SKIN

INSTRUCTOR: Jessie Forcucci, MD; Associate Professor, Department of Pathology

forcucci@musc.edu

792-4702

OUTLINE:

- 1. Skin Terminology and Structure
 - a. Structure and anatomic components of normal skin
 - b. Microscopic terminology
 - c. Clinical terminology
- 2. Acute Inflammatory Dermatoses
 - a. Urticaria
 - b. Eczema / Spongiotic Dermatitis
 - c. Erythema Multiforme
 - d. Drug Reaction/Eruption
- 3. Infectious Dermatoses
 - a. Bacterial Infections
 - i. Impetigo
 - ii. Folliculitis
 - iii. Cellulitis and Necrotizing Fasciitis
 - b. Fungal Infections
 - i. Candidiasis
 - ii. Tinea Versicolor
 - iii. Dermatophytosis
 - iv. Deep Fungal Infections
 - v. Onychomycosis
 - c. Viral
 - i. Warts
 - 1. Verruca Vulgaris
 - 2. Verruca Plana
 - 3. Condyloma
 - ii. Herpetic Vesicles
 - 1. HSV
 - 2. VZV
 - iii. Molluscum Contagiosum
 - d. Scabies
- 4. Chronic Inflammatory Dermatoses
 - a. Lupus Erythematosus
 - b. Morphea
 - c. Psoriasis
 - d. Lichen Planus
 - e. Sarcoidosis
 - f. Lichen Simplex Chronicus / Prurigo Nodularis
 - g. Post-Inflammatory Pigment Alteration
- 5. Blistering Disorders
 - a. Pemphigus Vulgaris

- b. Pemphigus Foliaceus
- c. Bullous Pemphigoid
- d. Dermatitis Herpetiformis
- 6. Benign Neoplasms and Non-Melanoma Skin Cancer
 - a. Seborrheic Keratosis
 - b. Actinic Keratosis
 - c. Squamous Cell Carcinoma
 - d. Basal Cell Carcinoma
 - e. Merkel Cell Carcinoma
- 7. Melanocytic Proliferations
 - a. Melanocytic Nevi
 - b. Melanoma

OBJECTIVES: After studying this unit you should be able to:

- 1. Identify normal anatomic skin structures microscopically
- Understand the meaning of common clinical and microscopic terms used to describe skin lesions
- 3. Describe the characteristic clinical and microscopic features of:
 - a. acute inflammatory and infectious dermatoses
 - b. chronic inflammatory dermatoses
 - c. blistering disorders
 - d. benign epidermal neoplasms and non-melanoma skin cancer
 - e. melanocytic nevi and melanoma

READING REFERENCE:

- 1. Robbins Basic Pathology, 10th Edition: Chapter 24, Skin (pg. 889-908) [https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20140017194]
- 2. Andrews' Diseases of the Skin, 13th Edition [https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20160013402]
 - a. Chapter 5, Atopic Dermatitis, Eczema, and Noninfectious Immunodeficiency Disorders (pg. 63-91)
 - b. Chapter 6, Contact Dermatitis and Drug Eruptions (pg. 92-139)
 - c. Chapter 7, Erythema and Urticaria (pg. 140-156)
 - d. Chapter 8, Connective Tissue Diseases (pg.157-183)
 - e. Chapter 10, Seborrheic Dermatitis, Psoriasis, Recalcitrant Palmoplantar Eruptions, Pustular Dermatitis, and Erythroderma (pg. 191-204)
 - f. Chapter 12, Lichen Planus and Related Conditions (pg. 215-230)
 - g. Chapter 14, Bacterial Infections (pg. 252-290)
 - h. Chapter 15, Diseases Resulting from Fungi and Yeasts (pg. 291-323)
 - i. Chapter 19, Viral Diseases (pg. 362-420)
 - j. Chapter 20, Parasitic Infestations, Stings, and Bites (pg. 421-452)

- k. Chapter 21, Chronic Blistering Dermatoses (pg. 453-474)
- I. Chapter 29, Epidermal Nevi, Neoplasms, and Cysts (pg. 636-685)
- m. Chapter 30, Melanocytic Nevi and Neoplasms (pg. 686-703)
- 3. Andrews' Diseases of the Skin Clinical Atlas

[https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20130186102]

- a. Chapter 5, Atopic Dermatitis, Eczema, and Noninfectious Immunodeficiency Disorders (pg. 53-64)
- b. Chapter 6, Contact Dermatitis and Drug Eruptions (pg. 65-85)
- c. Chapter 7, Erythema and Urticaria (pg. 87-99)
- d. Chapter 10, Seborrheic Dermatitis, Psoriasis, Recalcitrant Palmoplantar Eruptions, Pustular Dermatitis, and Erythroderma (pg. 125-138)
- e. Chapter 14, Bacterial Infections (pg. 185-202)
- f. Chapter 15, Diseases Resulting from Fungi and Yeasts (pg. 203-227)
- g. Chapter 19, Viral Diseases (pg. 263-289)
- h. Chapter 20, Parasitic Infestations, Stings, and Bites (pg. 291-307)

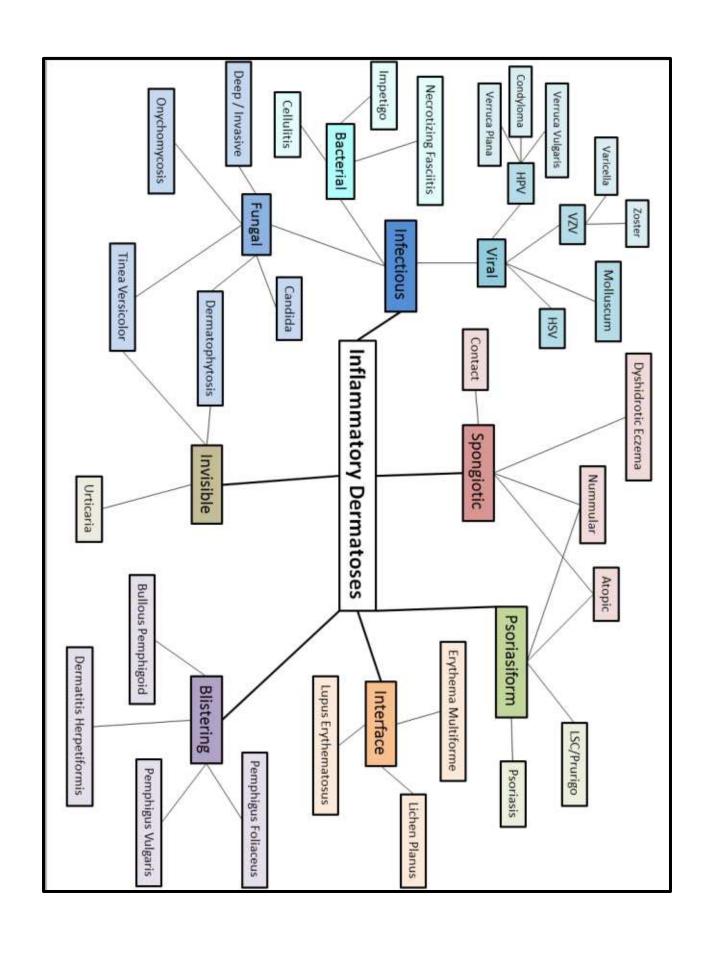
SKIN STUDY GUIDE

Terminology

Pathologic Terms		
Hyperkeratosis	Thickened cornified layer	
Acanthosis	Epidermal hyperplasia/thickening	
Papillomatosis	Surface elevation due to hyperplasia of dermal papillae	
Spongiosis	Epidermal intercellular edema	
Acantholysis	Lysis/disruption of intercellular keratinocyte adhesive junctions	
Dyskeratosis	Abnormal, premature keratinization	
Exocytosis	Lymphocytes migrating into epidermis	

Clinical Terms			
Macule	Circumscribed, flat lesion	< 5 mm	
Patch	Circumscribed, nat lesion	> 5 mm	
Papule		< 5 mm	
Nodule	Elevated, dome shaped lesion	> 5 mm	
Plaque	Elevated, flat topped lesion	> 5 mm	
Vesicle	Fluid filled blister	< 5 mm	
Bulla	Fluid Illied blister	> 5 mm	
Pustule	Raised, discrete, pus-filled lesion		
Wheal	Pruritic, elevated lesion with variable blanching and erythema		
Erosion	Loss of portion or the entire epidermis (heals without scar)		
Ulcer	Loss of epidermis and portion of dermis (heals with scar)		
Excoriation	Traumatic, self-inflicted break in skin due to scratching		
Lichenification	Thickened, rough skin due to chronic rubbing/scratching		
Crust/Scab	Dried serum, pus, blood, and epithelial debris		
Scale	Laminated or plate-like mass of keratin due to abnormal keratinization		

Common Terms		
Dermatitis	Inflammation of skin (epidermis/dermis)	
Folliculitis	Inflammation of hair follicle	
Vasculitis	Inflammation of vessels	
Hidradenitis	Inflammation of sweat glands	
Panniculitis	Inflammation of subcutaneous fat	
Alopecia	Decreased/absent hair	



Skin Appendix COM Flex Curriculum

Additional quick synopsis of various dermatologic conditions for those who are interested. For further information, the books below (available through MUSC library) are all wonderful resources.

Additional Resources:

Andrews' Diseases of the Skin, 13th Ed.

(https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20160013402)

Andrews' Diseases of the Skin Clinical Atlas, 2nd Ed. (https://www-clinicalkey-com.ezproxy-v.musc.edu/#!/browse/book/3-s2.0-C20190003032)

Dermatology, 4th Ed. (https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20131144449)

Dermatology Atlas for Skin of Color

(https://link.springer.com/book/10.1007%2F978-3-642-54446-0)

Dermatopathology, 3rd Ed.

(https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20150040916)

Weedon's Skin Pathology, 5th Ed.

(https://www.clinicalkey.com/#!/browse/book/3-s2.0-C20170008388)

General

Describing a dermatologic process

- Color
 - Pink, red, purple/violaceous, yellow, salmon
 - · Depigmented, hypopigmented, hyperpigmented
- Morphology
 - Size and topography
 - Secondary changes: excoriation, crust, erosion/ulceration, atrophy, lichenification
- Distribution
 - Location: generalized/diffuse, localized, symmetric, extensor, flexural, intertriginous, acral, photo
 - Grouping and configuration: corymbiform, concentric, linear, agminated, annular, arcuate, gyrate, polycyclic, serpiginous, guttate, nummular, linear, sporotrichoid, dermatomal, blaschkoid

Morphology

Flat

Elevated

Blister

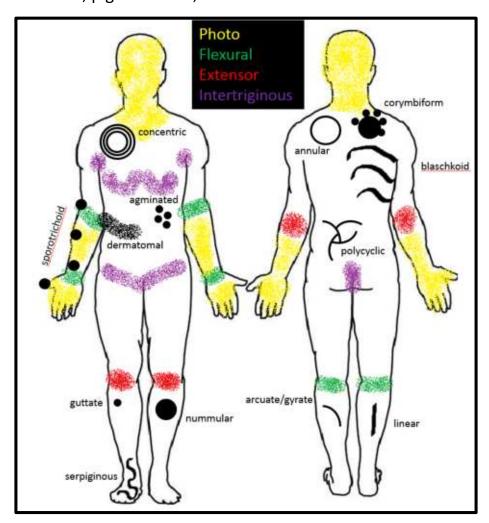
Term

macule $\rightarrow \rightarrow$ patch

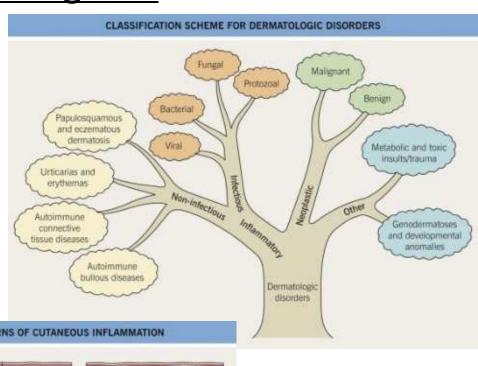
vesicle $\rightarrow \rightarrow$ bulla

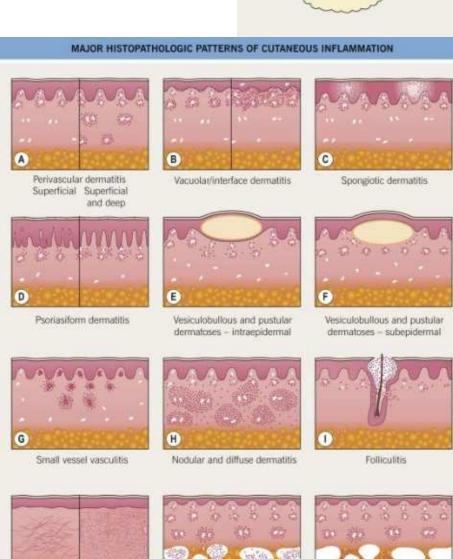
papule $\rightarrow \rightarrow$ plaque/nodule

- Evolution/Involution
 - Polymorphous vs uniform
 - Residual scar, pigmentation, etc.



Classification/Categories





Lobular panniculitis

Septal panniculitis

Fibrosing dermatitis

Physical/Environmental

Thermal Burns

- Type of burn and body surface involved are important for prognosis
- Scarring may lead to deformities, contractures, and increased risk of SCC

Туре	Description
First degree	Erythema and vascular congestion → desquamation Pain and increased surface heat Example: sunburn
Second degree	Superficial: edema, vesicle and bullae formation Recover without scarring Deep: pale, anesthetic, involves dermis → scarring ~1 month to heal
Third degree	Involves entire dermis and some subcutis, complete loss of skin appendages Ulcerated wound → scar (requires graft) + constitutional symptoms
Fourth degree	Involves skin, subcutis, and underlying tendons Constitutional symptoms (requires graft)

Miliaria

- Occlusion of eccrine ducts → increased pressure due to sweat production → rupture and sweat extravasation
- · Common in hot, humid climates



Erythema Ab Igne

Reticulated erythema or pigmentary alteration due to prolonged heat exposure (sitting by fire, heating pad, laptop / electronics)



Radiation Dermatitis

Acute and chronic changes; vary based on dose and length of exposure



crac Child

Perniosis/Chilblains

Erythema and swelling of toes, fingers, ears following exposure to cold, damp environment Predisposing factors: poor circulation, cryoglobulins, crack cocaine, lupus erythematosus

Child wears snow boots during school day after walking to school in snow, lateral thighs in female equestrians riding on cold day



Phytophotodermatitis

- Phototoxic reaction due to contact with plant furocoumarin and UVA exposure
- Vesicles and bullae form several hours after exposure → hyperpigmentation
- Common phototoxic plants: dill, fennel, fig, carrot, lime, bergamot, mustard, parsley, celery

Eruption on hands following day at beach/on boat drinking corona with lime

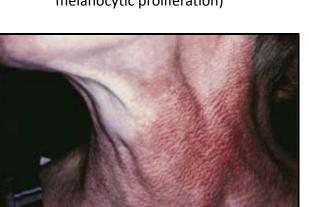


Image Source: Andrews' Diseases of the Skin, 13th ed

Physical/Environmental

Actinic Injury

- Sunburn (solar erythema): caused by UVB
 - Acute reaction to excessive sunlight exposure
 - Develops within 6 hours, may become tender and blister depending on severity → peaks at 24 hours → desquamation 1 week later
 - Increased UV exposure at higher altitudes, summer months in temperate climates, closer to equator, middle of day (9 am-4 pm)
 - Minimal treatment options available, prophylaxis is best
- Freckle (ephelis) and Lentigo (sun/age spots)
 - Brown macules on sun-exposed skin
 - More prominent with increased sun exposure
 - Freckles usually appear in childhood, lentigines usually appear in late adulthood
 - Increased production of melanin pigment (not a melanocytic proliferation)



poikiloderma of Civatte



dermatoheliosis





Solar lentigines

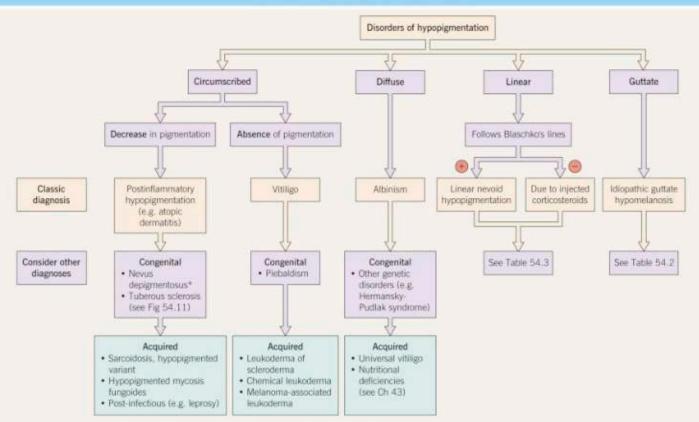
- Photoaging (dermatoheliosis)
 - Long-term excessive sun exposure (accelerated by cigarette smoking)
 - Most prominent on chest, neck, face, hands
 - Skin appears atrophic and wrinkled with uneven pigmentation
 - Microscopically, solar elastosis is evidence of chronic sun damage



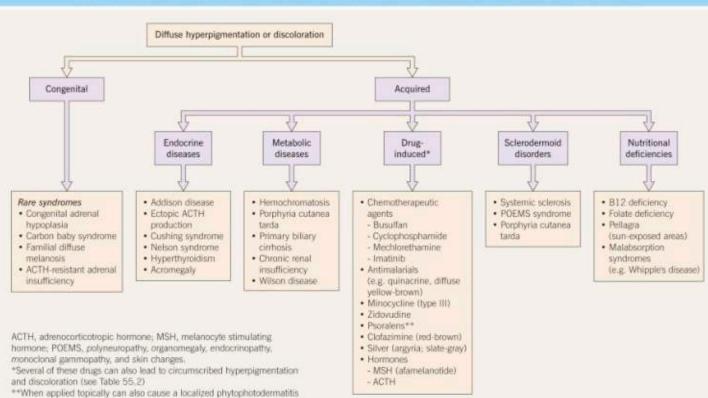
cutis rhomboidalis nuchae

<u>Pigmentation Disorders</u>



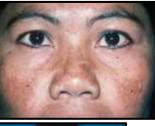


DIFFERENTIAL DIAGNOSIS AND CLINICAL APPROACH TO THE PATIENT WITH DIFFUSE HYPERPIGMENTATION OR DISCOLORATION



Pigmentary Disorder	s
Post-inflammatory pigment alteration	Hyper- or hypopigmentation due to inflammatory condition
Melasma	Brown patches on malar cheeks and forehead Predisposing factors: sun exposure, female hormones, and Fitzpatrick skin types IV and V Tx: sunscreen, bleaching creams, tretinoin
Vitiligo	Acquired, autoimmune depigmenting condition Localized, segmental, generalized, universal, acrofacial, and mucosal patterns Symmetric depigmented macules and patches Increased risk of other autoimmune conditions Tx: light therapy, topical steroid and steroid-sparing agents, systemic immunosuppressive agents
Peutz-Jeghers	Hyperpigmented macules on lips and oral mucosa GI polyposis
Albinism: reduced or absent melanin in skin, hair, and	Oculocutaneous albinism 7 types (may also have ↓ visual acuity) Autosomal recessive
eyes	Chediak-Higashi Syndrome Partial oculocutaneous albinism with giant granules (defective platelets, recurrent infections) Autosomal recessive
	Hermansky-Pudlak Syndrome Oculocutaneous albinism, defective platelets, interstitial lung disease Autosomal recessive (个in Puerto Ricans)
Piebaldism	White forelock and depigmented patches (congenital) Autosomal dominant
Drug Induced	Chemotherapy, antimalarials, heavy metals, OCP, amiodarone, AZT, clofazimine, diltiazem, minocycline
	Cit all call t















Hair

Hirsutism: male pattern hair growth in females



Hypertrichosis: ↑ hair

Alopecia: loss of hair

Categorized based on presence/absence of:

- Scarring
- Inflammation

Scarring

*CCCA: central centrifugal cicatricial alopecia



CCCA

Progressive scarring alopecia starting at crown in AA females



Traction

Due to prolonged tension from braids, ponytail, etc.; involves periphery of scalp with preserved frontal/temporal



Trichotillosis

Compulsive pulling/plucking hair Irregular patches and broken hair +/- trichophagia → bezoar



Pattern/Androgenetic

Female and male patterns May begin anytime after puberty Related to androgens



Telogen Effluvium

Excessive shedding (too many in telogen phase) Physical/psychological stressor 3-5 months prior

Hair Cycle

- Anagen phase: growing, 2-6 years
- Catagen phase: transition, 1-2 weeks
- Telogen phase: resting, 3-5 months
- Hair sheds/falls out

≈90% of scalp hair is in anagen phase Grows about 0.37 mm/day

Types

Lanugo: fine hair covering fetus

Terminal: coarse, thick hair (scalp, male face)

Vellus: fine, lighter colored (body)



Discoid LE

Erythema, follicular plugging **PIPA**



Lichen Planopilaris

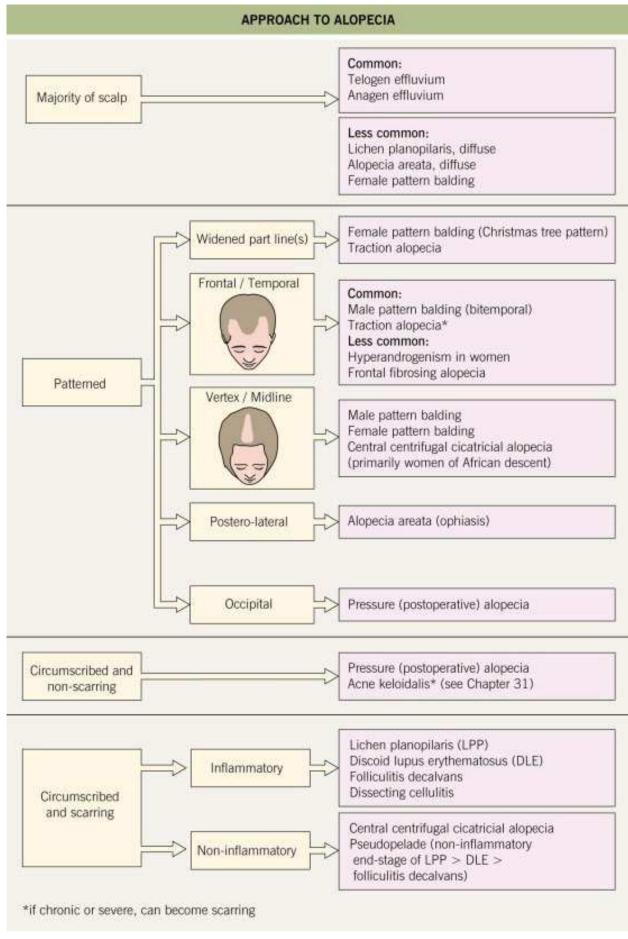
Perifollicular erythema Patches of progressive scarring



Alopecia Areata

Rapid, complete loss of round-oval patches Hx of regrowth, exclamation point hairs +/- nail pitting





Eczema

Atopic Dermatitis

Chronic, pruritic dermatitis often associated with other atopic conditions Presentation varies with age

Major Diagnostic Criteria (three of following):

- Pruritis
- Typical morphology and distribution
- Chronic or relapsing
- Personal or family history of atopic disease

Minor Diagnostic Criteria (three of following):

- Xerosis
- Perifollicular accentuation
- Ichthyosis/hyperlinear palms/keratosis pilaris
- Hand/foot dermatitis
- Nipple eczema
- Dennie-Morgan infraorbital fold or orbital darkening
- Facial pallor/erythema
- Pityriasis alba

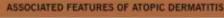
- Itch when sweating
- · Early age of onset
- Course influenced by environment or emotions
- · Tendency for cutaneous infections
- Intolerance to wool and lipid solvents
- Cheilitis
- Eyes: Recurrent conjunctivitis, keratoconus, or anterior subcapsular cataracts
- IgE reactivity or elevated serum IgE
- Food hypersensitivity

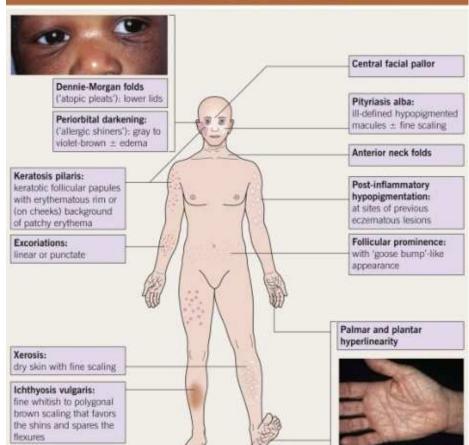
White dermatographism / delayed blanch to

cholinergic agents



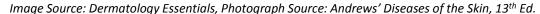






Treatment

- Education
- Barrier repair: gentle skin care, daily moisturization, limit hot water and scrubbing
- Antimicrobial therapy for infection
- Antihistamines for pruritis
- Topical corticosteroids and calcineurin inhibitors
- Phototherapy
- Systemic therapy: Dupilumab (IL-4 receptor inhibitor), corticosteroids, cyclosporine, methotrexate



DISTRIBUTION PATTERNS OF ATOPIC DERMATITIS AND REGIONAL VARIANTS Infantile atopic dermatitis Most common sites Other frequently involved sites Childhood and adolescent atopic dermatitis Head and neck dermatitis: Ear eczema: Erythema, scaling and fissuring primarily of face and neck after puberty; under earlobe and/or in may be triggered by retroauricular region, ± Malassezia overgrowth bacterial superinfection Eyelid eczema*: Nipple eczema: often has prominent exacerbated by rubbing of lichenification clothing (e.g. in joggers/ athletes) Dryness (chapping) of vermilion lips, ± peeling, Frictional lichenoid fissuring, angular cheilitis eruption: multiple, small, flat-Erythema and scaling topped pink to skin surrounding vermilion colored papules on lips, often due to irritation elbows > knees, from licking (lip licker's classically in atopic boys eczema) in spring/summer Dyshidrotic eczema: Prurigo-like lesions: deep-seated vesicles firm, dome-shaped favoring sides of fingers papulonodules with and palms central scale-crust, favoring extensor Juvenile plantar extremities dermatosis: glazed erythema, scaling Atopic hand eczema*: and fissuring of plantar often superimposed forefeet irritant contact dermatitis Most common sites Nummular lesions†: Other sites of predilection coin-shaped eczematous plaques, often with Specific variants oozing/crusting, favoring extremities

Eczema

Eyelid Dermatitis

Often related to atopic dermatitis or contact dermatitis Female>male

Thin skin is sensitive to airborne substances and transfer from hands Fragrance, nail polish, etc.



Nipple Eczema

Areola and surrounding skin

More common in women and infants

Atopic dermatitis, breastfeeding, contact dermatitis, friction (jogger's nipple)

r/o Paget disease



Hand Dermatitis

Very common, may be associated with atopic dermatitis 80% of occupation dermatitides

Components of contact dermatitis should be assessed

Consider: environmental allergens, topical medications, frequency of "wet" work (skin contact with liquid or in gloves, frequent hand washing), occupational chemical/allergen exposure

Tx: vinyl gloves +/- white cotton gloves underneath, moisturizing, topical steroids, phototherapy







Xerotic Eczema (Asteatoic Eczema, Eczema Craquele)

Dry, red skin ("winter itch")
Red, scaly patches with fine cracks in epidermis
Extensor extremities, flank
Common in elderly and during winter
Tx: gentle skin care, barrier repair



Nummular Eczema

Discrete, coin-shaped, erythematous, pruritic patches (2-4 cm) Lower legs, dorsal hands, extensor arms

Tx: topical corticosteroids or calcineurin inhibitors, antihistamine, phototherapy



Acneiform Disorders

Acne Vulgaris

Common condition of teenagers and young adults; face and upper trunk; mild – severe presentations, and may have associated systemic symptoms

May lead to post-inflammatory pigment alteration or scarring

Variants:

- Non-inflammatory: open and closed comedones
- Inflammatory: erythematous papules and pustules, nodules, and cysts
- Hormonal: predominantly adult females; may have hyperandrogenism and frequently have flares related to menstrual cycle (lower face, jawline, and neck)
- Acne excoriee: predominantly teenage girls and young women; picking leads to crusted erosions and scarring
- Acne mechanica: comedone formation due to friction or occlusion
- Acne cosmetica: comedone formation due to follicle occluding cosmetic products (hair products, makeup, occupational exposures)
- Acne fulminans: predominantly teenage boys; abrupt onset of inflammatory nodules on face and trunk that may coalesce with systemic symptoms
- Neonatal acne: 2 weeks 3 months; papules and pustules without comedones
- Infantile acne: 3 months 2 years; comedones, papules, pustules, and cysts

Therapeutic Options (consider severity, distribution, type, and patient preference):

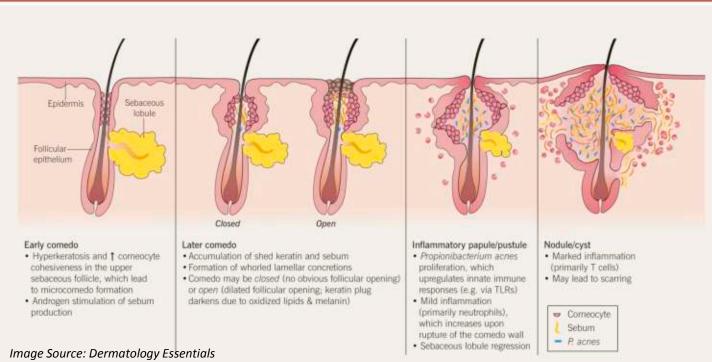
- Topical retinoids (tretinoin, adapalene, tazarotene): at least 3-4 weeks use before response, predominantly comedolytic
- Topical antimicrobials (benzoyl peroxide, clindamycin, erythromycin): reduces bacterial burden
- Oral antibiotics (tetracyclines): antibacterial and anti-inflammatory, 3-6 months
- Oral contraceptives and spironolactone: hormonal acne
- Oral isotretinoin: 4-6 months to reach target cumulative dose of 120-150 mg/kg
- Other options: lifestyle modification, azaleic acid, salicylic acid, topical dapsone, intralesional steroid







PATHOGENESIS OF ACNE



Acneiform Disorders

Rosacea

Typically begins in 4th decade with variable severity; central face Variants:

- Erythematotelangiectatic: flushing/blushing → central facial erythema, telangiectasia
- Papulopustular: papules and pustules
- Phymatous: irregular thickening of nose (bulbous)
- Ocular: telangiectasia, periorbital edema, blepharitis, recurrent styes, keratitis
- Rosacea fulminans

Treatment (consider severity and type): topical antibiotic, azelaic acid, oral tetracycline, oral isotretinoin, laser, surgical excision/electrosurgery







Periorificial Dermatitis

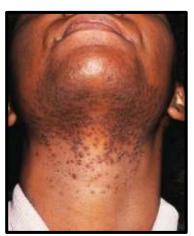
Children and adults
Pink papules and small pustules around orifices (commonly mouth and nose)
Exacerbated by topical steroids



Deep Folliculitis

Firm tender papules and nodules

"follicular occlusion tetrad": hidradenitis suppurativa, dissecting cellulitis, acne conglobate, pilonidal sinus



Pseudofolliculitis barbae



Acne keloidalis nuchae



Hidradenitis suppurativa

Genodermatoses and Congenital

AL ST	Disease	Inheritance	Dermatologic Presentation
	Neurofibromatosis Type 1	Autosomal dominant	≥ 6 café au lait macules, axillary/inguinal freckling, neurofibromas, Lisch nodules
	Noonan Syndrome	Autosomal dominant	Lymphedema, short curly hair, dystrophic nails, keloid formation, elastic skin, ulerythema of eyebrows, granular cell tumors, abnormal dermatoglyphs, café au lait macules
1.	LEOPARD Syndrome	Autosomal dominant	Lentigines, EKG abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, Retardation of growth, Deafness
	Proteus Syndrome	Autosomal dominant	Disproportionate, asymmetric overgrowth, epidermal nevi, vascular malformations, CT nevi
1	Tuberous Sclerosis	Autosomal dominant	Fibromas, shagreen patches, ash- leaf macules, café au lait macules, dental pits,
	Xeroderma Pigmentosum	Autosomal recessive	Extreme photosensitivity → freckling and skin cancer (defective DNA thymidine dimer repair)
	Bloom Syndrome	Autosomal recessive	Photosensitivity, malar telangiectasia, dwarfism, cataracts
=0	Rothmund- Thomson Syndrome	Autosomal recessive	Poikiloderma, photosensitivity, skin cancer
1	Gorlin-Goltz Syndrome	Autosomal dominant	BCC, palmar/plantar pits, hypertelorism, frontal bossing
	Reed Syndrome	Autosomal dominant	Multiple leiomyomas

Genodermatoses and Congenital



Disease	Inheritance	Dermatologic Presentation
Incontinentia Pigmenti	X-linked dominant	Vesicular, verrucous, and pigmentary stages with Blaschkoid distribution
Epidermolysis Bullosa	variable	Group of disorders; skin fragility and blistering due to physical injury
Hailey-Hailey Disease	Autosomal dominant	Recurrent vesiculobullous dermatitis of neck, axillae, and flexures
Ichthyoses	Variable	Disorders of keratinization leading to various types of scale
Darier Disease	Autosomal dominant	Brown papules in seborrheic distribution, nail changes, verrucous papules on hands and shins
Ectodermal Dysplasia	Variable	Group of disorders where components of the skin are absent, abnormal, or incomplete









