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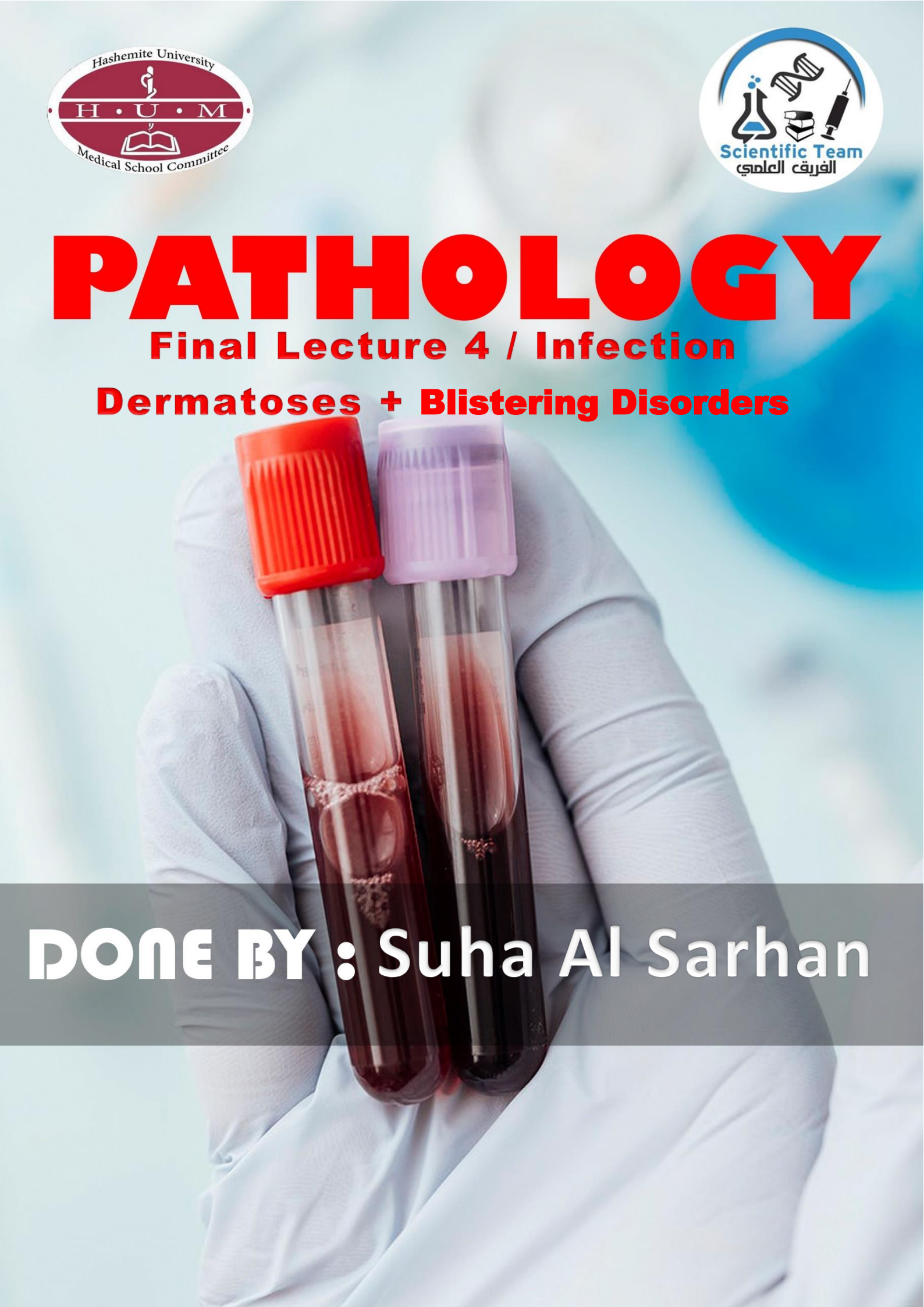
PATHOLOGY

Final Lecture 4 / Infection

Dermatoses + Blistering Disorders



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Infection Dermatoses

1. Bacterial Infection

- These range from superficial infections → caused by Staph. & Strept. spp., known as impetigo to deeper dermal abscesses → caused by anaerobes like Pseudomonas aeruginosa, associated with puncture wounds.
- **H:**
  skin biopsy typically shows spongiotic epidermis with a neutrophilic infiltrate.
  Cocci can be demonstrated using Gram stain in the superficial epidermis. Culture & sensitivity (C/S) to various antibiotics can be useful.
- **Clinically:**
  commonest skin bacterial infections is Impetigo primarily seen in children, but can affect adults.
  Impetigo transmitted by direct contact, usually caused by Staph. aureus, or less commonly Strept. pyogenes.
  Impetigo often begins as a single small macule that rapidly evolves into a larger lesion with a "honey-colored crust" (dried serum or scab).
  Impetigo most often involved the extremities, nose, & mouth

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2. Fungal Infection

- Fungal infections are varied & range from superficial infections with Candida species to life-threatening infections of immunosuppressed individuals with Aspergillus species.
- In general, a fungal infection can be:

(1) Very superficial (stratum corneum, hair, & nails)
(2) Deep, involving the dermis or subcutis
(3) Systemic involving skin by hematogenous spread (often in an immunocompromised host).

	Superficial infections	**deeper infections**
Pathogenesis	are often associated with a neutrophilic infiltrate in the epidermis.	*bacterial dermal infections induce neutrophil-rich abscesses, *fungal dermal infections often elicit a granulomatous response. *are usually more destructive; in particular, Aspergillus can be angio-(vascular) invasive.
Histopathological Features	Superficial candida infections induce a clinical response that can mimic psoriasis {this indicates that psoriasiform hyperplasia is a generalized response of skin to stimulation by the immune system}. therefore, it is essential to perform a fungal stain to exclude infection in a newly diagnose case of psoriasis	Deeper fungal infections produce greater tissue damage, probably induced by both the microbes themselves & the vigorous host immune response to their presence
Clinical Features	e.g. Candida usually show erythematous macules with superficial scale that can be pruritic	e.g. Aspergillus species in immunocompromised hosts are erythematous, often nodular, & sometimes show evidence of local hemorrhage.

3. Verrucae (Warts)

- Verrucae are common lesions of children & adolescents, although they may be encountered at any age.
- Verrucae are caused by human papillomavirus (HPV).
- Transmission is by direct contact between individuals or autoinoculation.
- Verrucae are generally self-limited, most often regressing spontaneously within 6 months to 2 years

- **Pathogenesis**:
  Some members of the HPV family (16 & 18) are associated with preneoplastic & invasive cancers of the anogenital region especially in cervix in female
  However, in contrast to HPV-associated carcinomas, most warts are caused by distinct low-risk HPV types that lack potential for causing malignant transformation.

  The virus subverts cell cycle control to allow ↑ proliferation of epithelial cells & production of new virus.
  Normal immune response usually limits the growth of these tumors, *but immunodeficiency can be associated with ↑ numbers & size of verrucae.

- **H, features**:
  common to verrucae include:
  1. Verrucous or papillomatous epidermal hyperplasia; often undulant in character (crown-like)
  2. koilocytosis = cytoplasmic vacuolization that preferentially involves the more superficial epidermal layers, producing halos of pallor surrounding infected nuclei (perinuclear hallow).
  3. Infected cells may also demonstrate keratohyaline granules & jagged eosinophilic intracytoplasmic protein aggregates as a result of impaired maturation

- **Clinically**:
  Warts can be classified into several types on the basis of their morphology & location. In addition, each type of wart is generally caused by a distinct HPV type.

Types of wart	Site	Characterictic
Verruca vulgaris	occuring anywhere, but are found most frequent on the hands, particularly on the dorsal surfaces & periungual (near the nail) areas	most common type of wart, they appear as gray-white to tan, flat to convex, 1-10mm papules with a rough, pebble-like surface
Verruca plana(flat wart)	common on the face or dorsal surfaces of the hands	These warts are flat, smooth, tan macules
Verruca plantaris	occur on the soles	These rough, scaly lesions may reach 1-2 cm in diameter
Verruca palmaris	occur on the palms	coalesce, & be confused with ordinary calluses منطقة من الجلد تكون سميكة جدا ويختلف تماما عن ال verruca palmaris & plantaris
Condyloma acuminatum (venereal wart)	occurs on the penis, female genitalia, urethra, & perianal areas	Caused by virus, it is very similar to condylomata lata which caused by syphilis (بميز بينهم بالسيرولوجيكال تيست)

BLISTERING (BULLOUS) DISORDERS

- These are disorders in which blisters are the primary & most distinctive features; although vesicles & bullae (blisters) occur as a secondary phenomenon in several unrelated conditions {e.g., herpesvirus infection, acute eczematous (spongiotic) dermatitis},
- Blisters can occur at multiple levels within the skin & assessment of their location within the skin is essential for an accurate histologic diagnosis.

1. Pemphigus (Vulgaris & Foliaceus)

- is a rare autoimmune blistering disorder resulting from loss of integrity of normal intercellular attachments within the epidermis & mucosal epithelium. التعريف مهم

- Most individuals who develop pemphigus are middle-aged & older.

- There are **3 major variants of pemphigus**;
  (1) vulgaris اخطر وحدة (2) foliaceus اقل من الاولى (3) paraneoplastic pemphigus (The latter is associated with internal malignancy & will not be discussed here.)

Types of pemphigus	Pathogenesis	H, Features	Clinically
pemphigus vulgaris	Both & are caused by a type II hypersensitivity reaction (Abs directed against a fixed tissue Ag) & show linkage to specific HLA types. Patient sera contain pathogenic IgG Abs to intercellular desmosomal proteins مهم(desmoglein types 1 & 3) of skin & mucous membranes. The distribution of these proteins within the epidermis determines the location of the lesions. By *direct immunofluorescence, lesional sites show a characteristic netlike "fishnet"* pattern of intercellular IgG deposits. The antibodies seem to function primarily by disrupting the intercellular adhesive function of the desmosomes & may activate intercellular proteases as well.	acantholysis selectively involves the layer of cells immediately above the basal cell layer = Suprabasal blister مهم	the most common type, involves mucosa & skin, especially on the scalp, face, axillae, groin, trunk, & points of pressure. Lesions are superficial vesicles & bullae that rupture easily, leaving erosions covered with serum crust
pemphigus foliaceus		acantholysis selectively involves the superficial epidermis at the level of the stratum granulosum = Subcorneal blisterمهم	a rare & benign form of pemphigus, results in bullae confined to skin, with infrequent involvement of mucous membranes. The blisters are so superficial that only zones of erythema & crusting site of previous blister rupture are detected

H, Common histologic denominator in all forms of pemphigus is acantholysis (lysis of the intercellular adhesion sites) within a squamous epithelial surface. Detached acantholytic cells become rounded.

Variable superficial dermal infiltration by lymphocytes, histiocytes, & eosinophils accompanies all forms of pemphigus.

2. Bullous Pemphigoid

- Affecting elderly individuals, bullous pemphigoid shows a wide range of clinical presentations, typically with generalized skin lesions & involvement of mucosal surfaces

- **Pathogenesis :**
  - ➔ Bullous pemphigoid is an autoimmune disease in which the characteristic finding is linear deposition of **IgG Abs** & complement in the basement membrane zone مهمم

  - ➔ Reactivity also occurs in the basal cell-basement membrane attachment plaques (hemidesmosomes; a protein involves normally in dermoepidermal bonding), where most of the bullous pemphigoid Ag is located.

  - ➔ IgG auto-Abs to hemidesmosome components fixes complement with subsequent tissue injury by means of locally recruited neutrophils & eosinophils.

- **H**:
  Bullous pemphigoid is characterized by a subepidermal, nonacantholytic blister. مهم
  Early lesions show a perivascular infiltrate of lymphocytes, eosinophils, & an occasional neutrophils; superficial dermal edema, & associated basal cell layer vacuolization. The vacuolated basal cell layer eventually gives rise to a fluid-filled blister

  Because the blister roof involves full-thickness epidermis, it is more resistant to rupture than blisters in pemphigus, & if uncomplicated by infection, heal without scarring.

- **Clinically:**
  lesions are tense bullae, filled with clear fluid, on normal or erythematous skin

  Sites of occurrence include the inner aspects of the thighs, flexor surfaces of the forearms, axillae, groin, & lower abdomen. Oral involvement is present in 1/3 of patients.

  Gestational pemphigoid occurs late in the 2 nd or 3 rd trimester of pregnancy & resolves after childbirth.

3. Dermatitis Herpetiformis

- is a rare disorder characterized by urticaria & grouped vesicles. The disease affects predominantly males, often in the 3rd & 4th decades.

- **Pathogenesis:**
  In some cases, dermatitis herpetiformis occurs in association with intestinal celiac disease. This association provides a clue to its pathogenesis.

  Genetically predisposed individuals develop IgA Abs to dietary gluten (derived from the wheat protein gliadin).مهممم
  The Abs cross-react with reticulin, (a component of the anchoring fibrils that tether the epidermal basement membrane to the superficial dermis). The resultant injury & inflammation produce a subepidermal blister.

  Some people with dermatitis herpetiformis & gluten- sensitive enteropathy respond to a gluten-free diet.

- **Morphology**
  a. As an early event, fibrin & neutrophils accumulate selectively at the tips of dermal papillae, forming small microabscesses
  b. The basal cells overlying these microabscesses show vacuolization & focal dermoepidermal separation that ultimately coalesce to form a true subepidermal blister.
  c. By direct immunofluorescence, dermatitis herpetiformis shows discontinuous, granular deposits of IgA selectively localized in the tips of dermal papillae النقطة مهمممممة

- **Clinical Features**
  The urticarial plaques & vesicles of dermatitis herpetiformis are extremely pruritic, bilateral, symmetric, & grouped, involving preferentially the extensor surfaces, elbows, knees, upper back, & buttocks

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SUMMARY: Blistering Disorders

- **Blistering disorders →** are classified according to the epidermal layer where the separation occurs. This group of diseases is often caused by autoreactive antibodies to constituents of the epithelium or basement membrane.

- **Pemphigus →** is associated with formation of IgG auto-Abs to intercellular (desmogleins) with resulting acantholysis in the epidermis; giving rise to bullae that are subcorneal (superficial) in the rare pemphigus foliaceus & suprabasal (deeper) in the more common pemphigus vulgaris.

- **Bullous pemphigoid →** shows deposition of IgG auto- antibodies to basement membrane proteins (hemidesmosomes) & produces a subepidermal blister.

- **Dermatitis herpetiformis →** is associated with deposition of IgA auto-Abs to (reticulin) fibrils that bind epidermal basement membrane to dermis, thus producing subepidermal blisters. This disease may be associated with celiac disease.