



e-Slide Exam

Answer Key

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Self-Paced Answer Key

Slide 1: Erythema Multiforme

- Interface dermatitis, mostly lymphocytes with individually necrotic keratinocytes early and confluent epidermal necrosis later with or without blistering.
- Normal basket weave cornified layer early
- If persistent, may have melanophages in papillary dermis which may give appearance similar to fixed drug eruption
- Ddx: GVHD—chronic form more lichenoid and/or sclerotic, acute form may be identical; DLE—thin epidermis, parakeratosis, thick BMZ; viral exanthema—sparse infiltrate with no interface changes

Slide 2: Granuloma Faciale

- Dense diffuse mixed infiltrate with eosinophils, neutrophils
- Features of leukocytoclastic vasculitis with nuclear dust and fibrin deposition in blood vessel walls
- End stage: perivascular “onion-skin” fibrosis
- Histologically similar to EED
- Ddx: Pseudolymphoma/persistent bite reaction: germinal centers and no vasculitis; LCV: no nodularity, fibrosis; Sweet’s—no vasculitis; abundant neutrophils; papillary dermal edema

Slide 3: Morphea

- Interstitial infiltrate of lymphocytes and plasma cells with some eosinophils in early lesions
- Sclerotic collagen
- Replacement of fat by sclerotic collagen and loss of adnexae.
- Ddx: radiation dermatitis—pleomorphic fibroblasts; nephrogenic fibrosing dermopathy—fibrosis as opposed to sclerosis; LE profundus—mummification of fat; lobular panniculitis; Scar—proliferation of fibroblasts; abundant collagen, minimal sclerosis; CT nevus—no sclerosis

Slide 4: Lupus Erythematosus Profundus

- Lobular panniculitis with hyalinization (“mummification”) of subcutaneous fat
- Nodular lympho-plasmacytic cellular infiltrate, occasionally with germinal centers
- Ddx: erythema nodosum: granulomatous septal panniculitis; erythema induratum: lobular suppurative and granulomatous panniculitis with vasculitis and fat degeneration; lipodermatosclerosis/sclerosing panniculitis: lipomembranous fat necrosis with overlying stasis change

Slide 5: Merkel Cell Carcinoma

- Diffuse basophilic neoplasm; individual cells with indistinct chromatin
- Numerous atypical mitotic figures; necrosis
- Fibrous strands—“trabecular” pattern
- May have a small cell variant
- CK 20 in a paranuclear dot pattern
- Positive staining for neuroendocrine markers: synaptophysin, neuron specific enolase, chromogranin
- Ddx: metastatic small cell carcinoma: positive staining with thyroid transcription factor 1; poorly differentiated lymphoma: positive staining with lymphoid markers

Slide 6: Metastatic Breast Cancer:

- Diffuse pattern with cords and strands of atypical epithelial cells between and among collagen bundles; may see ductal differentiation
- Nuclear molding; no desmosomes
- Progesterone and estrogen receptor positive
- May have mucin
- DDX: other diffuse interstitial neoplasms (see morpheaform BCC DDX above); Trichoadenoma—numerous follicular cyst-like structures in dermis with minimal epidermal changes

Slide 7: Compound Spitz Nevus

- Architectural features of benign lesion: sharply circumscribed, symmetrical, maturation
- Nests of epithelioid and spindle melanocytes usually with abundant cytoplasm at DE junction and in papillary and reticular dermis.
- May see Kamino bodies in epidermis—dull pink globules.
- May have features that simulate melanoma, including pagetoid spread, mitotic figures
- Ddx includes: Reticulohistiocytic granuloma (RHG) or JXG. Melanin commonly seen in Spitz and not in RHG or JXG. Xanthomatized cells seen in RHG/JXG but not in Spitz; Touton giant cells in JXG.

Slide 8: Kaposi's Sarcoma (Angiomatous Form)

- Diffuse proliferation of slit-like vascular spaces with extravasated erythrocytes, siderophages, plasma cells.
- Plump endothelial cells; over time, proliferate and lead to papule or nodule formation.
- Angiomatous form demonstrates ectatic blood vessels filled with sludged RBCs
- Promontory Sign: pre-existing blood vessels surrounded by slit-like vascular spaces.
- Ddx: Spindle cell hemangioma – a type of hemangioma with a few more spindle cells than usually seen; small blood vessels usually rounder than slit like as in KS.
Acroangiodermatitis – lobular proliferation of thick-walled stasis associated blood vessels.
Angiosarcoma - broad, diffuse poorly circumscribed neoplasm with much atypia;
Aneurysmal benign fibrocystoma -sclerosing hemangioma variant of dermatofibroma;
numerous blood vessels, histiocytes, siderophages.

Slide 9: Metastatic Malignant Melanoma

- Poorly differentiated atypical basophilic cells, some in nests
- Nodular dermal-based neoplasm; may involve blood vessels or lymphatics
- Ddx: eccrine acrospiromas: no atypia; ductal differentiation; cuboidal homogeneous cells

Slide 10: Desmoplastic trichoepithelioma

- Diffuse cords and strands of basophilic cells between collagen bundles.
- Structures resembling follicular germs are present.
- Stroma is thick and sclerotic.
- Calcification, small cysts
- Ddx: other diffuse sclerosing neoplasms: morpheaform basal cell carcinoma, MAC; trichofolliculoma, basaloid follicular hamartoma and trichoblastoma—not confused histologically.

Slide 11: PLEVA

- Interface dermatitis often with neutrophils in the parakeratotic cornified layer.
- Red cell extravasation.
- Infiltrate of mostly infiltrates “crashes” into the epidermis; dyskeratotic cells.
- Infiltrate often wedge-shaped; no eosinophils
- Ddx: PLC – same disease at different stage with less inflammation, parakeratosis.
Syphilis - plasma cells. Contact dermatitis - more spongiotic, minimal dyskeratosis and no interface dermatitis. Pityriasis rosea – much less dense infiltrate, no interface change;. Lichen striatus - periadnexal infiltrate, especially around eccrine gland

Slide 12: Incontinentia Pigmenti

- Eosinophilic spongiosis with dyskeratosis - may demonstrate “whorls” of dyskeratotic cells
- Lymphocytes and eosinophils in dermis
- Ddx: BP, contact dermatitis - lacks dyskeratotic cells; other conditions with eosinophilic spongiosis generally do not have dyskeratosis; Hand, Foot and Mouth—ballooning degeneration of cells in volar epidermis; variable inflammation, dermal edema; Pemphigus—suprabasilar acantholysis; Linear IgA—subepidermal neutrophils, blistering

Slide 13: Grover’s Disease (Transient Acantholytic Dermatitis)

- Focal acantholytic dyskeratosis
- Several different histologic forms: similar to PV, Hailey-Hailey, Darier’s, or spongiotic dermatitis
- Ddx: Hailey-Hailey - diffuse acantholysis, “dilapidated brick wall” without minimal dyskeratosis, diffuse, not focal; other conditions with acantholytic dyskeratosis require clinical distinction in most cases (wartlike dyskeratoma, “linear Darier’s”; Darier’s itself, familial dyskeratotic comedones, solitary acantholytic keratosis)

Slide 14: Discoid Lupus Erythematosus

- Superficial and deep perivascular and periadnexal lymphocytic infiltrate with vacuolar interface change; epidermal thinning late
- Mucin in the dermis between collagen bundles
- Thickening of the BMZ (“smudged”)
- Variant with thick epidermis and pseudocarcinomatous features simulates SCC
- Ddx: dermatomyositis - infiltrate less dense, no thickened BMZ; may be identical histologically to SCLE or ALE but not usually DLE; other lymphocytic infiltrates: no interface change; LP—may appear similar in some cases but usually more wedge shaped hypergranulosis; irregular saw-tooth rete, no BMZ thickening or follicular plugging usually

Slide 15: Lymphomatoid Papulosis

- Superficial and deep, often mixed, wedge-shaped infiltrate with large bizarre atypical cells
- CD 30 positive
- 3 types: A- anaplastic; B- cerebriform; C- mixed
- 15% associated with lymphoma and vasculitis
- Ddx: insect bite reaction: few or no atypical cells and if so, usually never as atypical; lymphoma: denser, deeper, clinical distinction; PLEVA: no eosinophils, more cornified layer changes

Slide 16: Trichoblastoma

- Diffuse proliferation of basaloid cells with primitive hair germ differentiation.
- Prominent sclerotic stroma with no clefts between stroma and basaloid cells.
- Ddx: Trichoepithelioma - more well-formed follicular structures; papillary mesenchymal bodies; cysts, calcification, smaller

Slide 17: Tumid Lupus Erythematosus

- Superficial and deep lymphocytic infiltrate with mucin; no epidermal change.
- Immunofluorescence stains often negative
- Ddx: PMLE - similar lymphocytic infiltrate with prominent papillary dermal edema; occasionally spongiosis in papulovesicular variant. Arthropod assault– mixed infiltrate with eosinophils. Morphea - sclerotic change. Reticular erythematous mucinosis: mild superficial and mid-dermal perivascular infiltrate with mucin, clinical info helpful. Other lymphocytic infiltrates: usually minimal mucin;

Slide 18: Sebaceous adenoma

- Proliferation of well-differentiated and well-circumscribed sebaceous lobules with crateriform pattern and central pustulous opening.
- Ddx Sebaceoma – more germinative basaloid cells comprising over 50% of the lesion. Sebaceous carcinoma –large and deep and asymmetrical with mitotic features of germinative cells; necrosis en masse often.

Slide 19: Interstitial granuloma annulare

- Diffuse infiltrate of histiocytes between collagen bundles in the dermis with perivascular infiltrate.
- Mucin between collagen bundles.
- Ddx: NLD - more sclerotic with degenerated collagen and more diffuse with plasma cells in the infiltrate. Rheumatoid Nodule - deeper with fibrin in center of palisade. Kaposi's Sarcoma - look for blood vessels, extravasated RBCs and siderophages. Epithelioid sarcoma much deeper and comprised of atypical cells.

Slide 20: Bowenoid Papulosis

- Overall histologic architecture similar to condyloma, especially from low power.
- "Windblown" keratinocytes, koilocytic change and gentle papillomatosis.
- Atypical cells represent a squamous cell carcinoma arising from HPV in the groin.
- Look for genital skin.
- Ddx: Condyloma has minimal if any atypia; other forms of SCC in situ: no signs of HPV infection, usually broader rather than papule

Slide 21: Microcystic adnexal carcinoma, nodular type

- Diffuse aggregates of small cuboidal cells in cords and strands.
- Deep and diffuse.
- Neurotropism.
- Ddx: Dermal Duct Tumor looks like a poroma that is no longer connected to the epidermis, aggregate of epithelial cells with homogeneous poroid pattern. Aggressive digital papillary adenoma - cystic aggregates with papillomatosis and atypical mitotic figures, often aggressive, may metastasize. Syringoma – small superficial lesion localized to papillary dermis, not deep and diffuse, small duct-like structures with sclerotic fibromatous stroma.

Slide 22: Mycosis Fungoides, tumor stage

- Dense diffuse infiltrate of atypical cells with cerebriform morphology
- Diffuse lymphoma with epidermotropism
- Sometimes superficial portion has features of residual patch or plaque stage disease
- Ddx: Syphilis- superficial and deep psoriasiform lichenoid pattern with plasma cells and no atypical cells. Pagetoid reticulosis – epidermotropic form of MF with no nodule or tumor stage. Nodular scabies/pseudolymphoma—nodular infiltrate of small lymphs; eosinophils; no epidermotropism, may see germinal centers

Slide 23: Clear cell hidradenoma

- Also known as acrospiroma and solid-cystic hidradenoma
- Circumscribed tumor in the upper or mid dermis composed of lobulated, sometimes cystic masses of cells and duct-like structures
- Focal apocrine decapitation secretion may be seen
- Biphasic cell population:
 - round cells with scant eosinophilic cytoplasm and round, oval nucleus
 - cells with abundant clear cytoplasm and small, dark nucleus
- DDX: Chondroid syringoma—mixed tumor of skin, abundant mucin with cartilaginous metaplasia containing small aggregates of basaloid cells with ductal differentiation; Spiradenoma—“blue balls in dermis”, homogeneous cuboidal cells, pink hyaline globules, ducts; Hidradenoma papilliferum—cystic dermal nodule with villous fronds of cells with apocrine differentiation, plasma cells; Renal cell ca—large clear cells; marked vascularity; atypia

Slide 24: Halo nevus

- Dense nodular infiltrate of lymphocytes in the papillary dermis; scattered residual nevus cells at DEJ and in papillary dermis on careful inspection.
- Ddx: Benign Lichenoid Keratosis (lichen planus-like keratosis) - Similar infiltrate but has dyskeratotic cells in epidermis; no nevus cells; features of solar lentigo. Lichen planus—true lichenoid infiltrate rather than dense nodular infiltrate in upper dermis; Melanoma—architecture of malignancy; pagetoid spread of cells in epidermis; more atypia of melanocytes than in halo nevus

Slide 25: Axillary granular parakeratosis

- Slight epidermal hyperplasia with parakeratosis and granular basophilic material on the outermost surface of the cornified layer. Often has a minimal infiltrate, but may have eosinophils and lymphocytes.
- DDX: irritant dermatitis--dyskeratotic cells; more inflammation; inverse psoriasis—more epidermal hyperplasia, PMN's in cornified layer; mounds of parakeratosis no granular material; LSC—no granular material. Epidermal nevus—papillomatosis, usually no granular appearance to cornified layer. Porokeratosis—cornoid lamella

Slide 26: Proliferating tricholemmal cyst

- Large bulbous aggregates of keratinocytes with differentiation toward the isthmus of the follicle.
- Pseudocarcinomatous hyperplasia with squamous eddies.
- Few if any mitotic figures, minimal cytologic atypia.
- Tricholemmal cornification.
- Ddx: SCC –much greater degree of atypia, mitotic figures. Pseudocarcinomatous hyperplasia - no tricholemmal cornification, usually no cyst morphology.

Slide 27: Epidermolytic Hyperkeratosis

- Compact hyperkeratosis
- Vacuolar degeneration of spinous and granular layers
- Coarse keratohyalin granules with basophilic clumping
- Blistering may or may not be histologically evident
- May be seen clinically in generalized, linear, palmoplantar, solitary, incidental (a/w cyst, SK, tag, nevus, etc), mucosal, or related to a solar keratosis
- Generalized form may be seen in offspring of those with linear (nevoid) form
- AD, defect in Keratin 1 and 10
- DDX—verruca vulgaris: koilocytes confined to upper epidermis; granular basophilic cytoplasm; no vesiculation; Hailey-Hailey disease—acantholysis; EDV—purplish homogeneous cytoplasm in vacuolated cells in epidermis; no abnormal cornification

Slide 28: Ichthyosis Vulgaris

- Sparse superficial perivascular lymphohistiocytic infiltrate if any
- Slight hyperkeratosis, often laminated
- Diminution or absence of the granular cell layer
- AD inheritance; mutation in profilagrin
- DDX: psoriasis-parakeratosis; inflammation; atopic dermatitis-compact hyperkeratosis, irregular epidermal hyperplasia; TV—basket weave cornified layer containing “spaghetti and meatballs” (Mallesezia furfur)

Slide 29: Sclerosing Hemangioma

- Variant of dermatofibroma
- Prominent proliferation of fibroblasts and histiocytes in the dermis with numerous extravasated RBC's and siderophages
- Fibroblasts dissect collagen (“keloidal collagen”) at the periphery (“doughnut” sign)
- Factor 13A positive, CD 34 negative
- DDX: AFX--more atypia; mitoses; traumatized angioma—fewer spindle cells, histiocytes; DFSP—fascicles of spindle cells; no histiocytes, no siderophages; KS—diffuse slit-like vascular spaces; nodular stage has fascicles of cells

Slide 30: Carbon tattoo

- Jet black pigment in dermis
- Often traumatically implanted by pencil lead injury or in industrial or firearm accident and so may be associated with scar
- Variable inflammation but may be minimal
- DDX: Cinnabar tattoo—red pigment; granuloma formation; Silicone—bubbly histiocytes; no pigment; Monsel's solution—refractile golden brown pigment because of iron, inflammation, scar, foreign body reaction

Slide 31: Chilblains (pernio)

- Acral site
- Superficial and often deep lymphocytic infiltrate with interface vacuolar alteration
- Papillary dermal edema
- Rarely lymphocytic vasculitis with true fibrin deposition in vessel walls
- DDX: Lichen striatus—infiltrate periadnexal; not as deep; may contain eosinophils; arthropod assault—wedge shaped infiltrate; eosinophils

Slide 32: Angiokeratoma

- Verrucous epithelial hyperplasia; hyperkeratosis and marked dilation of capillary dermal vessels
- Elongated epidermal ridges encircle dilated vessels in the superficial dermis and may completely enclose the vascular channels
- Minimal endothelial proliferation
- Thrombi in some
- DDX: Hemangioma—less epidermal proliferation, usually more endothelial proliferation; AV malformation—large vessels; dermal lesion; Lymphangioma—few red cells in spaces; valves; THH—thought by many to represent traumatized angioma; siderophages

Slide 33: Fibroepithelioma of Pinkus

- Variant of basal cell carcinoma on the lower part of the back most commonly
- Thin, anastomosing strands of basaloid cells in prominent loose stroma; some clefting
- DDX: TFI—less basaloid; differentiates towards isthmus of follicle; Reticulated SK—thicker cords of epithelial cells, cells more cuboidal; may see horn pseudocysts, no fibromucinous stroma; Basaloid follicular hamartoma—small solid aggregation of basaloid cells; no clefting

Slide 34: Fixed drug eruption

- Interface dermatitis; spongiosis, necrotic keratinocytes
- Superficial and deep mixed infiltrate with lymphocytes and eosinophils
- Late lesions have less prominent infiltrate and more pigment incontinence; may see many deep melanophages due to lesion recurring at the same site
- DDX: Phytophotodermatitis—parakeratosis; extensive necrosis with usually minimal inflammation; fewer melanophages; Erythema multiforme – superficial, less prominent infiltrate, no eosinophils, less pigment incontinence

Slide 35: Metastatic renal cell carcinoma

- Skin-colored or violaceous nodule, may resemble a pyogenic granuloma clinically
- More common in males with a predilection for the head and neck area
- Intradermal nodule composed of large clear cells (contains glycogen and lipid), often in a glandular configuration
- Stroma is vascular with presence of extravasated red blood cells
- DDX: Nodular hidradenoma—multilobular, vascular stroma absent, presence of ductal structures; Clear cell sarcoma—clear cells, often multinucleated cells present, melanin, common on foot; Balloon cell melanoma—nests of “balloon cell” melanocytes, sometimes junctional component, vascular stroma absent; Pyogenic granuloma—lobule composed of granulation tissue (vascular proliferation with an inflammatory cell infiltrate composed of lymphocytes and neutrophils)

Slide 36: Gout

- Yellow-white nodules commonly present over joints and on fingers and toes
- Due to deposits of monosodium urate (tophi); patients with arthritis symptoms
- Formalin-fixed specimens demonstrate amorphous, eosinophilic material surrounded by a rim of foreign body giant cells and macrophages
- Alcohol-fixed specimens demonstrate sharply demarcated needle-shaped crystals, often with a brownish color and doubly refractile on polariscopic examination (yellow=parallel, blue=perpendicular)
- DDX: Rheumatoid nodule—palisading granuloma around degenerated connective tissue and fibrin, only few multinucleated giant cells; Deep granuloma annulare—similar to rheumatoid nodule histologically, mucin may be present; Lipoid proteinosis—autosomal recessive deposition disorder, amorphous deposits, often perpendicular to epidermis and around vessels and adnexal structures; Calcinosis cutis—dark, basophilic calcium deposits (von Kossa or alizarin red positive)

Slide 37: Cellular blue nevus

- Blue nodule, 1-3 cm in diameter, most commonly located on the buttocks or sacrococcygeal region
- Densely packed melanocytes, with a broader expansion at its surface and a bulbous expansion at its base (“dumbbell shaped”) with frequent extension into the subcutaneous fat
- Most commonly with a biphasic appearance (mixture of plump epithelioid cells with somewhat clear cytoplasm and heavily pigmented spindle cells)
- DDX: Bednar tumor (pigmented DFSP)—cellular proliferation of spindled fibroblasts in a storiform pattern with presence of melanin; Metastatic melanoma—poorly circumscribed, atypical melanocytes; Neurothekeoma (Nerve sheath myxoma)—spindle cells in theques or fascicles in mucinous stroma; Nevus of Ito—dendritic melanocytes with fine granules of melanin

Slide 38: Granular cell tumor

- Usually solitary, 10% multiple; 40% involve the tongue
- Broad fascicles of tumor cells infiltrate between collagen bundles
- Large polygonal cells with granular cytoplasm (PAS positive/diastase resistant and S-100 protein positive)
- Larger intracytoplasmic granules are called pustule-ovoid bodies of Milian or residual bodies.
- May have overlying pseudoepitheliomatous hyperplasia (especially in mucosal lesions)
- DDX: Xanthoma—less granularity, positive for lipid stains, negative with S-100 protein; Other lesions with granular cytoplasm (BCC, dermatofibroma, etc)—may require special stains to differentiate; Primitive polypoid granular cell tumor—similar histology, more pleomorphism, S-100 protein negative

Slide 39: Mixed tumor of skin (chondroid syringoma)

- Firm intradermal or subcutaneous nodules most commonly on the head and neck area
- Composed of epithelial (eccrine or apocrine sweat duct structures) and mesenchymal elements with prominent mucinous stroma and focal chondroid change
- Two types recognized histologically based on epithelial component: one with tubular, cystic, partially branching lumina and the other with small, tubular lumina
- DDX: Eccrine spiradenoma—sharply demarcated nodule of basaloid cells, usually in a rosette-like pattern; Hidradenoma—epithelial neoplasm made up of one type of basaloid cell, absence of mucinous stroma; Merkel cell carcinoma—round, atypical, blue cells sometimes in clusters, rosettes, or a trabecular pattern, classic paranuclear dot staining pattern with low molecular weight keratins

Slide 40: Hibernoma

- Tumor of fetal "brown fat"
- Mulberry cells
- Generally well circumscribed
- Ddx: lipodermatosclerosis, granular cell tumor, lepromatous leprosy, liposarcoma