The Physician Pharmacist: Dermatology

Skin Layers:
-3 Layers = Epidermis, Dermis, SQ (Hypodermis, Subcutis)
-Corneum, Lucidum, Granulosum, Spinosum, Basalis
"Come Lets Get Some Beer"

Epithelial Cell Junctions:

-Tight junctions (Zonula Occludens) = prevents paracellular movement of solutes; composed of Claudins + Occludins

-**Adherens Junction** (Belt Desmosome, Zonula Adherens) = forms "belt" connecting Actin Cytoskeletons of adjacent cells w/ **Carherins** (Ca2+ dependent Adhesion proteins)

- Loss of **E-Cadherin** promotes Metastasis

-**Desmosomes** (Spot Desmosome, macula Adherens) = structural support via intermediate filament interactions

- Autoantibodies to **Desmoglein** 1 or 3 = Pemphigus Vulgaris

-Gap Junction = channel proteins called Connexons permit electrical + chemical communication btw cells

-Hemidesmosomes = connects Keratin in Basal cells to underlying basement membrane

- Autoantibodies = **Bullous Pemphigoid**

-Integrins = membrane proteins that maintain Integrity of Basolateral Membrane by binding to collagen, laminin, fibronectin in basement membrane

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Dermatologic Macroscopic Terms:

1. **Macule**
   a. Flat lesion w/ well-circumscribed change in skin color < 1 cm
   b. ex.) Freckle (Ephelide), Labial Macule
2. **Patch:**
   a. Macule > 1 cm
   b. ex.) Large birthmark (Congenital Nevus)
3. **Papule**:
   a. Elevated solid skin lesions < 1cm
   b. ex.) Mole (Nevus), Acne
4. **Plaque:**
   a. Papule > 1 cm
   b. ex.) Psoriasis
5. **Vesicle**:
   a. Small fluid-containing blister < 1cm
   b. ex.)Chickenpox (Varicella, Shingles (Zoster)
6. **Bulla**:
   a. Large fluid-containing blister > 1 cm
   b. ex.) Bullous Pemphigoid
7. **Pustule**:
   a. Vesicle containing pus
   b. ex.) Pustular Psoriasis
8. **Wheal**:
   a. Transient smooth papule or plaque
   b. ex.) Hives (Urticaria)
9. **Scale**:
   a. Flaking off of stratum corneum
   b. ex.) Eczema, Psoriasis, SCC
10. **Crust**:
    a. Dry exudate
    b. ex.) Impetigo

Dermatologic MICROscopic terms:

1. **Dyskeratosis:**
   a. Abnormal premature keratinization
   b. Ex.) SCC
2. **Hyperkeratosis:**
   a. thickness of stratum corneum
   b. ex.) Psoriasis, Calluses
3. **Parakeratosis:**
   a. Retention of nuclei in stratum corneum
   b. ex.) Psoriasis, Actinic Keratosis
4. **Hypergranulosis:**
   a. thickness of stratum granulosum
   b. ex.) Lichen Planus
5. **Spongiosis:**
   a. Epidermal accumulation of edematous fluid in intercellular spaces
   b. ex.) Eczematous dermatitis
6. **Acantholysis:**
   a. Separation of epidermal cells
   b. ex.) Pemphigus vulgaris
7. **Acanthosis:**
   a. Epidermal Hyperplasia (Spinosum)
   b. ex.) Acanthsis Nigricans, Psoriasis

Pigmented Skin Disorders:

1. Albinism:
-NORMAL melanocyte #, w/ melanin production due to Tyrosinase activity or defective Tyrosine Transport
- risk of skin cancer

2. Melasma (Chloasma):
-Acquired hyperpigmentation associated w/ pregnancy ("Mask of Pregnancy") or OCP use
-more common in pregnant pts w/ darker skin tones

3. Vitiligo:
-irregular patches of complete depigmentation
-caused by destruction of Melanocytes (autoimmune)
-Associated w/ other autoimmune dx

Seborrheic Dermatitis:
-Erythematous, well-demarcated plaques w/ greasy yellow scales in areas rich in sebaceous glands, such as scalp, face, and periocular region
-Common in infants (Cradle Cap) and Adults (associated w/ Parkinson's Dx)
-Sebaceous Glands are not Inflamed, but play a role in dx development
-Associated w/ **Malazzezia spp**
Tx → Topical antifungals + steroids

Common Skin Disorders:

1. Acne:
-Multifactorial etiology → sebum/androgen production, abnormal keratinocyte desquamation, Cutibacterium acne colonization of the Pilosebaceous unit (Comedones) and Inflam (papules/pustules, nodules, cysts)
-Tx = Retinoids, Benzoyl peroxide, ABx

2. Atopic Dermatitis (Eczema):
-**Type I HSR** = Pruritic eruption on skin flexures
-associated w/ other atopic dx (Asthma, Allergic Rhinitis, Food Allergies)
- Serum IgE
-Mutations in Filaggrin Gene predispose (via skin barrier dysfunction)
-appears on face (infancy) then in antecubital fossa in children/Adults

3. Allergic Contact Dermatitis:
-**Type IV HSR** = rxn secondary to contact allergen (Nickel, Poison Ivy, Neomycin)

4. Melanocytic Nevus:
-"Common Mole"
-Benign, but melanoma can arise in congenital or atypical moles
-intradermal nevi are papular
-Junctional nevi = flat macules

5. Pseudofolliculitis Barbae:
-foreign body inflammatory facial skin disorder
-Firm, Hyperpigmented papules + pustules that are Painful + pruritic
-located on cheeks, jawline, neck
-commonly occurs as result of Shaving "Razor bumps"
-Most commonly Black Males

6. Psoriasis:
-Papules + plaques w/ silvery scaling (especially on Knees + Elbows)
-Acanthosis w/ **Parakeratotic scaling** (nuclei still in Stratum Corneum)
-Munro microabscesses
- Stratum Spinosum, Stratum Granulosum (S, G)
-**Auspitz Sign** = pinpoint bleeding spots from exposure of Dermal Papillae when scales are scraped off
-Associated w/ nail pitting + psoriatic arthritis

7. Rosacea:
-inflammatory facial skin disorder = erythematous papules and pustules BUT no Comedones
-Facial flushing in response to external stimuli (alcohol, heat)
-Complications = Ocular involvement, Rhinophyma (bulbous Deformation of nose)

8. Seborrheic Keratosis:
-Flat, greasy, pigmented squamous epithelial proliferation of immature keratinocytes w/ Keratin-filled cysts ("Horn Cells")
-"looks stuck on"
-Lesions = head, trunk, extremities
-Common benign neoplasm of older persons
-**Leser-Trelat Sign** = Rapid Onset of Multiple of multiple seborrheic keratoses = GI Adenocarcinoma

9. Verrucae:
-Warts = caused by low-risk HPV stains (6 + 11)
-Soft tan-colored, cauliflower-liked papules
-**Epidermal Hyperplasia, Hyperkeratosis, Koilocytosis**
-Condyloma Acuminatum on Anus or genitals

10. Urticaria:
-Hives
-Pruritic wheals that form after Mast Cell Degranulation
-Superficial Dermal Edema + Lymphatic Channel Dilation

Vascular Tumors of Skin:

1. Angiosarcoma:
-rare blood vessel malignancy occuring in the head, neck, breast areas
-usually in elderly, on sun-exposed areas
-radiation therapy + chronic post mastectomy lymphedema
-Hepatic Angiosarcoma = vinyl chloride and Arsenic Exposures
-Very aggressive and difficult to resect due to delay in ddx

2. Bacillary Angiomatosis:
-benign capillary skin papules found in pts w/ AIDS
-**Bartonella** infxn causes
-mistaken for Kaposi Sarcoma, but has **Neutrophilic** Infiltrate

3. Cherry Hemangioma:
-benign capillary hemangioma commonly appearing in middle-aged adults
-does NOT regress
-frequency w/ age

4. Glomus Tumor:
-benign, painful, red-blue tumor **under fingernails**
-arises from modified smooth muscle cells of the thermoregulatory glomus body

5. Kaposi Sarcoma:****
-Endothelial malignancy affecting skin, mouth, GI tract, Respiratory Tract
-Older Eastern European males, AIDs pts, Organ transplant
-**HHV-8 and HIV (Lymphocytic infiltrate)**

6. Pyogenic Granuloma:
-Polypoid lobulated capillary hemangioma taht can ulcerate + bleed
-Associated w/ Trauma + Pregnancy

7. Strawberry Hemangioma:
-benign Capillary hemangioma of infancy
-appears in first few weeks of life → grows rapidly + regresses spontaneously by 5-8 yo

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Bacterial Skin Infxns:

1. Impetigo:
-skin infxn involving superficial epidermis
-Staph aureus + strep pyogenes
-highly contagious
-Honey-Colored Crusting
-Bullous Impetigo has bullae (usually Staph aureus)

2. Erysipelas:
-infxn involving upper dermis + superficial lymphatics (strep pyogenes - Group A)
-well-defined, raised demarcation btw infected + normal skin

3. Cellulitis:
-acute, painful spreading infxn of deeper dermis + SQ tissues
-strep pyogenes, Staph aureus
-occurs from break in skin from trauma or infxn

4. Abscess:
-Collection of pus from walled-off infxn within deeper layers of skin
-offending organism is almost always **Staph Aureus**

5. Necrotizing Fasciitis:
-deeper tissue injury, usually from anaerobic bacteria or Strep Pyogenes
-pain out of proportion to exam findings
-results = Crepitus from methane and CO_2 production
-"Flesh eating bacteria" → Bullae/skin necrosis → violaceous color of bullae
-Surgical emergency

6. Staphylococcal Scalded Skin Syndrome (SSSS):
-Exotoxin destroys keratinocyte attachments in stratum **Granulosum ONLY** (vs. Toxic- Epidermal Necrolysis = destroys epidermal-dermal junction)
-sxs = Fever, generalized erythematous rash w/ sloughing of upper layers of the epidermis
-tends to heal completely
-(+) Nikolsky Sign = separation of epidermis upon manual stroking of skin
-Newborns or children/adults w/ Renal Dx

Viral Infections:

1. Herpes:
-HSV-1 and HSV-2 of skin can occur anywhere from mucosal surfaces to normal skin
-"Herpes Labialis, Herpes, Genitalis, Herpetic Whitlow"

2. Molluscum Contagiosum:
-Poxvirus = umbilicated papules
-seen commonly in children
-sexually transmitted in adults

3. Varicella Zoster Virus (VZV):
-Varicella (Chickenpox) and Zoster (Shingles)
-Varicella = multiple crops of lesions **in various stages of healing (vesicles to crusts**)
-zoster = reactivation of virus in dermatomal distribution (unless disseminated)

4. Hairy Leukoplakia:
-Irregular, white, painless plaques on lateral tongue
-**can't be scraped off (Thrush Can be)**
-**EBV mediated** = occurring in HIV + Transplant pts
-precancerous lesion

Autoimmune Blistering Skin Disorders:

1. Pemphigus Vulgaris:
-Potentially fatal
-most commonly older adults
-**Type II HSR**
-IgG antibodies against **Desmoglein-1 and Desmoglein-3** (Components of **Desmosomes** = connect Keratinocytes in the Stratum **Spinosum**)
-sxs = Flaccid intraepidermal bullae caused by Acantholysis (Separation of keratinocytes) **"Row of Tombstones**", Oral mucosa involved
-(+) Nikolsky Sign
-reticular pattern around epidermal cells

2. Bullous Pemphigoid:
-less severe than pemphigus vulgaris
-most common in older adults
-**Type II HSR** (autoimmunity)
-IgG antibodies against **Hemidesmosomes** (Epidermal basement membrane; ANtibodies are "Bullow" the Epidermis (but above the Dermis))
-"Forms an outcropping/opening where the entire epidermis peels away from the Dermis"

Blistering Skin Disorders;

1. Dermatitis Herpetiformis:
-pruritic papules, vesicles, bullae (found on elbows, knees, buttocks)
-Deposits of IgA at tips of Dermal Papillae
-Associated w/ **Celiac Dx**
-Tx = Dapsone, Gluten-Free Diet

2. Erythema Multiforme:
-Infxns of **Mycoplasma Pneumonai, HSV**, Drugs (Sulfa, B-lactams, Phenytoin)
-Multiple types of lesions = macules, papules, vesicles, target lesions (look like targets w/ multiple rings + dusky center showing epithelial disruption)

3. Stevens-Johnson Syndrome (SJS):
-characterized by fever, bullae formation/necrosis, sloughing of skin at dermal-epidermal junction
-(+) Nikolsky + high mortality rate
-Typically mucous membranes involved, targetoid skin lesions may appear (similar to Erythema Multiforme)
-Associated w/ ADRs (Lamotrigine, Vancomycin)
-Toxic Epidermal Necrolysis (TEN) = more severe SJS involving > 30% of BSA

Lower Extremity Ulcers:

1. Venous Ulcer:
-chronic venous insufficiency
-MOST common type of ulcer
-location = Gaiter Area (Ankle to mid calf), Typically over malleoli
-Irregular border, shallow, exudative
-Mild/mod pain
-Telangiectasias, Varicose veins, edema, stasis dermatitis (Erythematous Eczematous Patches)

2. Arterial Ulcer:
-Peripheral artery dx (atherosclerotic stenosis)
-Location = Distal toes, anterior shin, pressure points
-Symmetric + well-defined punched out appearance
-SEVERE PAIN
-signs of arterial insufficiency (cold, pale, atrophic skin w/ Hair loss + nail dystrophy), Absent Pulses

3. Neuropathic Ulcer:
-Peripheral neuropathy (Diabetic Foot)
-Location = Bony Prominences (Metatarsal heads, heel)
-Hyperkeratotic edge w/ undermined borders
-Absent pain (NO PAIN)**
-Claw toes, Charcot Joints, Absent Reflexes

Miscellaneous Skin Disorders:

1. Acanthosis Nigricans:
-Epidermal Hyperplasia = symmetric, hyperpigmented thickening of skin (axilla, or neck)
-Associated w/ **Insulin resistance** (DM, Obesity, Cushing Syndrome, PCOS) or **Gastric Adenocarcinoma**

2. Actinic Keratosis:
-Premalignant lesions from sun exposure
-small, rough, erythematous/brownish papules or plaques
-Risk of SCC is proportional to degree of epithelial dysplasia

3. Erythema Nodosum: "Not the same as Multiforme"
-painful, raised inflammatory lesions of SQ fat (Panniculitis)
-usually anterior Shins + idiopathic
-Associated w/ Sarcoidosis, Coccidioidomycosis, Histoplasmosis, TB, Strep, Leprosy, IBD

4. Lichen Planus:
-Pruritic, Purple, Polygonal, Planar, Papules, and Plaques (6 P's)
-Mucosal involvement manifests as Wickham Striae (Reticular white lines) + Hypergranulosis
-Sawtooth infiltrate of Lymphocytes at Dermal-Epidermal Junction
-Associated w/ Hep C

5. Pityriasis Rosea: (NOT the same as Roseola = HHV-6/7)
-"Herald Patch" = followed days later by scaly erythematous plaques in a "Christmas Tree" Distribution on Trunk
-Multiple pink plaques w/ Collarette Scale
-Self-resolving in **6-8 weeks**

6. Sunburn:
-Acute cutaneous inflammatory rxn due to excessive UV irradiation
-causes DNA mutations, inducing apoptosis of keratinocytes
-UVB is dominant in SunBurn, UVA in tAnning and photoAging
-exposure to UVA and UVB risk of skin cancer

Burn Estimation: "Rule of 9's"
-entire head = 9%
-entire torso = 18%
-entire arm = 9% (18% for both)
-entire abdomen = 18%
-Perineum = 1%
-Entire leg = 18% (32% for both)

Superficial Burns:
-epidermis only
-similar to sunburn; localized, dry, blanching redness w/ no blisters
-Painful

Superficial Partial-Thickness Burn:
-epidermis + papillary dermis
-Blisters, blanches w/ pressure, swollen, warm
-Painful to temp and air

Deep Partial thickness burn:
-epidermis + reticular dermis
-blisters (easily unroofed), does not blanch w/ pressure
-PainLESS; perception of pressure only

Full-thickness Burn:
-epidermis and full-thickness dermis
-white, waxy, dry, inelastic, leathery, does not blanch w/ pressure
-PainLESS = perception of deep pressure only

Deep Injury Burn:
-Epidermis, dermis, and involvement of underlying tissue (Fascia, Muscle)
-white, dry, inelastic, does not blanch w/ pressure
-painLESS; some perception of deep pressure

Skin Cancer:
-Sun exposure strongly predisposes to skin cancer

1. Basal Cell Carcinoma;
-Most common skin cancer
-found in sun-exposed areas of body (Face)
-locally invasive, but rarely metastasizes
-Waxy, Pink, Pearly Nodules, w/ Telangiectasias, rolled borders, central crusting or ulceration
-Nonhealing ulcers w/ infiltrating growth or Scaling Plaque (superficial)
-**Palisading (Aligned) Nuclei**
-Basal Cell Carcinoma = more common above Upper Lip

2. Keratoacanthoma:
-middle-aged + elderly
-rapidly growing, resembles SCC
-Presents as DOme-shaped nodule w/ Keratin-Filled Center
-Grows rapidly (4-6 weeks) and may Spontaneously Regress

3. Melanoma:
-Common tumor w/ significant risk of Metastasis
-**S-100 tumor marker**
-Associated w/ Dysplastic Nevi (Moles); People w/ Lighter skin tones are at risk
-Depth of Tumor (**Breslow Thickness**) = correlates w/ risk of mets
-ABCDE's
- Asymmetry
- Border irregularity
- Color variation
- Diameter > 6 mm
- Evolution over time

-4 Different types:
- **Superficial Spreading**
- **Nodular**
- **Lentigo Maligna**
- **Acral Lentiginous** (Highest prevalence in people w/ Dark skin tones - soles/palms)

-Activating Mutation in **BRAF Kinase**
-Primary Tx = excision w/ wide margins
-Advanced melanoma Tx w/ Immunotherapy (Ipilumumab) and BRAF inhibs (Vemurafenib)

4. Squamous Cell Carcinoma (SCC):
-2nd most common skin cancer
-Associated w/ **immunosuppression**, Chronic non-healing wounds, occasionally Arsenic Exposure
-Appears on Face, Lower Lip, Ears, Hands
-Locally invasive, may spread to lymph nodes and will Rarely metastasize
-Ulcerative Red Lesions
-Histo = "**Keratin Pearls"**
-SCC = more common below lower lip

APAP:

- Reversibly inhibits Cyclooxygenase (mostly in CNS), inactivated peripherally
- Overdose produces hepatic necrosis (NAPQI) = depletes glutathione + forms toxic tissue byproducts in liver
- N-acetylcysteine (NAC) is antidote = regenerates Glutathione

ASA:

- NSAID that irreversibly inhibits Cyclooxygenase (COX-1 and COX-2) by covalent acetylation → synthesis of TXA2 + PGs
- bleeding time
- No effect on PT, PTT
- Effects lasts until new platelets are produced
- Low dose (< 300 mg/day) = platelet aggregation
- Higher doses = antipyretic and analgesic properties
- High high dose = anti-inflammatory
- Sxs = Gastric ulceration, tinnitus (CN VIII), allergic rxns (asthma and nasal polyp pts have it worse),
- Risk of Reye Syndrome (Kawasaki Vasculitis = only time we use it)
- Toxicity = Respiratory Alkalosis early → mixed metabolic acidosis-respiratory alkalosis
- OD = SodiumBicarb

Celecoxib:

- Selectively inhibits COX-2 (protecting gastric mucosa by avoiding COX-1 and spares platelet function as TXA2 production
- Risk of thrombosis, sulfa allergy

NSAIDs:

- COX-1, COX-2 inhibitor, blocking PG synthesis
- Used to close PDA
- Sxs = interstitial nephritis, gastric ulcer (PGs protect gastric mucosa), renal ischemia (PGs vasodilate afferent arteriole), Aplastic Anemia

Leflunomide:

- Mech = reversibly inhibits dihydroorotate dehydrogenase, preventing pyrimidine synthesis
- Suppresses T-cell proliferation
- Use = RA, Psoriatic Arthritis
- Sxs = Diarrhea, HTN, Hepatotoxicity, Teratogenicity

Bisphosphonates:

- Pyrophosphate analogs = bind hydroxyapatite in bone, inhibiting osteoclast activity
- Sxs = esophagitis, ONJ, Atypical Femoral Stress fractures

Teriparatide:

- Mech = recombinant PTH Analog (Osteoblastic activity when administered in pulsatile fashion)
- Use = Osteoporosis (causes bone growth compared to Antiresorptive therapies (Bisphosphonates)
- Sxs = risk of Osteosarcoma (avoid in pts w/ Paget Dx of Bone or unexplained elevation of Alk Phos)
- Avoid in pts who have had prior cancers or radiation therapy (Transient Hypercalcemia)

-LTB4 = neutrophil chemotactic agent
-PGI2 = inhibits platelet aggregation and promotes vasodilation

Purines → Hypoxanthine → Xanthine → Plasma uric acid → Urine (tubular secretion)

Allopurinol:
-competitive inhibitor of Xanthine Oxidase → conversion of Hypoxanthine and xanthine to Urate
-used in lymphoma and leukemia to prevent tumor lysis - associated urate nephropathy
- conc of Xanthine oxidase active metabolites, AZA and 6-MP

Pegloticase:
-recombinant uricase catalyzing uric acid to allantoin (more water-soluble product)

Febuxostat:
-inhibits Xanthine Oxidase

Probenecid:
-inhibits reabsorption of Uric Acid in PCT (also inhibits secretion of PCN)
-Can precipitate Uric Acid Calculi

Colchicine:
-binds and stabilizes tubulin to inhibit microtubule polymerization, impairing neutrophil chemotaxis and degranulation
-acute and prophylactic use
-GI neuromyopathic side effects, myelosuppression, nephrotoxicity

Etanercept:
-fusion protein (decoy receptor for TNF-a + IgG1 Fc)
“Etanercept Intercepts TNF”

References:

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