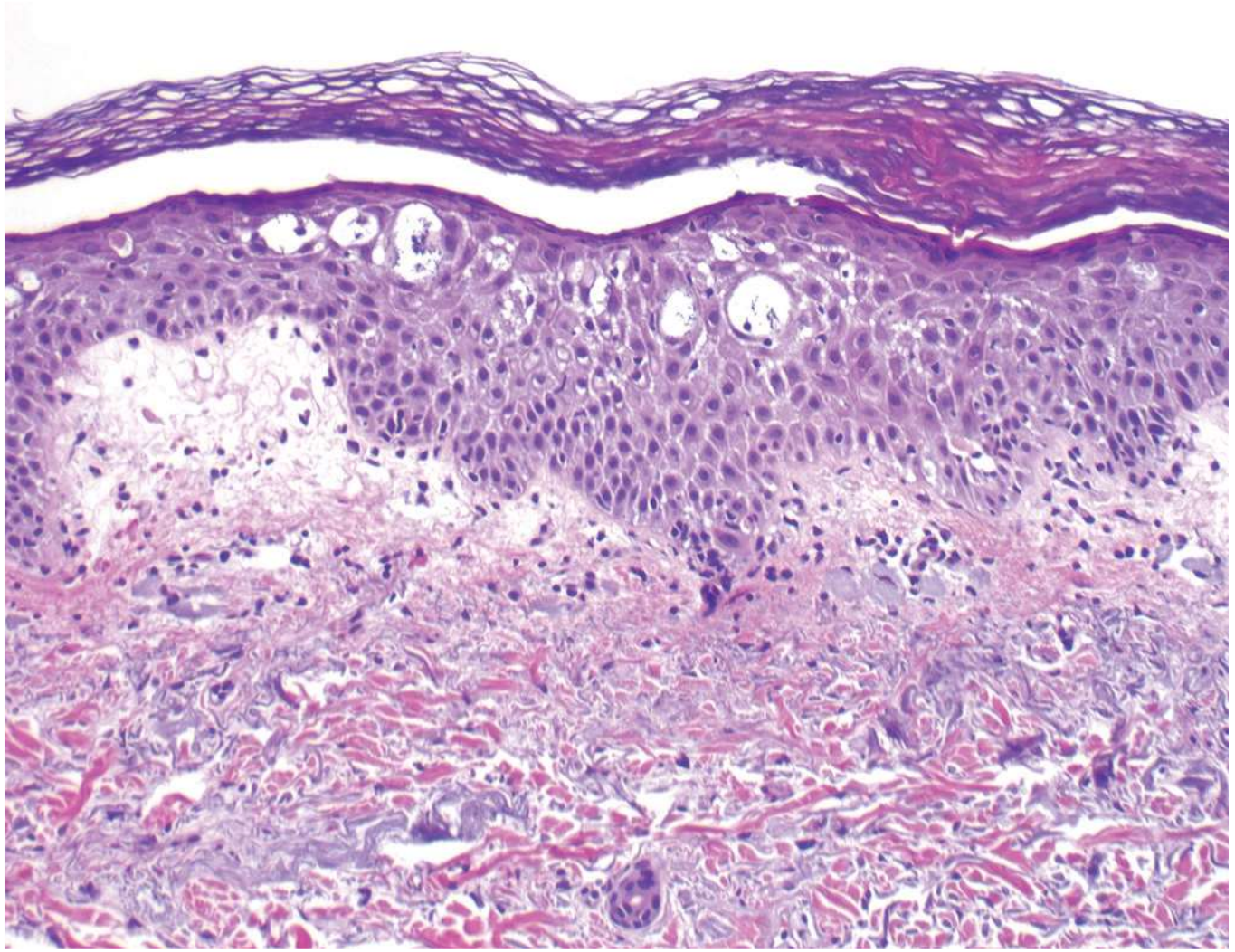
❖ Eczema:

- Is a clinical term for a number of pathogenetically different conditions, all are characterized by itchy, red, papulovesicular oozing & crusted lesions at an early stage, with time these lesions develop into raised, scaling plaques.
- **Examples:**

1. Allergic contact dermatitis (contact poisons)
2. Atopic dermatitis
3. Drug- related eczematous dermatitis

Mic:

1. Spongiosis, which is accumulation of edema fluid within the epidermis.
2. Superficial perivascular, lymphocytic infiltrate associated with papillary dermal edema.
3. Prominent eosinophils infiltrate.



2- Chronic inflammatory dermatoses:

- Have duration last for many months to years.
- Examples (psoriasis, lichen planus).

❖*Psoriasis:*

➢It is a common disorder affecting as many as 1% to 2% of people, that appears to have an autoimmune basis.

➢***Pathogenesis:***

As an immunologic disease, psoriasis is believed to be the product of environmental and genetic factors. that causes sensitized **T cells** enter the skin and accumulate in the epidermis, stimulating the secretion of cytokines and growth factors that induce **keratinocyte proliferation.**

➢***Sites:*** dorsal surfaces of limbs, scalp, lumbosacral areas & glans penis.

➢***Gross:*** Well defined, pink to salmon- colored plaques covered by loosely adherent silver- white scales.

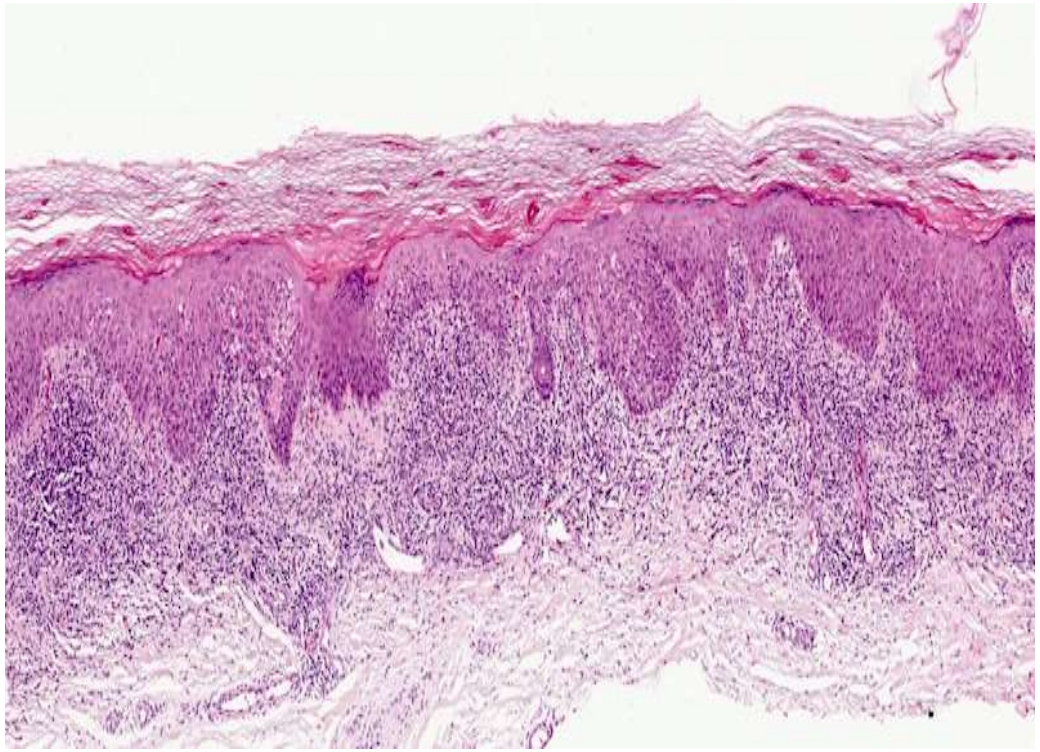
Mic.:

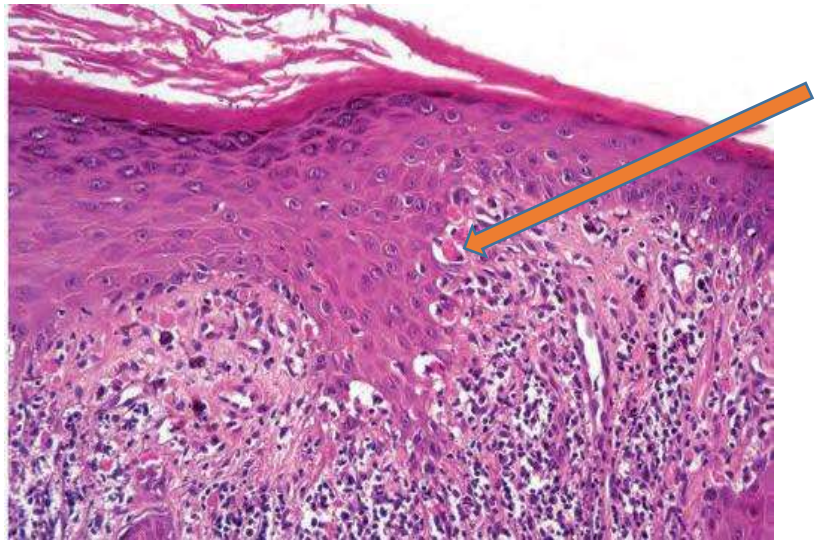
1. Prominent parakeratotic scale is seen.
2. Marked epidermal thickening (acanthosis), with regular downward elongation of the rete ridges.
3. Thinning or absence stratum granulosum
4. Neutrophils form small aggregates within the superficial epidermis.
4. Capillaries within dermal papillae are brought close to the surface, and lifting the scale from a plaque produces pinpoint areas of hemorrhage known as *Auspitz sign.*

❖ Lichen planus:

- Lichen planus is self-limited and usually resolves spontaneously 1 to 2 years after onset.
- ***Pathogenesis:***
- The lesions may result from a CD8+ T cell–mediated cytotoxic response against antigens in the basal cell layer and the dermoepidermal junction that are produced by unknown mechanisms.
- ***Sites:*** characteristically, there are bilateral symmetrical lesions, mainly on the limbs (about the wrists, elbows & glans penis, in 70% of cases associated with oral lesions.
- ***Gross:*** **itchy, violaceous, flat topped papules,** which may coalesce focally to form plaques.

- ***Mic:***
- Continuous infiltrate of lymphocytes along the dermoepidermal junction.
- Dermoepidermal junction shows sawtoothing appearance.
- **Civatte bodies** a nucleated, necrotic basal cells incorporated into the inflamed papillary dermis.





Infectious dermatoses

❖ *Wart (Verrucae):*

- Affects any age, a self limiting, regress spontaneously within 6 months- 2yrs.
- ***Etiological agents are HPV*** (low-risk HPV subtypes that lack transforming potential)

- ***Divide according to sites into:***

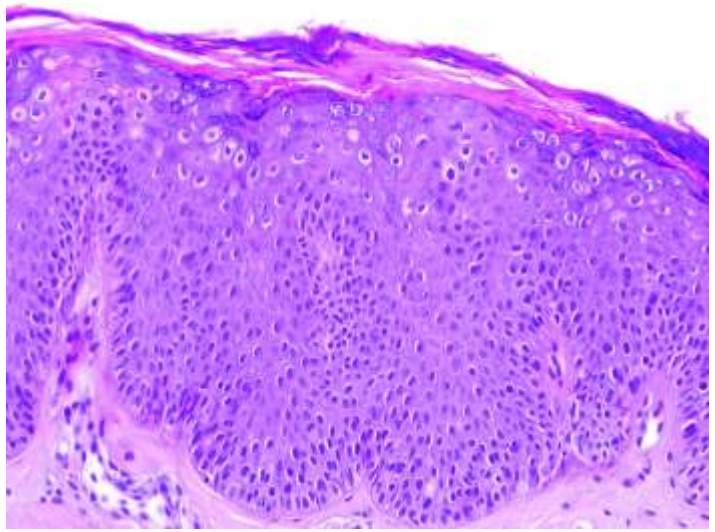
1. Verruca Vulgaris: the commonest one, most frequently on the dorsal surface of the hands
2. Flat warts (verruca plana): common on the face & also dorsal surface of hands
3. Verruca palmaris & plantaris: on the palms & soles
4. Venereal warts (condyloma accuminatum): on the penis , female genitalia , perianal & rectal areas.

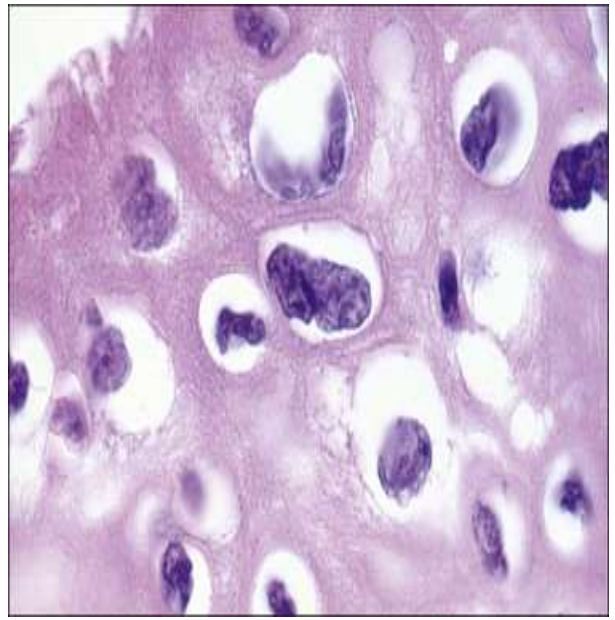
➢Gross:

- Multiple papules with rough surfaces

➢***Mic***:

- Papillomatosis (papillomatous epidermal hyperplasia) and cytopathic alterations including Koilocytosis (nuclear enlargement, hyperchromasia, and a wrinkled nuclear contour and a cytoplasmic perinuclear halo).





Blistering (bullous) diseases:

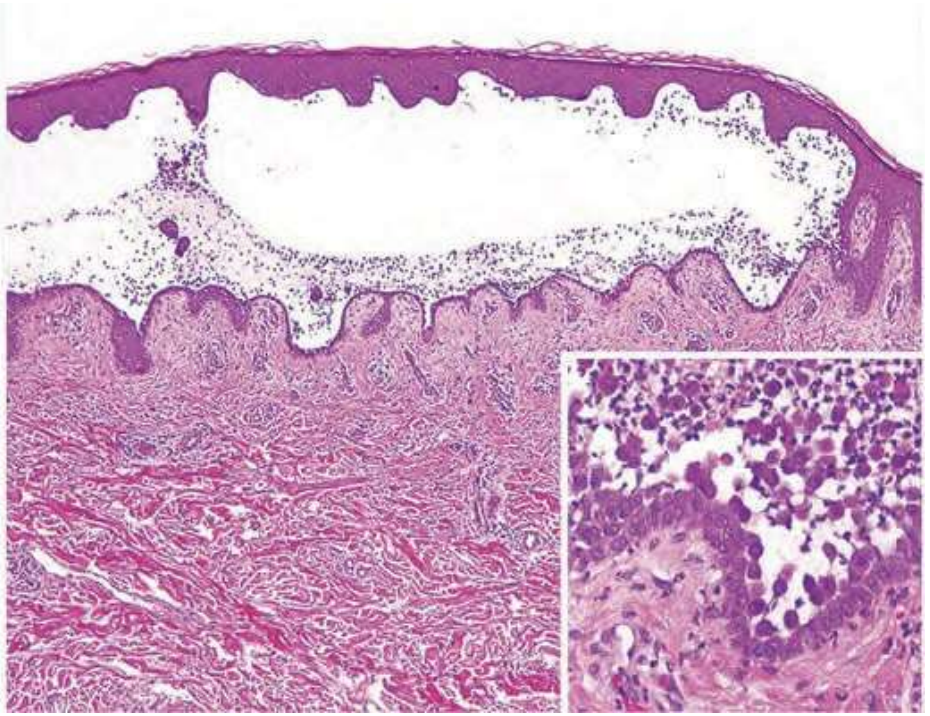
- A group of autoimmune disorders characterized by formation of bullae.
- These bullae are either subepidermal or supraepidermal in their location.
- These bullae are **due to acantholysis** of epidermal cells junctions.
- Examples of bullous diseases are Pemphigus vulgaris, Bullous Pemphigoid, &dermatitis herptiformis.

1. Pemphigus vulgaris:

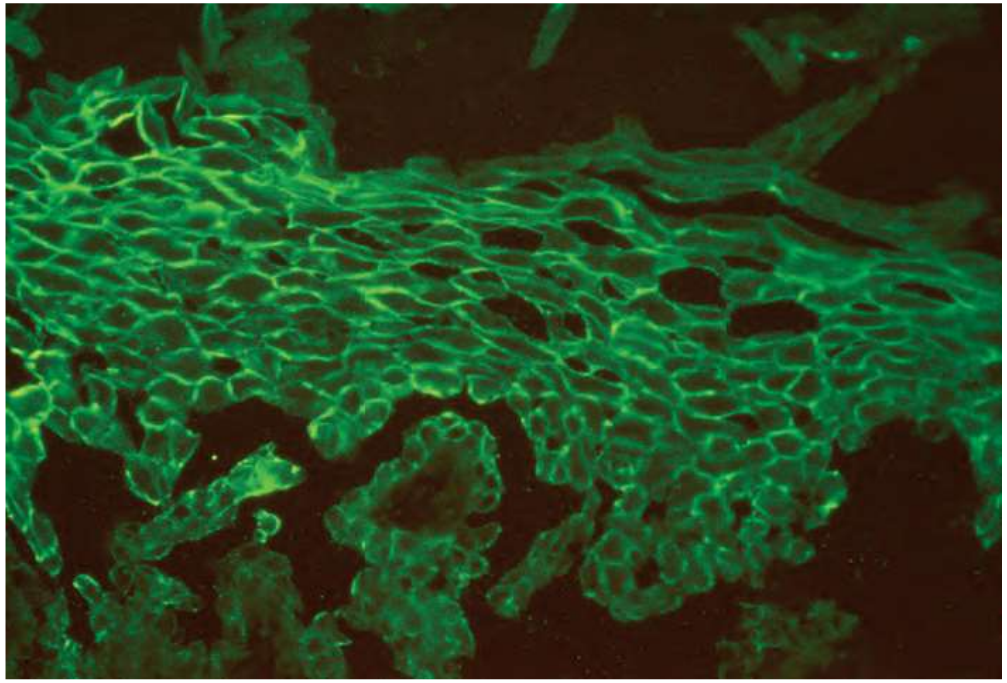
- Characterized by suprabasal acantholytic blisters or bullae.
- Bullae involve skin & rare the mucous membranes.
- The disease is due to type II hypersensitivity reaction.
- By immunoflourscent technique, there is netlike pattern of intercellular IgG deposits at the sites of acantholysis

Pemphigus vulgaris

Eroded plaques are formed following the rupture of confluent, thin-roofed bullae.



Suprabasal acantholysis results in an intraepidermal blister.



Netlike pattern of IgG deposits at the sites of acantholysis.

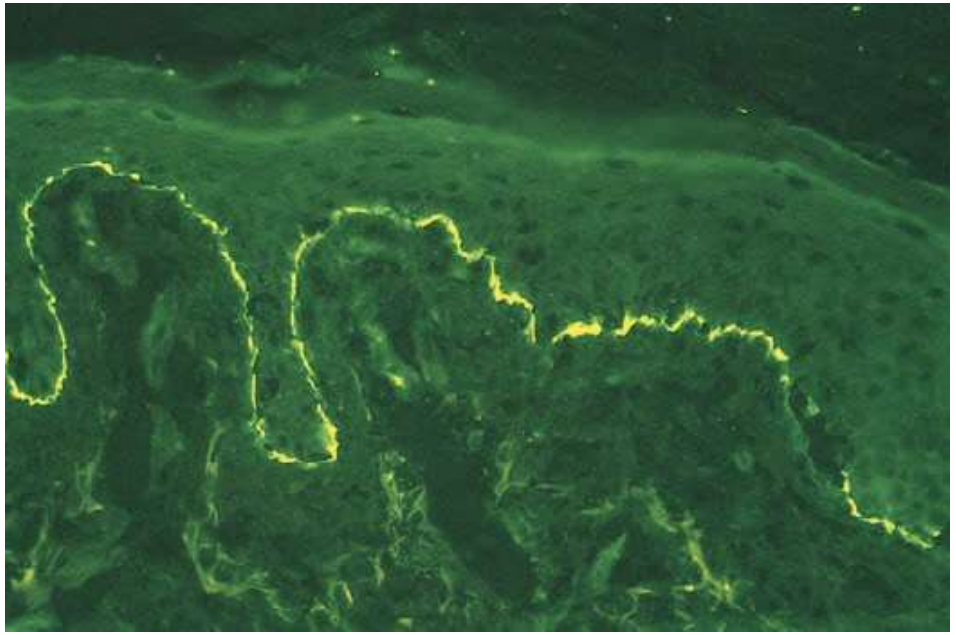
2. Bullous Pemphigoid:

- Affects skin & commonly the mucous membranes (in 30% of cases).
- Characterized by subepidermal, nonacantholytic blisters.
- Also caused by type II hypersensitivity reaction.
- By Immunoflourscent shows linear deposits of Immunoglobulins along the basement membrane zone.

Bullous Pemphigoid

Bullae consist of tense blisters that usually fail to rupture, as their roof consists of intact epidermis.

Intact subepidermal blister associated with eosinophils, lymphocytes, and occasional neutrophils.



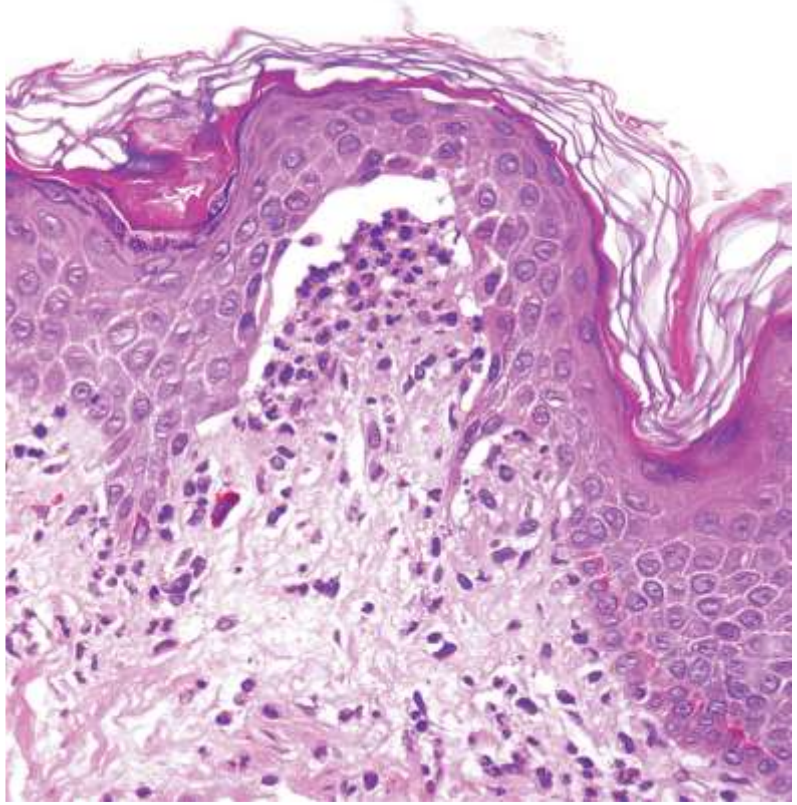
Linear deposition of Immunoglobulins along the basement membrane.

3. Dermatitis heptiformis:

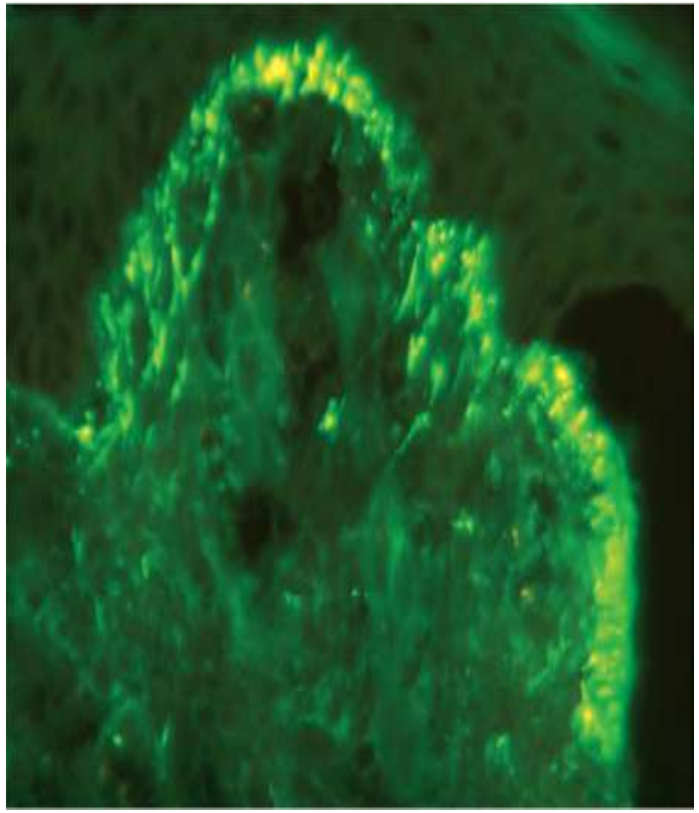
- Affects male > female, at 3rd- 4th decades of life.
- In 10%- 20% of cases associated with celiac disease.
- The lesions of dermatitis herpetiformis are **bilateral, symmetrical,** involve the extensor surfaces elbows, knees, upper back, and buttocks.
- Characterized by **subepidermal bullae and** neutrophils accumulate selectively at the **tips of dermal papillae** forming small microabscesses
- By immunoflourscent, there are granular deposits of IgA along the tips of dermal papillae.

3. Dermatitis heptiformis:

Intact and eroded erythematous blisters, often grouped (seen here on elbows and arms).



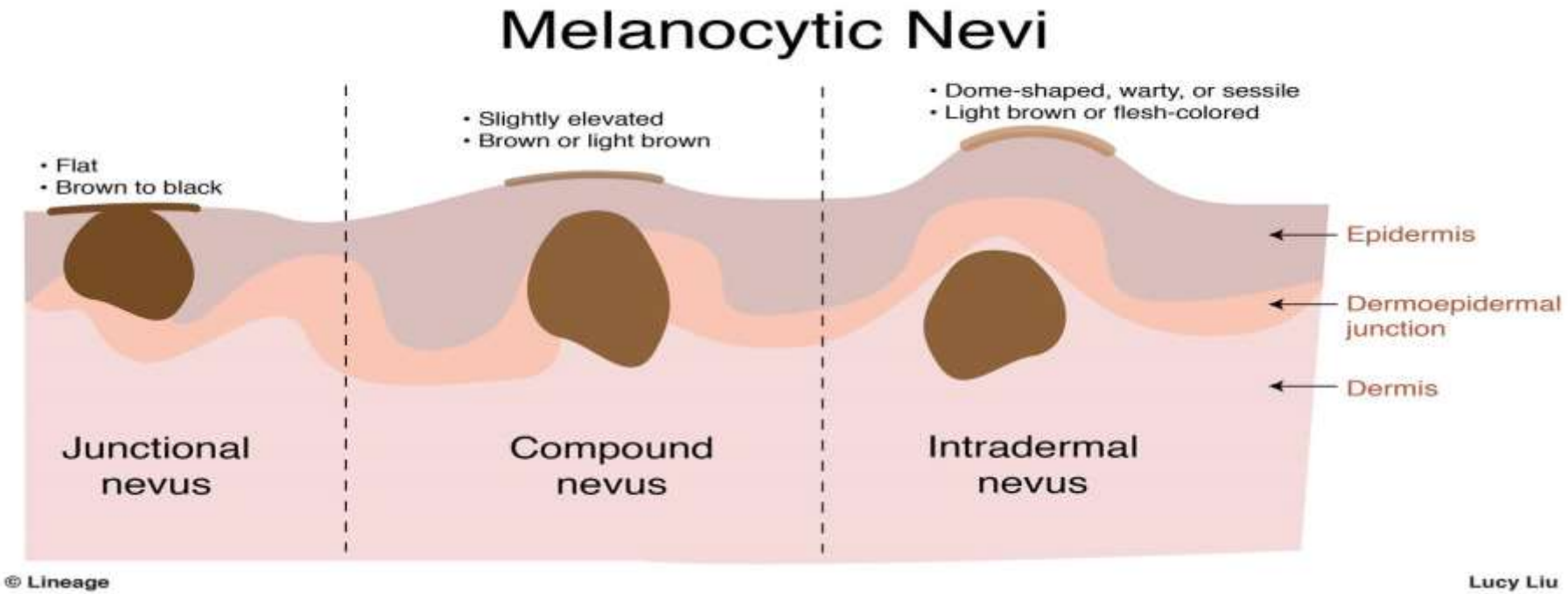
Subepidermal blisters associated with accumulation of neutrophils (microabscesses) at the tips of the dermal papillae.



Deposition of IgA autoantibody at the tips of the dermal papillae.

Tumors of Skin

- The most common benign skin tumor is **nevus** which composed microscopically from:
- Round to oval cells that grow in nests along dermoepidermal junction **(junctional nevi)** that may grow into the underlying dermis **(compound nevus**) & in older lesions only the dermal nests persist **(pure dermal nevus).**



Malignant tumors of skin

1. Squamous cell carcinoma:

- The most common tumor arising on the sun exposed sites in older people
- Male> female
- ***Etiology*:**

1. Sunlight (ultraviolet). 2. Industrial carcinogens (tar, oils)

3. Chronic ulcers. 4. Sinus of chronic osteomyelitis

5. Old burn scars. 6. Arsenic compounds

7. Ionizing radiation. 8. Tobacco (squamous cells carcinoma)

9. Immunocomromised patients. 10. Xeroderma pigmentosum

❖***Gross:***

I. In situ carcinoma is usually sharply defined red plaques.

II. Invasive carcinoma is nodular lesion, sometimes ulcerate.

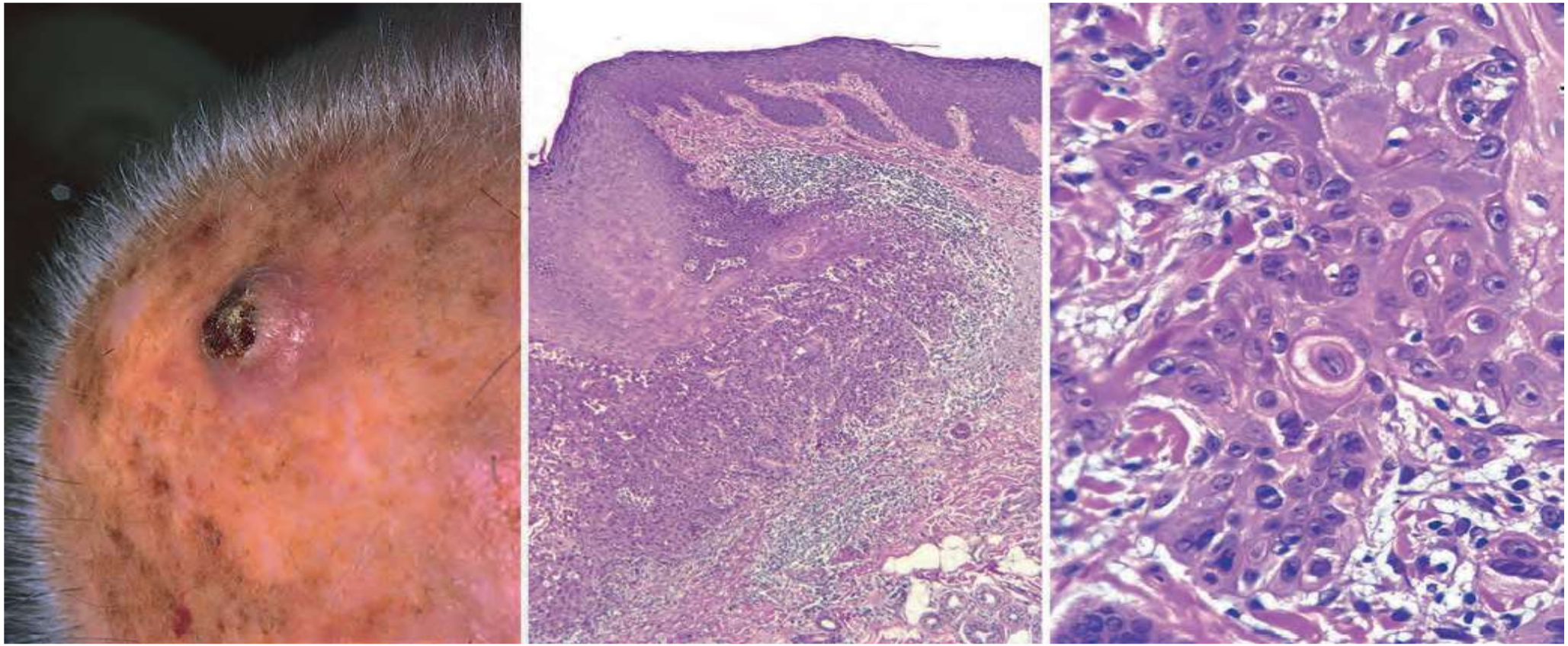
❖***Mic***:

I. In situ carcinoma: atypical malignant cells are involved the all levels of epidemis without break through the basement membrane.

II. Invasive carcinoma: malignant cells are break through the basement membrane. Invasive carcinomas show variable degrees of differentiation ranging from tumors well differentiated carcinoma to a highly anaplastic carcinoma.

❖Less than 5% of squamous cells carcinoma shows metastases to regional lymph nodes.

(A) (B) (C)

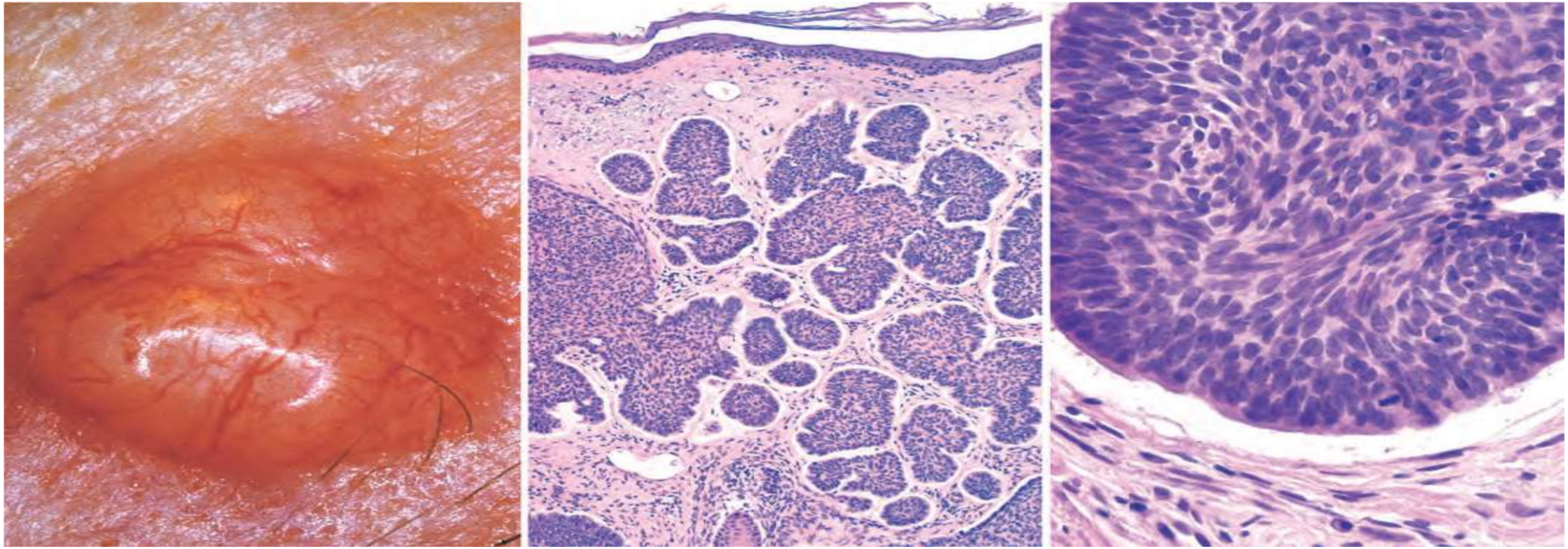


Invasive squamous cell carcinoma. (A) Lesions are often nodular and ulcerated, as seen in this scalp tumor. (B) Tongues of atypical squamous epithelium have transgressed the basement membrane and invaded deeply into the dermis. (C) Invasive tumor cells show enlarged nuclei with angulated contours and prominent nucleoli.

2. Basal cell carcinoma:

Are common, **slowly growing tumors that are rarely metastasizing.**

Has the same etiology of Squamous cell carcinoma.



(A) Pearly, telangiectatic nodule (B) nests of **uniform basaloid cells** within the dermis that are often separated from the adjacent stroma by thin clefts (C), an artifact of sectioning.

3. Melanoma:

- Melanoma is less common but much more deadly than basal or squamous cell carcinoma.

➢ ***Sites*:** skin, oral cavity, anogenital areas, esophagus, meninges& eyes.

➢ ***Etiology:***

- Sunlight
- Preexisting nevus (dysplastic nevus)
- Industrial carcinogens
- Hereditary & familial factors

➢*Gross & clinical features:*

- ***Warning clinical signs of malignant melanoma; are***

1. Enlargement of preexisting mole
2. Itching & pain in preexisting mole
3. Irregularity of borders of pigmented lesion
4. Variegation of color within the pigmented lesion
5. Development of new pigmented lesion during adult life

➢ ***Mic*:**

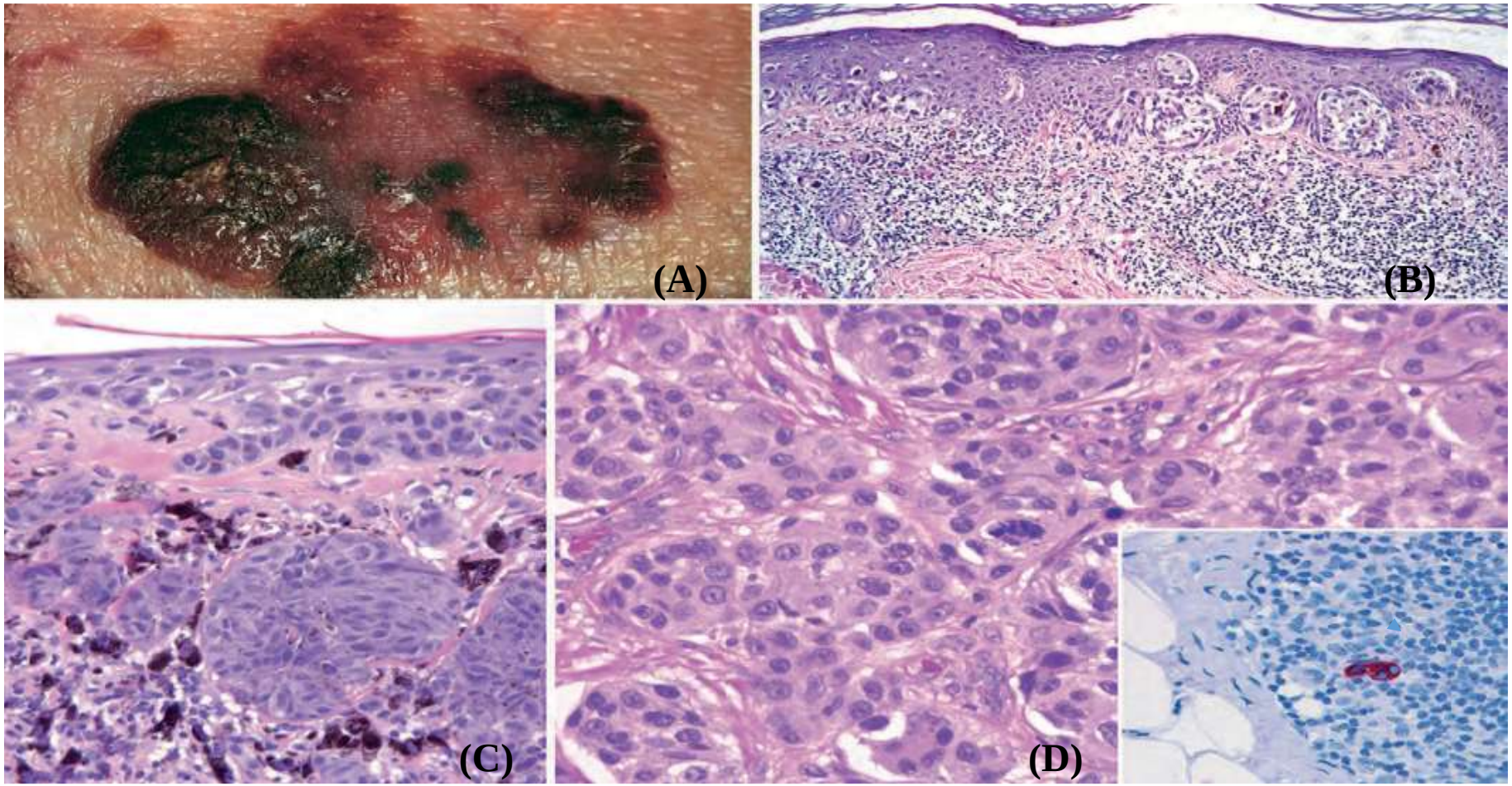
There are two patterns of growth in malignant melanoma.

- *Radial pattern of growth*: represent the initial tendency of malignant melanoma to grow horizontally within the epidermis & superficial dermal layers, for long period of time, such pattern of growth have no tendency of metastasis & angiogenesis.
- *Vertical growth:* with the time melanoma now grows downward into the deeper dermal layers as an expansile mass, with high tendency of metastasis & angiogenesis.

➢Characteristics of melanomas cells:

- Melanoma cells are larger than cells of nevus
- Malignant cells have large nuclei, with irregular contour, & clumped chromatin
- Have prominent eosinophilic nucleoli
- Cells grow either in nests or single.

➢**Sites of metastasis**: regional lymph nodes, liver, lung, brain, & heart



Melanoma. (A) Typical lesions are **irregular in contour and pigmentation**. (B) **Radial growth** phase showing irregular nested and single-cell growth of melanoma cells within the epidermis and an underlying inflammatory response within the dermis. (C) **Vertical growth** phase demonstrating nodular aggregates of infiltrating cells. (D) High-power view of melanoma cells. The *inset* shows a sentinel lymph node with a tiny cluster of melanoma cells staining for the melanocytic marker HMB-45. Even small numbers of malignant cells in a draining lymph node may confer a worse prognosis.


Always have faith
in your ability; success will
come your way eventually.
Best of Luck!
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