

LO1 Pigmentation & Sweating Disorders

★ major determinant of skin color is melanocyte activity ★
= intracytoplasmic organelle density

★ UV Radiation

Size of melanocytes & tyrosinase activity

UVA: immediate darkening

UVB: delayed tanning, carcinogenic

★ Melanin produced from tyrosine via tyrosinase (Cu dependent)

★ [pheomelanin: yellow/red — round
eumelanin: black/brown — elliptical
stimulated by MSH & ACTH on MC1-R

★ Acanthosis Nigricans

★ type I: insulin-resistant, obesity, PCOS

★ type II: GI malignancies (rapid onset)

★ Melasma sharply demarcated dark patches

young women Fitz type IV, V, VI; tx: sun protection

★ Onychomycosis Hyperpigmented plaques d/t excessive hydroquinone use

tx: stop medication

★ Transient Neonatal Pustular Melanosis

@ BIRTH

NEUTROPHILS

★ Erythema Toxicum Neonatorum

2-4 days after birth

EOSINOPHILS

★ Vitiligo progressive loss of functional melanocytes

d/t autoimmune destruction via IFN-gamma JAK-STAT

white patches w/ sharp demarcation

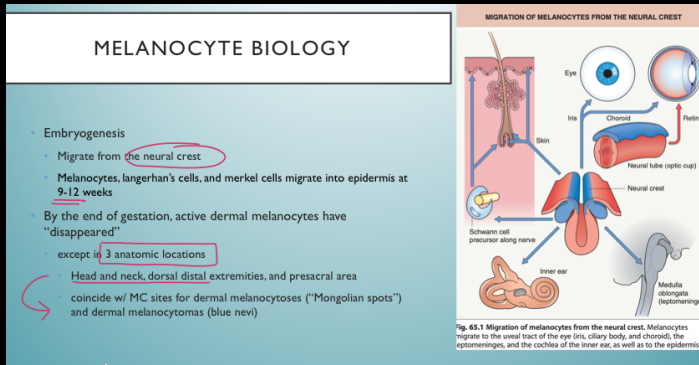
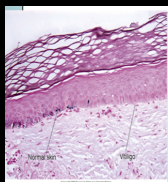
treatment resistant - esp. acrofacial type

topical/oral steroids, calcineurin inhib, depigment.

Halo nevi = common

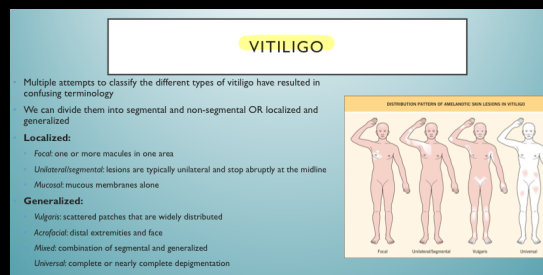
Histo: loss of melanocytes, inflammation ★

MC comorbidity = autoimmune thyroiditis



FROM NEURAL CREST

TO



★ Oculocutaneous albinism (OCA) type of AR leukoderma

★ # melanocytes = normal ★

OCA I → mutation in tyrosinase gene

OCA1A: most severe, no melanin but normal # melanocytes

OCA1B: some tyrosinase activity, some pigmentation

MC OCA II → mutation in OCA2 gene on chromosome 15

europeans mostly, still have tyrosinase activity

no transport melanosomal proteins

★ Pautz-Jeghers syndrome

- STK11 mutation in MTOR pathway

- oral mucosal lentiginosis + small bowel polyposis

★ ↑ risk GI & pancreatic CA → [NEED video endoscopy @ 8yo then q3y] ★

★ Drug Induced Hyperpigmentation

Minocycline

MC blue/black in areas of prior inflammation

- II blue/black @ shins
- III muddy brown all over

Chloroquine blue/black pretibial, face, cartilage
Amiodorone slate grey on sun exposed areas
Chlofazamine pink discoloration
Zidovudine blue/black nails

DRUG-INDUCED PIGMENTATION

- Chlorpromazine, thioridazine, imipramine, and clomipramine may cause a slate-gray hyperpigmentation in sun-exposed areas after long periods of ingestion
- Frequently, corneal and lens opacities are present
- Therefore all pts with hyperpigmentation from these meds should have ophthalmologic exam

Rifampin = red/orange bodily secretions

SWEATING controlled through SNS but functionally CHOLINERGIC *

TQ

* Primary Hyperhidrosis

- localized excessive sweating; onset <25 yrs; bilateral/symmetric
- * STOPS DURING SLEEP! *

* Secondary

d/t another condition

* Auriculotemporal Nerve syndrome

aberrant regen of PSN fibers
sweating in auriculotemp. distribution after FOOD *

* Anhidrosis / hypohidrosis

d/t ectodermal dysplasia
results in hyperthermia!

tx: Qbrexex (glycopyrinium)

SE: blurry vision

tx: botox

BROMHIDROSIS smelly sweat

- Apocrine bromhidrosis: bacterial degradation of apocrine sweat → chain fatty acids
- Exaggeration of typical axillary body odor
- Eccrine bromhidrosis: 3 types
- Keratinogenic: bacterial degradation of stratum corneum macerated by excess eccrine sweat
- Metabolic: abnormal secretion of amino acids or breakdown products
- Heritable metabolic disorders:
 - PKU: mousey odor
 - Maple syrup urine disease: sweet odor
- Exogenous: odorogenic compounds
 - ie: garlic, asparagus & curry → cotton ming!
- Treatment:
 - Antibacterial soaps, commercial deodorants, changing under clothes, Drysol, topical ABX (e.g. clindamycin), surgical removal of the glands

VOGT-KOYANAGI-HARADA SYNDROME

immune system attacks melanocytes

inflammation everywhere
 Th1 cells
 melanocytes

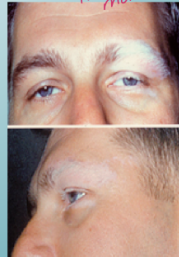
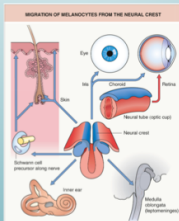
Multisystem disorder

- Uveitis, aseptic meningitis and otic involvement (e.g. dysacusia)
- Vitiligo (especially of head and neck region) and poliosis
- Only 20-60% of patients have cutaneous vitiligo like lesions

Affects primarily pigmented races, F>M, all ages

Autoimmune

Auto-antigens solely expressed in melanin containing cells

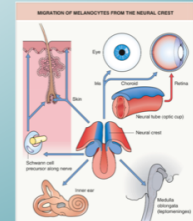


VOGT-KOYANAGI-HARADA SYNDROME

4 phases

- 1. Prodromal phase (meningoencephalic phase)** Meningitis!
 - fever, malaise, HA, N/V, tinnitus
 - can include meningismus, headaches, mental status changes
 - Recovery is usually complete
- 2. Uveitic phase**
 - Anterior or posterior uveitis
- 3. Convalescent phase**
 - begins 3 weeks-3 months after the uveitis appears
 - alopecia, vitiligo, poliosis whitened hair
- 4. Recurrent attacks of uveitis** → permanent decreased visual acuity, cataracts, glaucoma

Treat flairs with CS and steroid sparing immunosuppressive therapy aggressive



CHEPIAK HIGASHI

AR, LYST-CHS1 mutation

Lysosome dysfunction

- bleeding
- bacterial infx
- brain problems
- pigment dilution (grey hair)



HERMANSEK-PUDLAK

- AR, HPS1 gene, PUERTO RICANS
- disordered biogenesis of melanosome
- glycosome-related organelles

- bleeding
- pulmonary fibrosis
- ceroid lipofuscin = neuro degeneration



WAARDENBURG

inability of melanoblasts to reach target

sxs of piebaldism (KIT mutation)
 white forelock
 hypopigmentation
 premature greying

PLUS

unibrow (synophrys)
 congenital deafness
 ocular Δs



WAARDENBURG SYNDROME

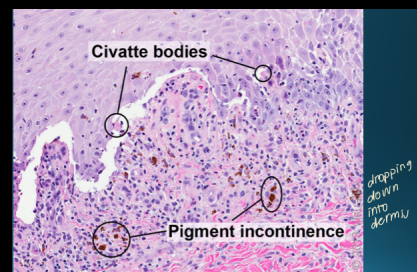
- Four types of Waardenburg syndrome (WS) exist
- Six genes are associated with WS.
- Types I and III are caused by mutations in the PAX3 gene
- causing a transcription factor
- Most cases of WS type II are caused by mutations in the MITF gene
- however, some have SOX10, EDN3, EDNRB, and SNR12
- No dystopia canthorum
- Type 3- PAX3 gene
- upper limb abnormalities
- WS type IV is caused either by a mutation in SOX10 or by mutations in the endothelin-3 (EDN3) or the endothelin receptor (EDNRB) gene.
- impair the ability of melanoblasts to reach their final target sites (inner ear, eye, skin) during embryogenesis.
- Hirschsprung's disease

(TQ)
 melanoblasts migrate to white forelock

LO2 Skin of Color

Post-inflammatory Hyperpigmentation Mechanism:

- ① ↑ melanocyte activity → tan / dark brown
- ② melanocyte drop out → grey-blue / brown



* Erythema Dyschromicum Perstans (EDP)

Hispanics, @ neck / trunk ; sparse mucosa

* Erythematous bordered lesions progress to grey / brown
tx: clofazamine



* Lichen Planus Pigmentosus

grey / brown patches in photo or intertriginous distribution

* Ø erythematous borders!

* Sarcoidosis immune mediated granulomatous condition

grant hilar lymph nodes on CXR

papular eruption; **NON CASEATING GRANULOMAS**



* Lofgren syndrome → arthritis, erythema nodosum, bilateral hilar lymphadenopathy

* Congenital Dermal Melanocytosis melanocytes in epidermis don't regress

benign blue-grey patches peak @ 1-2 y/o

short wavelengths seen better = blue

* Keloid

dense fibrotic nodule that expands area of trauma

* Pseudofolliculitis Barbae

flesh colored erythematous papules w/ hair shaft @ center

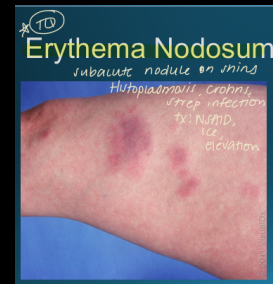
MC beard area from shaving against grain

* Acne keloidalis Nuchae

mechanical trauma

pustules & keloid-like papules on post neck

TO



HAIR LOSS

Non-scarring = Ø destruction of follicular ostia

dx: punch biopsy

* Scarring / Cicatricial alopecia = scar on opening of hair follicle

- central centrifugal cicatricial alopecia

AA females w/ progressive hair loss from VERTEX w/ clumps of normal growth

d/t chemical straightening

tx: stop hair styling

- lichen planopilaris

acute or insidious w/ perifollicular scale & erythema

tx: topical steroids / TC1

- frontal fibrosing alopecia

variant of lichen planopilaris ... only @ front, complete loss

- traction alopecia

d/t tight braiding

incomplete temporal & frontal hair loss

- dissecting cellulitis of scalp

painful firm / boggy scalp nodules that rapidly connect

tx: oral ab ± steroids



TO

LO3 Skin & Systemic Dz 1

* Acanthosis Nigricans → insulin resistance & obesity

oral/mucosal → GI malignancies

* Sweet's Syndrome (acute febrile neutrophilic dermatosis)

painful erythematous plaques w/ FEVER

TG-CSF ↑ Neutrophils but Ø infection

myeloid leukemia

* Erythema Gyratum Repens

pruritic, wavy "wood-grain" pattern rash; spares face, hands & feet

Tesinophils

→ d/t cross reactivity ★★

LUNG CANCER; & TB, SLE, U.C.

* Subcorneal Keratosis

- epidermal inclusions "pasted on"

* FGFR3 mutation

- Leser-Trélat sign: GI malignancy (Adenocarcinoma of stomach)

* Epidermal Inclusion Cysts

- sebaceous cyst/epidermoid cyst filled w/ keratinaceous debris

- Gardner Syndrome: germline APC mutation (FAP)

- osteomas of sinuses, mandible, & desmoid tumors

* Muir Torre Syndrome

★ sebaceous adenomas associated w/ internal malignancies (colorectal & urothelial)

★ MSH2 & MLH1 mutations (mismatch repair)

HPNCC subtype (AD)



* Cowden Syndrome

multiple hamartoma & trichotemnomas

PTEN germline mutation

plus colon polyps ★



* Putz-Jeghers Syndrome

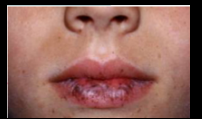
STK11 mutation

oral/mucosal lentiginos + hamartomatous GI polypsis (small bowel)

* Gorlin Syndrome / Nevoid Basal Cell Carcinoma

PTCH germline mutation

medulloblastoma & jaw cysts



GI Dz / DISORDERS

* Necrodermatitis enteropathica

Zn deficiency; child w/ no hair

* Necrolytic Migratory Erythema

glucagonoma → elevated glucose & diarrhea

* Hereditary Hemorrhagic Telangiectasias → AVMs

telangiectasias / oral petechiae blanches w/ pressure; epistaxis

* Pyoderma Gangrenosum

NO dermatitis w/ painful ulcers w/ dusky border

leukemia



ulcerative
colitis

* Erythema Nodosum

- panniculitis, red, elevated, painful [Ø vasculitis]

- TB, histo, coccidio, drugs

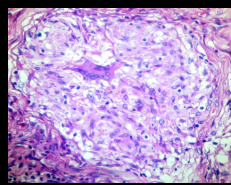
- ↑ NO



★ Sarcoidosis

TO

- unknown cause, dx of exclusion
- noncaseating granulomas
- hypercalcemia



asteroid
& Schaumann
bodies

LD4 Skin & systemic dz II

NEURO DZ

★ Tuberous Sclerosis

- (AD) TSC & TSC2 mutation
- hamartomas & benign neoplasms involving brain & other tissue
→ epilepsy, mental retardation, autism

- ★ [- derm: ash-leaf patches, shagreen patches, angiofibromas, & subungal/perilungal fibromas]
- giant cell astrocytoma, rhabdomyoma

★ Familial Neurofibromatosis

Neurofibromatosis I

- (AD) NF1 gene mutation = tumor suppressor gene
- ★ [- neurofibromas, optic nerve gliomas, lisch nodules, cafe au lait spots]
- tumor of schwann cells
"bag of worms"



NF1
Neuro
tumors
& cafe au
lait spots

Neurofibromatosis II

more CNS involvement → schwannomas

★ Sturge-Weber Syndrome

- port wine stain, venous angiomas, vascular ectasia (V1)
- glioma in a baby ★ leptomeningioma
- GNAQ mutation (sporadic)

★ Ataxia Telangiectasia

- (AR) ATM gene defective DNA repair
- death in adolescence from infection or malignancy

CARDIAC DZ

★ Leopard Syndrome

- ★ Lentigines, cardiac conduction abnormalities, ocular hypertelorism, abnormal genitalia, pulmonary stenosis, growth retardation, sensorineural deafness
- (AD) PTPN11 gene (same as Noonan)

★ Carney Complex

- ★ LAMB: lentigines, atrial myxomas, mucocutaneous myxomas, & blue nevi
- ★ NAME: nevi, atrial myxomas, neurofibromatosis, ephelides, & endocrine neoplasia
- ★ PRKAR1A gene mutation
- Hypercortisolism & GH pituitary adenomas

AUTOIMMUNE

★ Scleroderma

excess collagen deposition, vascular damage
generalized = CREST syndrome

★ SLE

malar/butterfly rash

★ Discoid lupus erythematosus (DLE)

- Ø systemic, Ø ANA antibodies
- raised scar-like atrophic red plaques
→ scarring alopecia

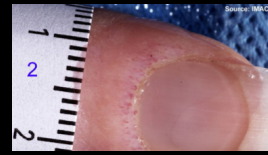


TO?

- ★ SLE-like drug eruptions
 - ⊕ ANA antibodies & anti-histone
 - SHIP-E

★ Dermatomyositis T-cell mediated [CD4⁺]

- heliotrope discoloration of upper eyelids
- Gottron papules - scaly rash on joints



★ VISCERAL CANCERS

★ Poikiloderma

hyper/hypopigmentation & telangiectasias

★ Histo: [perivascular inflammatory infiltrates]

ENDOCRINE

- ★ Necrobiosis lipoidica diabetorum
 - collagen degeneration
- ★ Pretibial Myxedema
 - Graves/Hashimoto's
 - Nonpitting edema → deposition of GAGs (hyaluronic acid)

★ Xanthomas

severe chylomicronemia/triglyceridemia // underlying lipoprotein disorder
 (eruptive) [tuberous]
 (palmar, xanthomas & xanthelasma)



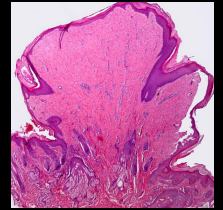
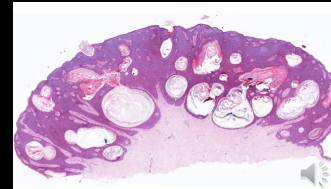
local = lipoprotein

LO5 Benign Skin Neoplasms

★ Seborrheic keratosis: hyperkeratotic lesions of the epidermis

ring sign - uniform depth

Leser-Trélat sign - adenocarcinoma of stomach



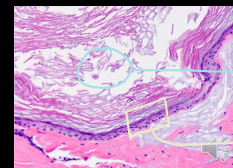
- ★ Acrochordon = skin tag (hyperplastic, soft dermis & epidermis)
- metabolic syndrome
- Ø malignant threat

★ Epidermal cyst: implantation & proliferation of epidermal elements WITHIN the DERMIS

multiple: Gardner syndrome → APC mutation // FAP
 central punctum

★ GRANULAR LAYER

Ø eccrine, sebaceous glands or hair follicles



→ keratin flakes
 → granular layer

- ★ Trichilemmal (Pilar) cyst: 90% on scalp
- derived from outer root sheath

Ø granular layer, Ø central punctum

★ Sebaceous tumors: adnexal lesions on dermis

- Muir-Torre syndrome ~ HNPCC

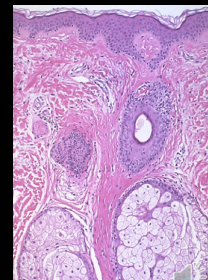
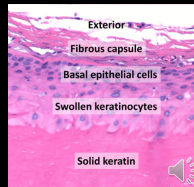
→ MSH2, mismatch repair gene

→ visceral malignancies

★ microsatellite instability

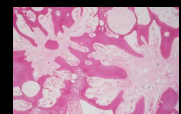
- filled w/ oil
- nodular / lobulated growth

★ LOOKS LIKE BASAL CELL



★ Eccrine Poroma

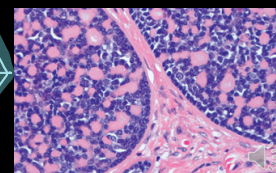
- red scaly nodule on palm/soles → often mistaken for melanoma
- round, bland cells w/ elongated rete ridges



★ Cylindroma

- Hereditary - Brooke Spiegler syndrome
- CYLD gene

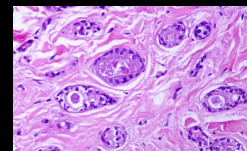
★ blue, basaloid geometric nodules in DERMIS only



* abundant BM deposition, + spherical pink droplets

* Syringoma: fleshy papules on face/body

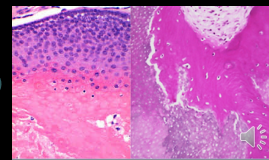
- tadpole shaped epithelial tubes w/ sclerotic background
- double layer of cells



* Pilomatricoma: solitary firm lesion from hair follicle

* Gardner syndrome - like (?)

- activating β -catenin (CTNNB1 gene)
- located in dermis/hypodermis -- DEEP



- * [① ghost/shadow cells - sheets of dead keratinocytes
- ② germinative matrix epithelial component (blue cells)

- metaplastic bone formation *

* Trichoepithelioma: from rudimentary hair follicles

- multiple familial trichoepithelioma (MFT) - adolescence

* papillary mesenchymal bodies @ bases of abortive hair follicles

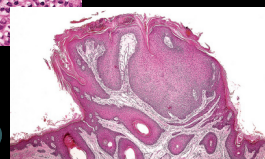
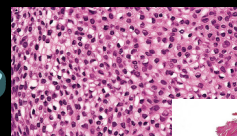
* Trichilemmoma: follicular proliferation -- outer root sheath

* Cowden syndrome (③ hamartomas - visceral malignancy)

* PTEN mutation

- glycogenated, clear cytoplasm
- basophilic palisading cells w/ thick/hyaline, BM material

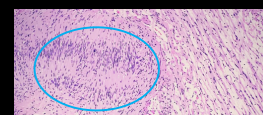
* PAS④ PASD④, diastase resistant



* Schwannoma: peripheral nerve sheath tumor

* Verocay bodies - parallel columns of elongated nuclei

- Antoni A - more cellular
- Antoni B - loose, less cellular *



* Neurofibroma: peripheral nerve sheath tumor (schwann cells + nervous tissue)

* NF1 biallelic inactivation

[RAS cell growth signaling]

- nonencapsulated dermal lesion
- proliferation of all elements of peripheral nerves (not just schwann cells)

- café au lait spots, optic gliomas, lisch nodules, multiple cutaneous neurofibromas

* [HETEROZYGOSES (AD), complete penetrance, variable expressivity] *

1/2 de novo, 1/2 genetic

* NF2: bilateral vestibular schwannoma - CNVIII & other CNS tumors

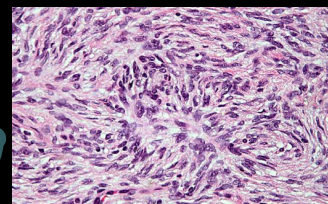
AD -- heterozygotes

* Fibrous Histiocytoma (dermatofibroma): proliferation of fibroblasts

- asymptomatic, ③ Fitzpatrick sign → dimples when squeezed
- multiple = immunocompromised

* [ill defined dermal lesion hyperplasia

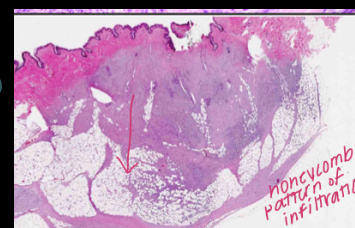
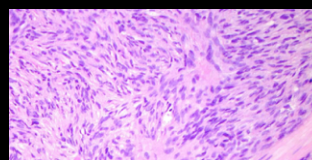
storiform/fascicular pattern



* Dermatofibrosarcoma protuberans: low grade, aggressive malignancy

- males 25-40, high recurrence
- spindle shaped pattern
- invades fat & muscle (honeycomb)

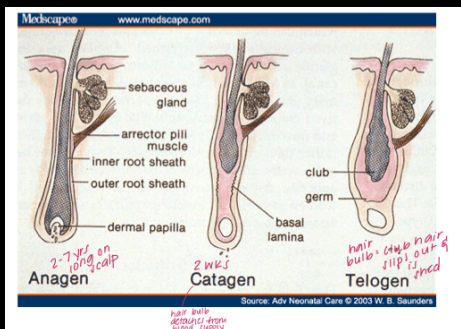
* t(17;22)(q22;q13) COL1A1-PDGFB fusion



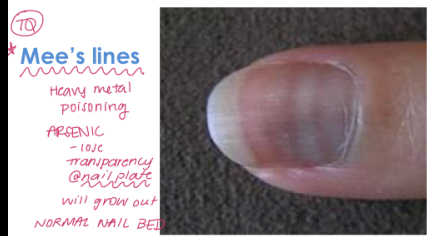
TQ

plexiform
ML subtype

LOW Hair & scalp



Leukonychia - striated



@ nail plate NOT NAIL BED

Nail bed Muercks nail = blanching

TO

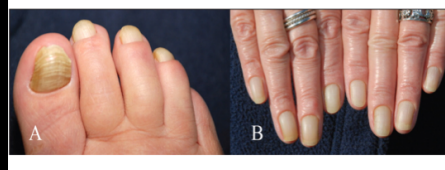
Alopecia areata

- exclamation hairs = active stage, give steroid
- pitting nails

TO

Yellow nails

TRIAD
yellow nail + pulmonary + chronic LE edema



Hair excess

INDEPENDENT OF ANDROGENS

Hypertrichosis

Hairy new anorexia nervosa survivors
yellow hairs grow in patches



Effluvium

happens all @ once

- Stressors that cause hair roots to be pushed prematurely into resting state

Telogen effluvium

inflammation or scarring
women after childbirth



Chemotherapy

causes hair to bypass the normal telogen shedding and come out in the anagen phase

Anagen effluvium

lose hair during growth phase (anagen)



onychomadesis → prox shedding
trauma, illness, Kawasaki

- Apply Osteopathic tenets to determine appropriate treatment of dermatologic conditions
- Utilize knowledge of the underlying pathology of dermatologic conditions, patient's physical and mental state to determine appropriate treatment with OMT
- Apply knowledge of dermatomes and neurologic pathways to determine appropriate OMT for given dermatologic conditions
- Apply knowledge of **lymphatic and vascular systems** to determine appropriate OMT for given dermatologic conditions

Rational Treatment

#1

- **Examine the patient** – Inspect, palpate and check **range of motion** if appropriate

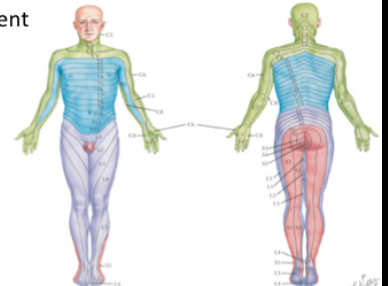
– What **dermatomes** are involved → *shingles!*

- Helps direct treatment

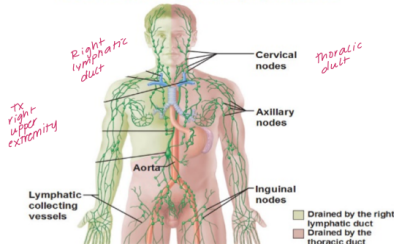
– **TART findings**

- Bogginess
- Hypertonicity
- Edema
- Skin Temperature
 - Increase/Decrease

*chronicity
tactatness*



General Distribution of Lymphatic Collecting Vessels and Regional Lymph Nodes



Lymphatic Considerations

- When treating conditions with edema or localized infections → *weeping*
- **Check for somatic dysfunctions at**
 - Thoracic Inlet – Sibson's Fascia, 1st Ribs, Clavicle
 - Thoracic Diaphragm
 - OA/AA
 - SI Joint/Hip
 - Popliteal Fossa/Fibular Head

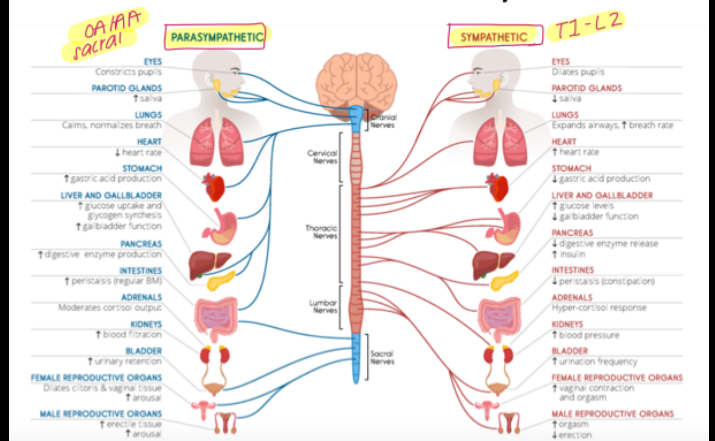
★ check points

check areas, if good fix

Osteopathic Approach to Treatment

- What can be done to **enhance the medical treatment** of skin disorders?
 - Counseling
 - Support groups
 - Dietary modification - *the GUT*
 - OMT!
 - Stretching and Exercise! *↑ blood flow / lymph*

Autonomic Nervous System



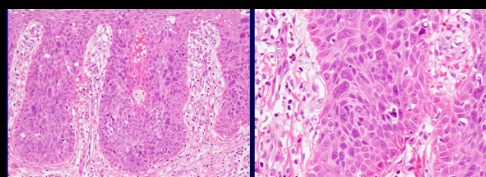
LO8 Nonmelanocytic skin cancer

★ SQUAMOUS CELL CARCINOMA

RF: UV light → DNA damage & p53 mutation
UVB = most carcinogenic (intermed. wavelength)

★ Bowen dz - SCC in situ

full thickness keratinocytic abnormality
rough irregular / scaly patches
pleomorphic cells w/o invasion



★ Invasive SCC

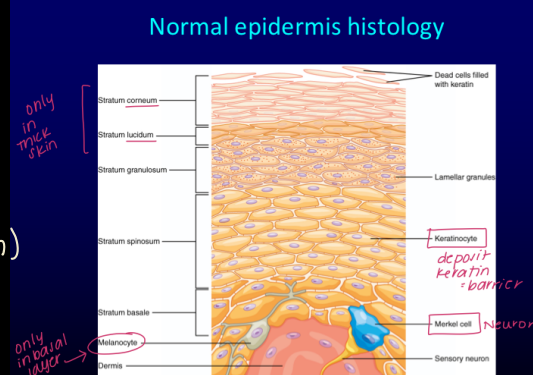
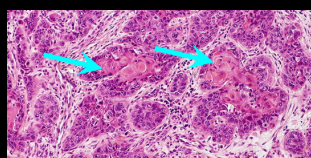
thin plaque / scaly papule / ulcer / nodule

→ well differentiated type

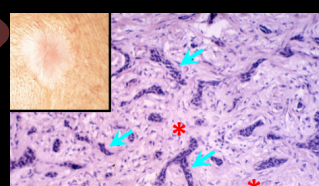
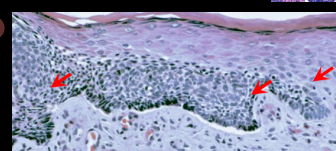
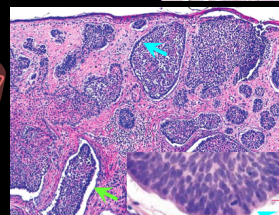
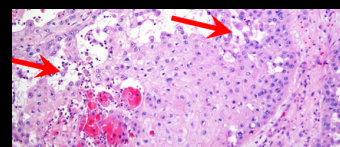
★ keratin pearls ★

→ Acantholytic type

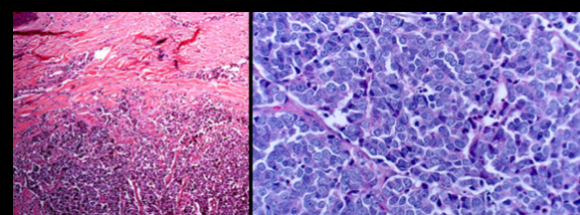
★ floating tumor cells ★



Squamous cell carcinoma				
	Normal skin	AK actinic keratosis	USCC	Metastatic cSCC
Clinical description		Scaly skin colored/pink macule or papule	Persistent firm or scaly papule or red nodule which may spontaneously bleed	Multiple nodular lesions in skin or internal organs
Histopathology				
Histological description	Well-defined stratum basale, spinosum, and granulosum with orthokeratotic scale	Enlarged, atypical keratinocytes confined to the epidermis with parakeratotic scale	Enlarged, atypical keratinocytes invading the dermis	Enlarged, atypical keratinocytes in the dermis, lymph nodes, or internal organs, typically with no epidermal connection
Increased signaling (activation, overexpression, or amplification)		ras, Fyn/SFKs, Src-2	ras, Fyn/SFKs, c-myc, bcl-2, STAT-3, p-1 integrin, MMP	In addition to cSCC alterations: VEGF (ras), MMP7, MMP12 (ras)
Decreased signaling (inactivation, transcriptional or translational repression, or gene deletion)		p53, Brca1	p53, Src, Notch (p53), PKC, E-cadherin	In addition to cSCC alterations: E-cadherin, P-cadherin
Genomic changes		Genomic instability with few chromosomal alterations	Increased genomic instability resulting in chromosomal translocations, isochromosomes, gene deletions, and amplifications	



Worst one!
perineural invasion



Palisading, cleft

★ Actinic keratosis = precancerous @ sun exposure spots

- rough patches on skin

- basal layer atypia, hyperkeratosis & parakeratosis

- dermal elastosis

★ BASAL CELL CARCINOMA

RF: UV light

Patn: PTCH, p53

px: papule/nodule

w/ telangiectasias

→ Nodular

basaloid, palisading & peritumoral clefting

→ Superficial

budding, MULTIFOCAL

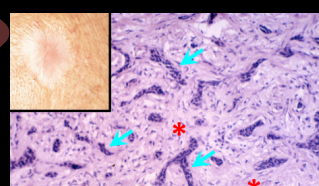
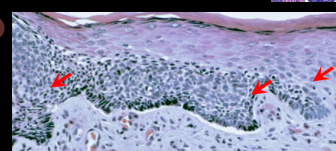
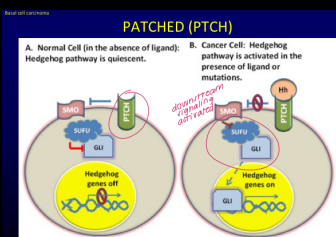
→ Morphoeiform

scar-appearing

★ cords of basaloid cells

in desmoplastic stroma

Tx: cut, burn, freeze



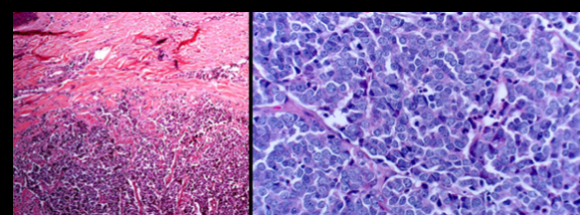
★ MERKEL CELL CARCINOMA

aggressive neuroendocrine tumor

CK20, CD56, synaptophysin, chromogranin, EMA

rapid growing - fatal

salt & pepper nuclei!



* MYCOSIS FUNGOIDES *

* cutaneous T cell lymphoma → **CD4+ cells** (CD8⁻)

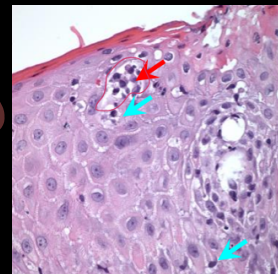
TO

- patch
- plaque
- tumoral
- Sezary cell

→ **Sezary syndrome**

erythroderma + lymphadenopathy + Sezary cell < 80%

Pautrier Abscesses

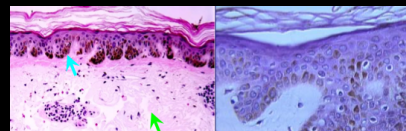


CD4+ only!

LO9 Melanocytic Lesions

* Lentigo: age spots, overproduction of melanin

- elongation of rete ridges & ↑ pigmentation
- linear melanocytic hyperplasia



* melanocytic nevus: moles

acquired BRAF/NRAS mutations
regular shape, border, symmetry

→ junctional type

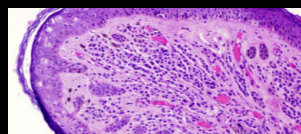
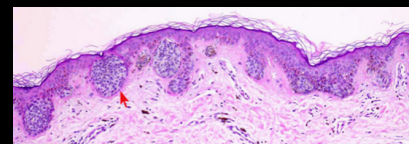
macule w/ nests of melanocytes @ DE jxn

→ intra dermal type

nodule w/ nests in upper dermis

→ compound

mixed features



* dysplastic nevus

cytologic atypia, potential melanoma

px: >5mm, irregular, variable colors/borders

LOOKS LIKE MELANOMA ON OUTSIDE

* [melanocytic nests extending beyond 3 rete ridges]

* melanoma

d/t UV light +

path: BRAF/RAS

CKND2A

TERT promoter

Hutchinson's sign

ABCs → asymmetry, border, color

[+ S100, HMB-45, melanA, tyrosinase]

[if seen in DERMIS, its invasive]

↳ in situ = epidermis only

* GROWTH

- radial - horizontal - in situ
- vertical - deep into dermis

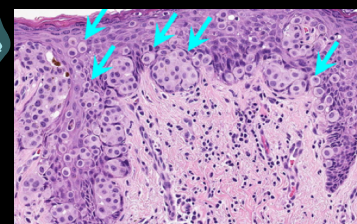
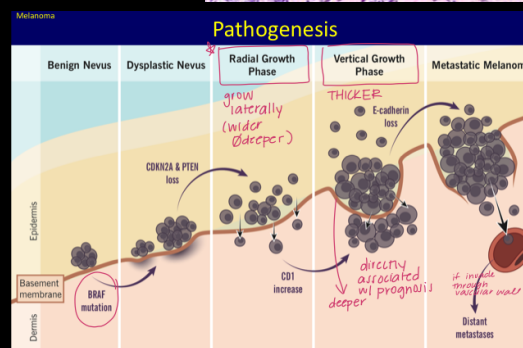
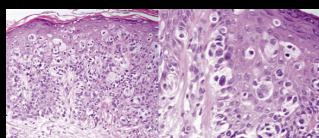
* SPREAD

- pagetoid - in situ

pale cytoplasm clumps in epidermis

* INVASIVE

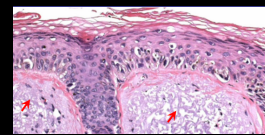
- Ø maturation
- Beyond basal layer!



→ lentigo maligna melanoma

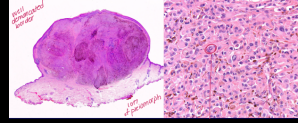
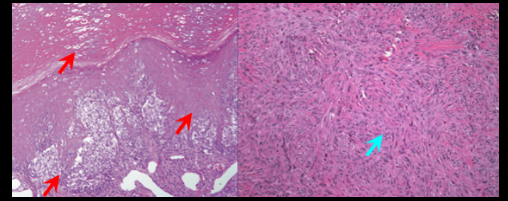
atypical cells in basal layer

Flat growth
 multinucleated melanoma cells @ DE jxn
 marked elastosis (red)



→ acral lentiginous melanoma
 thick skin

→ nodular melanoma
 vertical growth
 intranuclear inclusions
 ↑ metastases



⑦ melanoma prognosis
 based on depth of invasion

Breslow's system thickness (FYI)

- Measure tumor thickness with ocular micrometer at right angles to surface of adjacent normal skin from (a) **top of granular layer** of overlying epidermis OR from **ulcer base** over deepest point of invasion to (b) **deepest invasive tumor cells**
- 2009 AJCC Staging System employs following thresholds for thickness: T1: ≤ 1.00 mm thickness, T2: 1.01 to 2.00 mm thick, T3: 2.01 to 4.00 mm thick, T4: more than 4.00 mm
- 10 year survival: 92% for melanoma < 1.00 mm thick; 80% if 1.01 to 2.00 mm thick; 63% if 2.01 to 4.00 mm thick; 50% if > 4.00 mm thick

THICKER = poor prognosis
 → distance from top to bottom

Invasive melanomas		
	Radial Growth	Invasive components
Superficial spreading	Nests and pagetoid spread	Epithelioid
Lentigo maligna	Basal layer, Pagetoid spread uncommon	Spindled or epithelioid, solar elastosis
Acral lentiginous	Pagetoid spread	Spindled elongated nuclei
Nodular	None	Most commonly epithelioid

all [⊕ HMB45
 ⊕ S100
 ⊖ cytokeratin]

- Keep in mind: HMB45, melanA and S100 are melanocytic markers, that can be positive in both benign nevus and melanoma

WANG PQS

Skin tumors 1

- ✓ 1. C or D? tan nodule w/ greasy colored surface → seborrheic keratosis
- ✓ 2. B
- ✓ 3. C
- ✓ 4. C
- ✓ 5. A
- ✓ 6. B
- ✓ 7. B
- ✓ 8. D
- ✓ 9. B
- ✓ 10. C
- ✓ 11. E
- ✓ 12. C
- ✓ 13. D
- ✓ 14. C
- ✓ 15. E
- ✓ 16. D or E lobular, plate-like growth of pale pink, glassy cells w/ palisading → tricholemmoma
- ✓ 17. A
- ✓ 18. B CD34+
- ✓ 19. D
- ✓ 20. D spindle cell prolif. & S100+ = Neurofibroma
- ✓ 21. C
- ✓ 22. E
- ✓ 23. B

Skin tumors 2

- A 1. C dysplasia limited to basal layer = actinic keratosis → can develop into SCC or BCC
- ✓ 2. E
- ✓ 3. E
- ✓ 4. B Morphea BCC → perineural invasion
- ✓ 5. C
- C 6. B? Invasive = Mohs surgery
- ✓ 7. B
- B 8. C? rough scaling macule / waxy lesion → Basal Cell
- ✓ 9. B superficial type → multifocality
- ✓ 10. E nodular basal cell → PTCH mutation
- ✓ 11. D ⊕CK ⊕CD56 ⊖CD45
- ✓ 12. D → Merkel cell
- C 13. E * only in epidermis! ⊖S100 beyond basal layer
- ✓ 14. E * * → full thickness epidermal dysplasia = Bowen Dz
- ✓ 15. D
- ✓ 16. A pruritic rash; ⊕CD3 ⊖CD20 Mycosis Fungoides → ⊖ lymphadenopathy
Rash < 80% body
- C 17. E
- ✓ 18. D CD40 CD80
- ✓ 19. A
- ✓ 20. E Erythroderma, lymphadenopathy, & Sezary cells → Sezary Syndrome
> 80%

Skin Tumors 3

- ✓ 1. E
- ✓ 2. C
- ✓ 3. C melasma d/t estrogen? *pregnancy*
- ✓ 4. E
- ✓ 5. D
- ✓ 6. E
- ✓ 7. D
- ✓ 8. E
- ✓ 9. C
- ✓ 10. B
- ✓ 11. A / B compound nevus
- ✓ 12. A
- A 13. ~~B / E?~~ Dysplastic Nevus → basal layer only; >3 rete ridges long
- ✓ 14. C
- ✓ 15. C pagetoid spread — melanoma in situ
- ✓ 16. D ↳ Beyond basal layer! (w/o dermal involvement)
- ✓ 17. B
- ✓ 18. E
- ✓ 19. C
- B 20. ~~C~~ Nodular type BCC