

Dermatology Lecture List

- 1. Introduction**
- 2. Eczematous Dermatitis & Urticaria**
- 3. Common Dermatologic Problems**
- 4. Path of Inflammatory Skin Disease**
5. Pathophysiology of Non-Melanoma Skin Cancer
6. Blistering Disorders
7. Nevi and Malignant Melanoma

Definitions

Primary Lesions	<i>Initial (and sometimes the only) manifestation of skin disorder</i>
Macule	flat lesion, can be any shape, size, or color, can't palpate!
Papule ↔ Plaque	raised lesion, any shape or color. 1 cm is the cutoff (papule is smaller)
Nodule	spherical-ish lesion from dermis or subQ fat. If large = "tumor"
Wheal	= "hive" round lesion results from edema in dermis
Bulla ↔ Vesicle	blister. 1 cm is the cutoff (bulla is smaller)
Pustule	a bulla or vesicle filled with pus
Secondary Lesions	<i>Δ's in skin which are superimposed upon or occur subsequently to primary lesions</i>
Erosion	all or part of epidermis is lost. heals WITHOUT scarring (dermis not involved)
Ulcer	hole in skin: loss of full thickness of epidermis + part/all of dermis. heals WITH scarring
Excoriation	linear erosion from scratching
Fissure	crack/split in skin
Scale	thick stratum corneum
Crust	scab: dried stuff
Atrophy	thinning of skin. generalized: physiologic aging; or localized: stretch marks
Lichenification	thickening of skin. exaggeration of normal skin markings, results from repeated rubbing or scratching
Arrangement of Lesions	
Linear	curved (just kidding)
Annular	ring-shaped
Serpiginous	wandering or twisting, like a snake
Herpetiform	tight clustering of lesions heaped on top of on another; taken from the fashionable style of paris herpes
Dermatomal	lesions in a dermatome: shingles!

O2: Eczematous Dermatitis & Urticaria

Atopic Dermatitis

Definition

Atopic Dermatitis (AD) = chronic pruritic inflammation of skin associated with allergy
Eczema = often used synonymously with AD, but it technically means a specific reaction pattern of erythema, scaling, and vesicles; can have many causes

acute: erythema, vesicles, edema, serous exudate

chronic: lichenification, scale, hyperpigmentation

Pathophysiology

Complicated: involves T cells, Langerhans cells, Eos, keratinocytes, cytokines, IgE

Type I HSR: ↑ IgE in most. IL-4 may play major role in causing ↑ IgE (IL-4 inhibits IFN- γ)

Immunology review: dependent on which cytokines are present, Th0 are driven towards Th1 (IL-12) or Th2 (IL4)

IL-4 stimulate B cells to make IgE

Aeroallergens: seasonal variation, + test to skin dust in most patients

Hyperresponsive Langerhans cells and T cell activation

Defective epidermal barrier: ↓ ceramides → ↑ penetration of irritants, allergens, and microbes

S. aureus: up to 90% colonization; anti-staph antibiotics leads to rapid response

Food: Specific food elimination (nuts, etc) may be useful with severe AD, but not much of a difference in mild/moderate cases.

Defective cell-mediated immunity: pts susceptible to viral and fungal skin infections

due to ↓ epidermal barrier and lack of β defensins in skin

Over 2/3 have family or personal history of atopy (allergy)

Clinical

60% get AD in first year of life; only 10% get it between the ages of 6-20

Pruritis is universal feature: **itch** → **rash**
dry skin

Skin

poorly-demarcated, erythematous, scaly plaques
oozing, excoriations, crusts

lichenification (if chronic)

any area can be affected, but distribution varies with age, typically in flexor creases

Associated Findings

ichthyosis vulgaris: fish-like scaling

pyriasis alba: scaly hypopigmented plaques

dennie-morgan sign: infraorbital eyelid folds

follicular prominence

hyperlinear palms

Histopathology

not needed for diagnosis

acanthosis: thickened epiderms

spongiosis: intraepidermal intercellular edema
dermal infiltrate of lymphs, monocytes, mast cells

Course

60% spontaneous remission by age 5

95% remission by age 20

Treatment

hydration: no soap

topical anti-inflammatory agents (corticosteroids)

topical calcineurin inhibitors

calcineurin is a protein phosphatase that activates IL-2 transcription

IL-2 ↑ growth and differentiation of T cells

calcineurin is inhibited by pimecrolimus, tacrolimus, and cyclosporine

may ↑ risk of skin cancer and lymphoma

antihistamines

antistaph antibiotics (topical or systemic)

Contact Dermatitis

Definition

An acute, subacute, or chronic inflammation of epidermis and dermis caused by external agents

two types

primary irritant: something irritates the skin directly. Not immune-mediated.

allergic: Type IV HSR

Etiologic Agents

allergic dermatitis:

poison ivy, oak, etc. → contain Rhus antigen
nickel

most allergens are haptens

irritant dermatitis:

frequent hand washing, diaper contents

Clinical

pruritis/burning of skin

delayed onset of 7-10 days in allergic dermatitis (but with repeated exposure, can be accelerated to 12 hrs)

Skin

acute: erythema, edema, vesicles, erosions

subacute: mild erythema, less vesiculation, some thickening

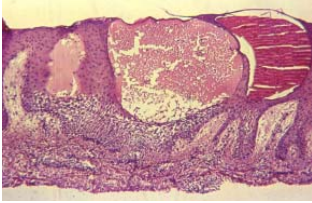
chronic: lichenification, hyperpigmentation, scale, excoriations, NO vesicles

lesions are localized to areas that were exposed to irritant

O2: Eczematous Dermatitis & Urticaria

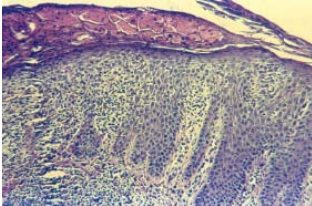
Histopathology

acute: spongiosis in epidermis, vesicles and lymphocytes in dermis



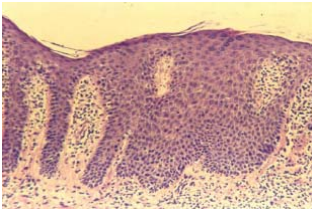
intraepidermal vesicles, spongiosis, mixed perivascular infiltrate in upper dermis

subacute: acanthosis and scale/crust

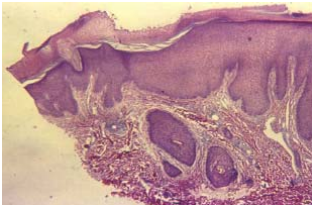


less epidermal edema, but exocytosis, scaling, crust

chronic: psoriasiform epidermal hyperplasia, parakeratosis, dermal fibrosis



minimal edema, but acanthosis, parakeratosis



lichen simplex chronicus: pronounced acanthosis and hyperkeratosis

irritant dermatitis has more superficial vesicles and PMN's compared with allergic

Lab

patch test: apply allergen to skin

Treatment

antihistamines, topical (or systemic if severe)
corticosteroids, dressings

Urticaria and Angioedema

Definition

Urticaria (Hives) = pruritic eruption of transient edematous papules and plaques called wheals.

Angioedema = large edematous plaques of the dermis and subcutaneous tissue

Types

IgE-mediated

complement-mediated

physical (vibration, cold)

mast cell degranulators (morphine, etc)

hereditary angioedema: ↓ C1 inactivator

C1 is always active → continues to generate vasoactive C3a & C5a →

↑ capillary permeability

Treat with Danazol (↑ concentration C1 inactivator)

Pathophysiology

Most IgE mediated

complement-mediated urticaria triggered by immune complexes → anaphylatoxin release → mast cell degranulation

Clinical

pruritic lesions that last hours rather than days
wheals occur within 36 hours after challenge with causative agent

angioedema → swelling of mucous membranes involving larynx, can compromise airway

Skin

wheals can have multiple shape, size

dermographism: a linear wheal with flare occurs where skin is stroked with a firm object

Histopathology

edema of dermis and subq tissue

infiltrate is eosinophil-rich if IgE mediated or PMN-rich of complement mediated

Course

new lesions may develop for weeks after offending agent removed

only 50% of patients are free of the problem in 1 year

hereditary angioedema can be fatal

Treatment

antihistamines are mainstay of therapy

symptomatic: cool bath, antipruritic lotions

epinephrine for laryngeal edema & anaphylaxis

danazol for hereditary angioedema

03: Common Skin Disorders: Acne, Warts, Psoriasis, Seborrheic Dermatitis

Acne

Definition: disease of pilosebaceous follicle

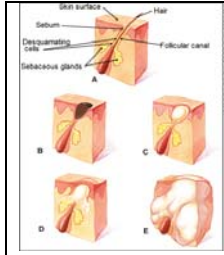
pathognomonic lesion: comedo

Pathophysiology

pilosebaceous follicle is a special type of hair follicle that produces a tiny vellous (fine) hair

a big sebaceous gland is attached to the follicle
→ produces sebum (TGL's)

How acne happens



A: normal follicle
B: open comedo (blackhead)
C: closed comedo (whitehead)
D: papule
E: pustule

1) Microcomedo formation

At puberty, infundibular orifice of the pilosebaceous follicle gets narrowed due to retention hyperkeratosis, resulting in a **microcomedo**

"retention hyperkeratosis" = accumulation of plates of keratin in lumen

genetics and FFA in follicle promote this process
microcomedo = plug of keratin

If microcomedo enlarges

→ forms **macrocomedo = open comedo = blackhead**

If microcomedo doesn't enlarge → plug allows sebaceous secretion in follicle

→ **closed comedo = whitehead**

2) sebaceous gland secretion (↑ by androgens)

3) Propionibacterium acnes: anaerobic, G+

P. acnes loves sebum → makes FFA → further stimulation of retention hyperkeratosis

P. acnes is chemoattractive to PMN's

4) Neutrophils

PMN's release proteolytic enzymes → whole mess is extruded into dermis →

inflammatory papule → **pustule**

(superficial abscess in dermis)

inflammatory nodule results when inflammatory infiltrate and abscess in region of sebaceous gland → seen in **nodulocystic acne**

Treatment

1) treat retention hyperkeratosis

tretinoin (retin-A) and adapalene (differin) are vitamin A analogues: ↓ keratin
→ no microcomedo formation

most important (earliest in pathogenesis)

peeling agents (sulfur-salicylic acid) peel retained keratin from follicle infundibulum

2) treat sebum secretion

isotretinoin (accutane) is systemic vit A derivative (13-cis-retinoic acid)

causes irreversible squamous metaplasia of sebaceous glands

turns off all sebum secretion

⚠ extremely teratogenic!

antiandrogens (estrogens, glucocorticoids, flutamide, spironolactone)

ortho tricyclen was approved for treatment of acne

3) treat *P. acnes*

systemic antibiotics (erythromycin, tetracycline, doxycycline, minocycline)

benzoyl peroxide: topical agent, suppresses growth of *P. acnes*

4) treat PMN's

systemic agents that inhibit PMN's (steroids, dapsone, colchicine) are not really used due to side effects

Note that tetracycline and erythromycin also seem to inhibit PMN chemotaxis

Warts

Etiology: HPV

Clinical

keratinocytes above granular layer are infected
transmission by direct contact

incubation 1-12 months

↑ incidence in small children → usually have spontaneous involution

Findings: different appearance in different sites

extremities: common wart

face: filiform or flat

plantar surfaces: thickened plaques or punctate hyperkeratoses

nether regions: cauliflower = condyloma acuminata, spread by sex

Laboratory

clinical diagnosis, but sometimes warts can be hard to distinguish from benign growths such as seborrheic keratosis or precancers/cancerous growths such as actinic keratoses or squamous cell carcinoma → biopsy!

characteristic histological finding is vacuolated cells in upper dermis

Treatment

no single effective therapy: physically destroy (laser, freeze, burn)

interferon may be helpful: imiquimod may involve local release of endogenous interferon

Complications

infants born to mom with condyloma acuminata may rarely develop laryngeal papillomas
cervical cancer!

03: Common Skin Disorders: Acne, Warts, Psoriasis, Seborrheic Dermatitis

Psoriasis

Definition: chronic skin dz of unknown cause
affects ~1% of US/european population, but uncommon in native americans and asians
M=F

Clinical presentation: can mix and match these types

Psoriasis Vulgaris

plaque-type, most common form
sharply-demarcated red plaques with silver-white scale
elbows, knees, lower legs, scalp
chronic & stationary

Guttate Psoriasis ("drop-like")

papules with sharp borders and silver scale
usually erupts acutely in generalized fashion
triggered by GAS

Erythrodermic Psoriasis

a cause of exfoliative erythroderma
entire skin surface becomes red and scaly
may occur suddenly

Generalized Pustular Psoriasis

usually acute and generalized
no scale, but surfaces of bright red plaques are studded with pustules

Localized Pustular Psoriasis

planter & palmar aspects of hands, feet, fingers, toes
pustules may occur in crops or waves on a base of atrophic erythematous plaques

Histopathology: all forms have same pathology

- 1) psoriasiform epidermal hyperplasia with loss of granular layer
- 2) elongated dermal papillae and enlarged capillaries
- 3) PMN's in dermis and within epidermis
- 4) lymphocytes in dermis
- 5) parakeratotic scale

Associated diseases

psoriatic arthritis: destructive arthritis which may accompany psoriasis

Pathogenesis: vicious cycle

- 1) rapidly growing epidermis
 - 2) inflammatory cells in dermis and epidermis
- inflammation induces growth and vice versa

genetic factors (B27)

environmental factors (trauma = Koebner phenomenon), drugs, strep infections, stress, can set the disease in motion

Treatment aimed at controlling, not curing

Antiinflammatory (AI), antiproliferative (AP), or immunomodulatory (IM) treatments are used

mild/moderate disease: AI & AP

moderate/severe disease: AI, AP & IM

Seborrheic Dermatitis ("dandruff")

Definition

inflammatory disorder with erythematous scaly plaques involving areas of skin rich in sebaceous glands (scalp, face, chest)

Clinical

Who gets it?

common in infancy and adulthood

uncommon between age 6 and puberty

↑ with HIV or Parkinsons (of all things)

In infants

scalp and diaper area

"cradle cap" = scalp covered with erythematous scaly dermatitis

in children, it's not pruritic, but may become bacterially superinfected

Leiner's disease = SD → exfoliative erythroderm

sepsis + diarrhea + wasting

In adults

involves scalp: pruritus and scaling

more severe with HIV or PD

only rarely progresses to exfoliative erythroderm

bacterial superinfection → pustules or impetiginized crusting

can develop seborrheic

blepharoconjunctivitis if extensive facial involvement

Histopathology

spongiotic dermatitis with moderate acanthosis, intracellular edema and spongiosis

mounds of parakeratotic scale around ostia of hair follicles

perivascular lymphocytic infiltrate in dermis

Pathogenesis

lipophilic yeast *Pityrosporum ovale* produces inflammatory rxn

Treatment

inhibit growth of *P. ovale*, reduce inflammation, remove scale

antiseborrheic shampoo

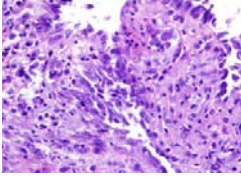
can use topical corticosteroids

is there any skin disease that is not treated with topical corticosteroids?

04: Pathology of Inflammatory Skin Diseases

Terminology

Acantholysis

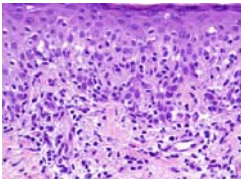


broken intercellular bridges between keratinocytes → normally polygonal cells become round

Eczema/Eczematous

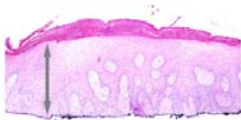
eruption with erythema, scale, and vesicles
histological correlated is spongiosis

Epidermotropism



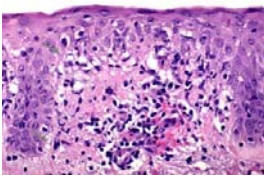
random permeation of epidermis by atypical lymphocytes
hallmark of mycosis fungoides

Exocytosis



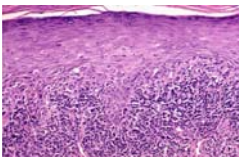
entry of normal lymphocytes into epidermis during inflammatory event
normally permeation at all levels with associated spongiosis and scale formation

Interface



rxn affecting dermoepidermal junction (DEJ)
two main forms: lichenoid and vacuolar

Lichenoid



clinical meaning: flat-topped violaceous papules with enhanced skin markings
pathological meaning: band-like inflammatory infiltrate, with obscures DEJ
associated with keratinocyte necrosis

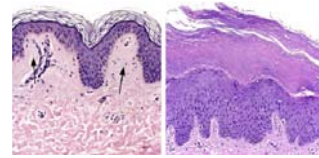
Lichenification

palpable thickening of skin with accentuated markings, a secondary change

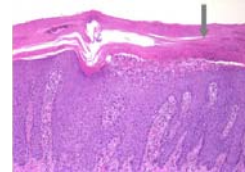
Hyperkeratosis (Ortho- and Parakeratosis)

too much stratum corneum → clinically manifests as scale

ortho: no nuclei

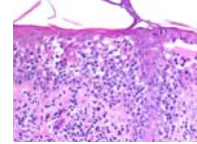


para: retained nuclei (always abnormal)



hallmark of eczematous (spongiotic) dermatitis

Spongiosis



intercellular edema, evident by enhanced visualization of spines (intercellular bridges)

Inflammatory reaction patterns

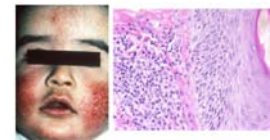
Spongiotic:

Characteristics

characteristic feature of eczematous dermatitis



▶ atopic dermatitis

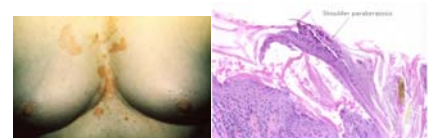


▶ nummular dermatitis

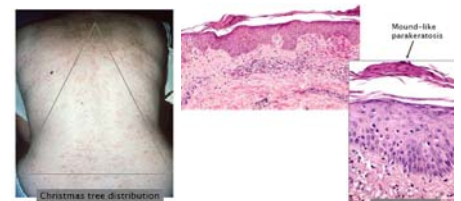
▶ contact dermatitis

other spongiotic processes

▶ seborrheic dermatitis



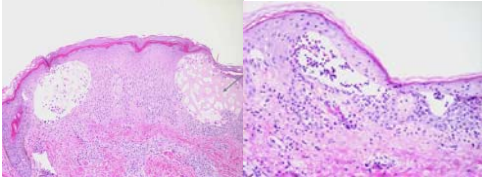
▶ pityriasis rosea



O4: Pathology of Inflammatory Skin Diseases

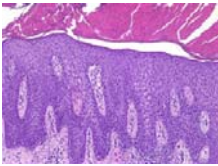
Phases may overlap (acute, subacute, chronic)

Acute eczematous (spongiotic) dermatitis



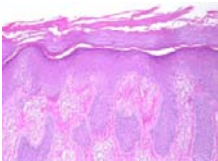
- ▶ minimal epidermal hyperplasia
- ▶ spongiotic vesicles
- ▶ langerhans cell-rich microvesiculation
- ▶ dermal inflammatory infiltrate
- ▶ scale has NOT yet formed

Subacute



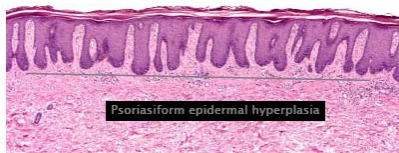
- ▶ ↑ hyperplasia
- ▶ mild spongiosis
- ▶ parakeratosis

Chronic

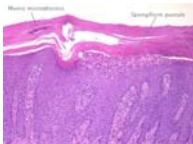


- ▶ ↑↑ hyperplasia (may even be psoriasiform)
- ▶ ↓ spongiosis
- ▶ more hyperkeratosis

Psoriasiform

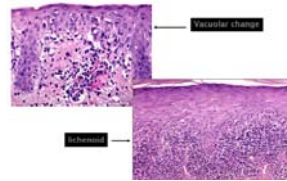


- ▶ like psoriasis, duh
- ▶ regular elongation of rete ridges, with bulbous expansion of tips
- ▶ thinning of supra-papillary plates (portion of epidermis above dermal papilla)
- ▶ extensive parakeratosis
- ▶ PMN's
- ▶ munro's microabscesses = PMN aggregates layered within parakeratosis



Less commonly: spongiform pustules of Kogoj = intercalation of PMN's between keratinocytes

Interface dermatitis

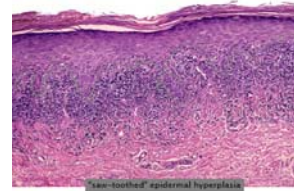


characteristics

these processes disrupt the DEJ → keratinocyte necrosis & pigment incontinence

Lichenoid

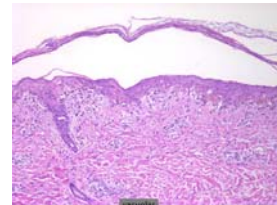
band-like infiltrate obscures jxn
prototype: lichen planus
orthokeratosis
saw-toothed epidermal hyperplasia with hypergranulosis



mononuclear inflammatory infiltrate (↓ eosinophils)

Note: in drug-induced lichenoid HSR, see ↑↑ eosinophils

Vacuolar



presence of clear vacuoles on either side of DEJ

seen in SLE, erythema multiforme, and acute GVH disease

Erythema Multiforme

- ▶ Herpes-associated: EM minor
- ▶ Drug associated: EM major (Stevens-Johnson)

04: Pathology of Inflammatory Skin Diseases

Vesiculobullous

characteristics

divided into two categories depending on where the skin splits in the blistering process

intra-epidermal

gross

flaccid bullae (blisters)

histology

acantholysis

primarily pemphigus disorders

rarely see in diseases of epidermal maturation & keratinization:

grover's, darrier-white, hailey-hailey

sub-epidermal

tense blisters, less susceptible to rupture

non inflammatory:

epidermolysis bullosa acquisita

↑ Eos:

bullous pemphigoid

↑ PMN's:

dermatitis herpetiformis

bullous lupus

linear IgA dz

Hair follicle-based inflammation

Acne vulgaris

comedo = keratin-plugged follicle infected with bacteria

inflammation → papules, cysts, nodules

Rosacea

gross

erythematous facial rash with flushing triggered by hot beverages, EtOH, stress

histology

follicular spongiosis

demodex mites within follicles

telangiectasias

Granulomatous

characteristics

activated ("epithelioid") macrophages

Sacoidal

non-necrotizing grandma-lomas

↓ necrosis

↓ inflammation

Necrobiotic granulomatous inflammation: "living dead" (degenerative connective tissue interspersed with macrophages)

Granuloma annulare

gross

papular eruption

may coalesce to form annular plaques on extremities

histology

collagen degeneration with ↑ dermal mucin

surrounding palisaded granulomatous rxn

Necrobiosis lipoidica

gross

yellowish waxy plaques over shins

associated w/ DM

histology

pan-dermal granulomatous rxn

lymphoplasmacytic inflammation

granulomas with giant cells

Necrotizing granulomas

infectious granulomas

caseating if TB or fungal

Vasculopathic

most common: leukocytoclastic (hypersensitivity vasculitis)

necrotizing small vessel vasculitis

seen w/drug HSR rxns or w/CT dz