Handbook of Dermatology

A PRACTICAL MANUAL

Margaret W. Mann
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Handbook of Dermatology: A Practical Manual Margaret W. Mann
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A Practical Manual

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Preface

Welcome to the first edition of *Handbook of Dermatology: A Practical Manual*, a pocket guide designed for practicing dermatologists, dermatology residents, medical students, and physicians in other fields who may be interested in dermatology. Written and edited by former residents and attending physicians in the Division of Dermatology at Washington University School of Medicine, this book is based on an in-house resident handbook which has been used by our department for the past five years. Our goal was to compile and consolidate need-to-know dermatologic information for daily use in patient care and resident and fellow education. As such, it represents the indispensable pocket-sized quick reference which we had wanted during our training and which we now use in our practices.

Currently, there are multiple in-depth dermatology textbooks and atlases, most of which are too bulky to be carried around in the clinic. Our manual concisely presents data in outline, bullet-point, and table formats such that information is manageable and easily retrievable. The compact design is lightweight, allowing information to be accessible in seconds during clinics, facilitating patient care. We have tried to balance space limitations with the need to cover a subject in sufficient detail.

Our manual has three main sections – medical dermatology, surgical dermatology, and pharmacology/treatment. Each section is designed to provide the reader with up-to-date, comprehensive yet concise information for patient care. In addition to core material, we sought to consolidate the information which we found ourselves most often looking up, which our attendings most frequently quizzed us on, and which were emphasized on the dermatology board exam. The manual consolidates the dermatologic algorithms, protocols, guidelines, staging and scoring systems which we find most essential. Each section is designed for easy reference, with tabular and graphic information throughout. The diseases covered are those which we frequently encountered in clinic, on call, during teaching conferences, and on board exams.

We hope you will find this manual helpful to you in providing care to your patients. We welcome your input as this manual continues to evolve.

Margaret W. Mann
David R. Berk
Daniel L. Popkin
Susan J. Bayliss

Dedication

We wish to express our thanks to the many people who have inspired us to write this book and supported us in our careers. Special thanks to the following physicians who contributed to the manuscript: Drs. Paul Klekotka, Alison Klenk, and Neel Patel – who helped make the prototype possible – without you, this manual would never have happened; Drs. Milan Anadkat, Grace Bandow, Amy Cheng, Michael Heffernan, Yadira Hurley, and David Smith for their valuable contributions; Drs. Stacey Tull and Quan Vu for the beautiful drawings; Drs. Senait Dyson, Kristen Kelly, and Anne Lind for their proofreading and comments; and finally Drs. Lynn Cornelius, Arthur Eisen, and all the faculty in the Division of Dermatology at Washington University for their support and encouragement.

Margaret Mann would like to thank her parents and her ever-patient husband, Daniel, for all the love and support over the years.

David Berk wishes to thank his family, especially his wife Melissa and his parents, for their constant support and patience.

Daniel Popkin would like to thank his parents and his wife Margaret.

Susan Bayliss wishes to thank her grandsons Cai and Eli Kenemore, and her daughters Elizabeth Kenemore and Meredith Mallory for all the joy they constantly bring her.

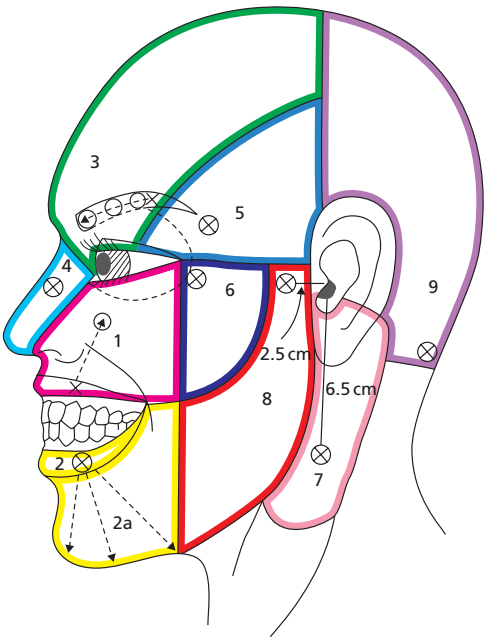
Abbreviations

ACD	allergic contact dermatitis
AD	autosomal dominant
AFB	acid fast bacilli
AK	actinic keratoses
ANA	anti-nuclear antibody
ANCA	anti-neutrophilic cytoplasmic antibody
APS	antiphospholipid syndrome
AR	autosomal recessive
ASO	antistreptolysin O titer
asx	asymptomatic
BCC	basal cell carcinoma
BID	twice daily
BM	bone marrow
BMP	basic metabolic panel
BMZ	basement membrane zone
BP	bullous pemphigoid
BP	blood pressure
Bx	biopsy
Ca^{++}	calcium
CAD	coronary artery disease
CBC	complete blood count
CCB	calcium channel blocker
CF	cystic fibrosis
cGVHD	chronic graft-versus-host disease
CH50	total hemolytic component
CMP	complete metabolic panel
CMV	cytomegalovirus
CN	cranial nerve
CNS	central nervous system
CP	cicatricial pemphigoid
CR	creatinine
CRF	chronic renal failure
CRP	C-reactive protein
Cryo	cryoglobulinemia
CT	computed tomography
CTCL	cutaneous T-cell lymphoma
CTD	connective tissue disease
CVA	cerebral vascular accident
Cx	culture
CXR	chest X-ray
DCN	doxycycline

DEJ	dermal–epidermal junction
DF	dermatofibroma
DFA	direct fluorescent antibody
DFSP	dermatofibrosarcoma protuberans
DH	dermatitis herpetiformis
DHEA-S	dehydroepiandrosterone sulfate
DI	diabetes insipidus
DIF	direct immunofluorescence
DM	dermatomyositis
DM2	diabetes mellitus type II
Dsg	desmoglein
Dz	disease
EBA	epidermolysis bullosa acquisita
EBV	Epstein–Barr virus
EDS	Ehlers–Danlos syndrome
EED	erythema elevatum diutinum
EKG	electrocardiogram
EM	electromicroscopy
EMG	electromyogram
ENA	extractable nuclear antigen
eos	eosinophils
ESR	erythrocyte sedimentation rate
ETOH	alcohol
F	fever
FLP	fasting lipid panel
FMF	Familial Mediterranean fever
G6PD	glucose-6-phosphate dehydrogenase
GA	granuloma annulare
GF	granuloma faciale
GI	gastroenterology
GVHD	graft-versus-host disease
h/o	history of
HA	headache
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high density lipoprotein
Hep	hepatitis
HSM	hepatosplenomegaly
HSV	herpes simplex virus
HTN	hypertension
IBD	inflammatory bowel disease
IIF	indirect immunofluorescence
IL	intralesional
IM	intramuscular

IV	intravenous
IVIG	intravenous immunoglobulin
KOH	potassium hydroxide
LAN	lymphadenopathy
LCH	Langerhans Cell Histiocytosis
LCV	leukocytoclastic vasculitis
LDH	lactate dehydrogenase
LDL	low density lipoprotein
LE	lupus erythematosus
LFT	liver function test
LN	lymph nodes
LP	lichen planus
MCN	minocycline
MCTD	mixed connective tissue disease
MEN	multiple endocrine neoplasia
MF	mycosis fungoides
MM	malignant melanoma
MR	mental retardation
MRI	magnetic resonance imaging
MTX	metrotrexate
nl	normal
NLD	necrobiosis lipoidica diabeticorum
NSAIDs	non-steroidal anti-inflammatory drugs
NXG	necrobiosis xanthogranuloma
OCP	oral contraceptive pill
OTC	over the counter
PAN	polyarteritis nodosa
PCN	penicillin
PCR	polymerase chain reaction
PCT	porphyria cutaneous tarde
PET	positron emission tomography
PFTs	pulmonary function tests
PIH	post inflammatory hyperpigmentation
PMLE	polymorphous light eruption
PMNs	polymorphonuclear leukocytes
po	per oral
PPD	tuberculosis skin test
PT/PTT	prothrombin time/ partial thromboplastin time
PUVA	psoralen + ultraviolet A
PV	pemphigus vulgaris
QD	once a day
QHS	every night
QOD	every other day
RA	rheumatoid arthritis

RF	rheumatoid factor
ROS	review of systems
RPR	rapid plasma reagin (screening test for syphilis)
Rxn	reaction
SCC	squamous cell carcinoma
SCM	sternocleidomastoid
SJS	Stevens–Johnson syndrome
SLN	sentinal lymph node
SPEP	serum protein electrophoresis
SQ	subcutaneous
SS	systemic sclerosis
SSRI	selective serotonin reuptake inhibitor
SSSS	staphylococcal scalded skin syndrome
Sxs	symptoms
szs	seizures
TB	tuberculosis
TBSA	total body surface area
TCA	tricyclic antidepressant
TCN	tetracycline
TEN	toxic epidermal necrolysis
TG	triglycerides
TIBC	total iron binding capacity
TID	three times a day
TNF	tumor necrosis factor
TSH	thyroid stimulating hormone
Tx	treatment
UA	urinalysis
UPEP	urine protein electrophoresis
VLDL	very low density lipoprotein
WBC	white blood cell count
WLE	wide local excision
XD	x-linked dominant
XR	x-linked recessive
X-RXN	cross reaction
XP	xeroderma pigmentosa
yo	year old



1. **Infraorbital** (30 g, 1", 2 cc): nose, cheek, upper lip, lower eyelid
   Intraoral: Enter above first premolar (third lateral) in gingival-labial sulcus, aim toward foramen in mid-pupillary line 1 cm below orbital rim.

2. **Mental** (30 g, 1", 2 cc): Lower lip
   Intraoral: Enter gingival-labial sulcus at base of second lower bicuspid

2a. **Mental plus** (30 g, 1.5", 2–4 cc): Chin
   After the mental nerve is blocked, pass 1 cm beyond in all directions toward inferior mandibular border

3. **Supraorbital**: Meid/lat forehead, anterior scalp (30 g, 1.5", 3 cc)
   Supratrochlear: Mid-forehead
   Infratrochlear: Medial upper eyelids, upper side of nose
   Enter along the orbital rim at the lateral 1/3 of the eyebrow aiming toward the supraorbital notch. Inject 1 cc lateral to the notch, 1 cc medial to the notch, and 1 cc when the needle advances to the nasal bone.

4. **Dorsal nasal** (30 g, 1", 1–2 cc): Cartilaginous nasal dorsum and tip.
   Inject ~1 cc lateral to the distal tip of the nasal bone.

5. **Zygomaticotemporal** (30 g, 1.5", 1–2 cc): Lateral orbital rim/temple.
   Inject inferior to the zygomaticofrontal suture, 1 cm lateral to the orbital rim.
   Inject 1 cc over the lacrimal gland for upper lateral eyelid (lacrimal nerve).

6. **Zygomaticofacial** (30 g, 1.5",1–2 cc): Superior/lateral cheek.
   Inject just lateral to the lateral/inferior border of the orbital rim.

7. **Great auricular** (30 g, 1", 1–2 cc): Lower 1/3 ear, lower postauricular
   Inject over mid-SCM, 6.5 cm below the external auditory meatus.

8. **V3-mandib** (22–23 g spinal needle, 3–4 cc): Most of cheek, upper preauric.
   Insert 90° at the sigmoid notch (b/n condyle and coranoid process)
   2.5 cm anterior to the tragus. Advance to the ptyergoid plate, mark needle, retract to skin, redirect 1 cm posterior, insert to mark, then aspirate and inject.

9. **Occipital** (30 g, 1", 5 cc): Posterior scalp
   Inject medial to the occipital artery (palpate at the superior nuchal line)
   OR inject along superior medial line b/n occipital protuberance and mastoid.

Plate 1. Facial nerve blocks. (Courtesy of Dr. Stacey Tull.)

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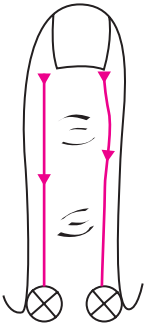
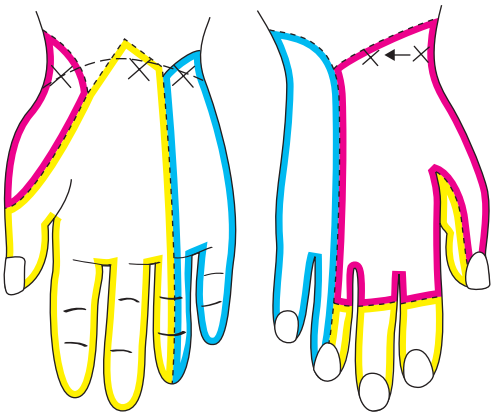


- 2 dorsal and 2 volar nerves
- Inject 1–2 cc of 2% plain lido on each side of digit distal to the MCP (or MTP) joint
- Maximum of 6–8 cc to avoid circulatory compromise

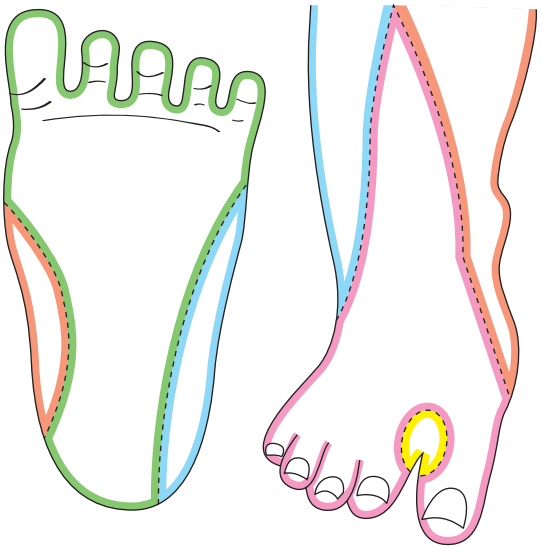
Plate 2. Digital nerve block. (Courtesy of Dr. Stacey Tull.)



Wrist

- **Radial:** Inject lateral to the radial artery at the proximal wrist crease to the midpoint of the dorsal wrist
- **Ulnar:** Inject at the proximal wrist crease medial to the flexor carpi ulnaris (ring finger)
- **Median:** Inject at the proximal wrist crease b/n palmaris longus and flexor carpi radialis (long finger)

Plate 3. Nerve block of the hand. (Courtesy of Dr. Stacey Tull.)



Ankle

- **Sural:** Inject 5 cc midway between Achilles and lateral malleolus
- **Post tibial:** Inject 3–5 cc posterior to PT artery below the medial malleolus
- **Saphenous:** Inject 5 cc along the long saphenous vein 1 cm above the medial malleolus
- **Supra peroneal:** Inject 5 cc from 5 cm above lateral malleolus to the anterior tib
- **Deep peroneal:** Skip it (mostly for deep structures)–use local for skin here.

Plate 4. Nerve block of the foot. (Courtesy of Dr. Stacey Tull.)

Part 1
General Dermatology

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Work-up Quick Reference

CTCL	CBC, LDH, Sezary prep, flow cytometry, CXR
Vasculitis	CBC, ESR, BMP, UA, consider drug-induced vasculitis, further testing guided by ROS and type of vasculitis suspected (CRP, SPEP, UPEP, cryo, LFT, HBV, HCV, RF, C3, C4, CH50, ANA, ANCA, ASO, CXR, guaiac, cancer screening, HIV, ENA, echo, electromyogram, nerve conduction, biopsy (nerve, respiratory tract, kidney))
Urticaria	In children, often due to Strep Consider ASO, Rapid Strep
Urticarial vasculitis	CBC, UA, ANA, C1, C3, C4, CH50, anti-C1q, ESR
Lupus	ANA, ENA (Ro/La), CBC, BMP, ESR, C3, C4, UA, G6PD
Sarcoid	BMP, Ca^{++}, CXR, PFTs, G6PD, EKG, ophtho consult
Angioedema	CBC, C1 est inhib, C1,C2,C4; Hereditary: C1-nl; C2,C4 and C1 est inhib-↓ (C1est inhib levels may be nl but non-functional); Acquired: C1-$^{-}$↓; C2,C4 and C1 est inhib-↓
Photosensitivity	ENA (Ro/La)
Hypercoagulable	CBC, PT/PTT, Factor V Leiden, Anti-phospholipid Ab, protein C&S, prothrombin G20210A, anti-thrombin III activity, homocysteine
TEN	Tx: IVIG 2–4 gm/kg (total dose, divided over 2–5 days) use GammaGard if possible (low IgA) Check for IgA deficiency. See TEN protocol p. 282–283

Direct immunofluorescence – where to biopsy?

Diseases	Where to biopsy
LE, MCTD, PCT, LP, Vasculitis	Erythematous border of active lesion/involved skin (avoid old lesions, facial lesions, ulcers)
Pemphigus group, Pemphigoid group, Linear IgA	Erythematous perilesional skin (avoid bullae, ulcers, erosions)
DH	Normal-looking perilesional skin (0.5–1 cm away)
Lupus band	Uninvolved, non-photoexposed skin (buttock)

Source: http://www.mayoclinic.org/dermatology-rst/immunofaqs.html

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False positive/negative DIFs

False negative in BP: (1) low yield of biopsy on distal extremity (esp. legs) (controversial), (2) predominantly IgG4 subclass of auto-antibody (poorly recognized on DIF)

False positive in LE: chronically sun-exposed skin of young adults

To increase DIF yield: transport in saline (reduces dermal background) – cannot do DIF on formalin-fixed specimen

Biopsy for GVHD

Biopsy for GVHD vs. lymphocyte recovery vs. drug eruption

- In general, path is indistinguishable between GVHD, lymphocyte recovery, and drug eruption except high grade GVHD
- Lymphocyte recovery occurs in the first 2 weeks after transplant
- Acute GVHD occurs between 3 weeks and 100 days (or longer in persistent, recurrent, or late-onset forms)
- Chronic GVHD classically was considered to occur after 40 days but has no time limit
- Eosinophils may be found in both drug eruption and acute GVHD.

Marra DE *et al.* Tissue eosinophils and the perils of using skin biopsy specimens to distinguish between drug hypersensitivity and cutaneous graft-versus-host disease. *JAAD.* 2004; 51(4):543–545.
Zhou Y *et al.* Clinical significance of skin biopsies in the diagnosis and management of graft vs host disease in early postallogeneic bone marrow transplantation. *Arch Derm.* 2000; 136(6):717–721.

The Dermatologic Differential Algorithm

1. Is it a rash or growth?
2. If it is a rash, is it mainly epidermal, dermal, subcutaneous, or a combination?
3. If the rash is epidermal or a combination, try to define the characteristics of the rash. Is it mainly papulosquamous? Papulopustular? Blistering?
4. After defining the characteristics, then think about causes of that type of rash (CITES MVA PITA):
   Congenital, **I**nfections, **T**umor, **E**ndocrinologic, **S**olar related, **M**etabolic, **V**ascular, **A**llergic, **P**sychiatric, **I**atrogenic, **T**rauma, **A**utoimmune. When generating the differential, take the history and location of the rash into account.
5. If the rash is dermal or subcutaneous, then think of cells and substances that infiltrate and associated diseases (histiocytes, lymphocytes, mast cells, neutrophils, metastatic tumors, mucin, amyloid, immunoglobulin, etc.).

6. If the lesion is a growth, is it benign or malignant in appearance? Think of cells in the skin and their associated diseases (keratinocytes, fibroblasts, neurons, adipocytes, melanocytes, histiocytes, pericytes, endothelial cells, smooth muscle cells, follicular cells, sebocytes, eccrine cells, apocrine cells, etc.).

Alopecia Work-Up

Hair	Duration	% of Hair	Microscopic/Hair pull
Anagen	2–6 years	85–90	Sheaths attached to roots
Catagen	2–3 weeks	<1	Intermediate appearance (transitional)
Telogen	3 months	10–15	Tiny bulbs without sheaths, 'club' root
Exogen	Active shedding of hair shaft		
Kenogen	Rest period after shedding telogen; empty follicle		

Associations

1. Medications? Telogen effluvium-associated meds: anticonvulsants, anticoagulants, chemotherapy, psychiatric meds, antigout, antibiotics, beta-blockers
2. Hormones (pregnancy, menstruation, OCPs)?
3. Hair care/products?
4. Diet (iron or protein deficiency)?
5. Systemic illness/stress?

Cicatricial or non-cicatricial?

1. **Non-cicatricial:** Is hair breaking off or coming out at the roots? Is hair loss focal or diffuse?

Breakage	Coming out at roots
Hair shaft defects, trichorrhexis nodosa, hair care (products, traction, friction), tinea capitis, trichotillomania, anagen arrest/chemotherapy	Telogen effluvium, alopecia areata, androgenetic, syphilis, loose anagen, OCPs

Focal loss	Diffuse loss
Hair care (traction), tinea capitis, trichotillomania, alopecia areata, syphilis, hair shaft defects	Telogen effluvium, anagen effluvium, androgenetic alopecia, hair shaft defects

2. **Cicatricial:** Is biopsy predominantly lymphocytic, neutrophic, or mixed?

Classification of cicatricial alopecia

Lymphocytic	Neutrophilic	Mixed
• LPP (including classic, frontal fibrosing, Graham-Little) • Central centrifugal • Alopecia mucinosa • Keratosis follicularis spinulosa decalvans • Chronic cutaneous LE • Pseudopelade (Brocq)	• Folliculitis decalvans • Dissecting cellulitis/ folliculitis	• Folliculitis/acne keloidalis • Folliculitis/acne necrotica • Erosive pustular dermatosis

Adapted from Olsen EA *et al.* North American hair research Society Summary of sponsored Workshop on Cicatricial Alopecia. *J Am Acad Dermatol* 2003; 48:103–10.

Structural hair abnormalities classified by hair fragility

Increased fragility	No increased fragility
Trichorrhexis invaginata (bamboo)	Loose anagen
Monilethrix	Pili annulati
Trichorrhexis nodosa	Uncombable hair (spun-glass)
Trichothiodystrophy	Woolly hair
Pili torti	Pili bifurcati
	Pili multigemini
	Acquired progressive kinking

Adapted from Hordinsky MK. Alopecias. In: Bolognia JL, Jorizzo JL, Rapini RP. *Dermatology* Vol. 1, Mosby; London. 2003, p. 1042.

Pull test and hair mount

1. **Pull test** – reveals telogen hairs in telogen effluvium, and anagen hairs in loose anagen syndrome. Helpful to identify active areas in cicatricial alopecia or alopecia areata.
2. **Hair mount**

Disorder	Hair mount findings
Monilethrix	Beaded, pearl necklace, knots
Trichorrhexis nodosa	Fractures, paint brushes
Trichorrhexis invaginata	Bamboo/golf tee hair
Trichothiodystrophy	Trichoschisis, tiger-tail on polarization
Loose anagen	Anagen hairs with ruffled cuticles and curled ends and lacking root sheaths
Pili torti	Flattened, 180° irregularly spaced twists

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Uncombable hair	Pili canaliculi et trianguli, triangular in cross section
Pili annulati	Abnormal dark bands on polarization, air bubbles in cortex
Elejalde	Pigment inclusions
Griscelli	Pigment clumping
Menkes	Multiple – pili torti, trichorrhexis nodosa, trichoptilosis

Hair count – helpful in quantifying hair loss

1. Daily hair count: collect all hairs before shampooing (Normal is <100)
2. 60 second hair count: comb for 60 seconds (Normally yields 10–15 hairs).

Biopsy – helpful in persistent alopecia, may help determine if an alopecia is cicatricial

1. 4 mm punch biopsy for horizontal sectioning
   - **a.** Hair count: Caucasians should have ~40 total hairs (20–35 terminal, 5–10 vellus) while African Americans should have fewer (18 terminal, 3 vellus) – assess catagen vs. telogen at isthmus level and terminal vs. vellus at infundibular level.
   - **b.** Look at terminal to vellus* hair ratio:

     Normal >4 (~7–10T: 1V)
     Androgenic <2–4T: 1V

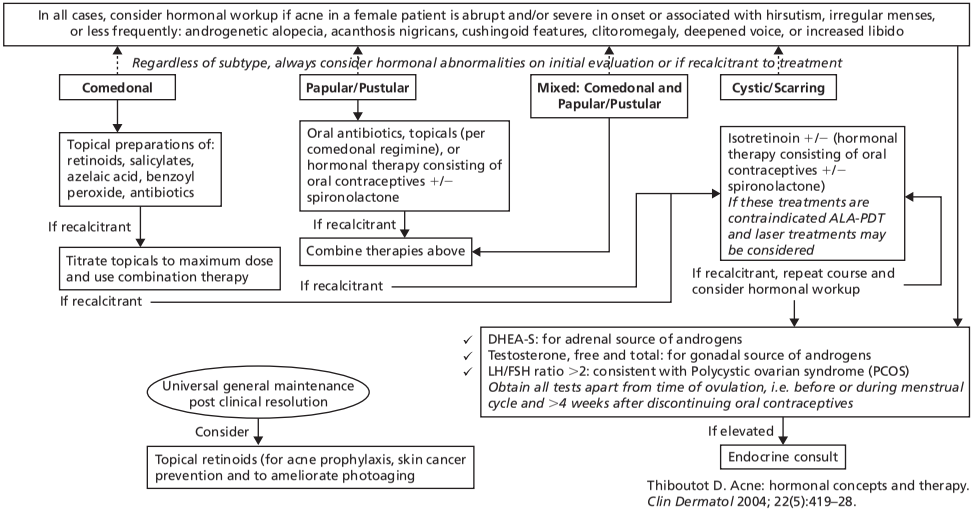
   - **c.** Look for characteristic findings:
     Alopecia areata: lymphocytes around anagen bulbs
     Trichotillomania: pigment casts, trichomalacia, catagen hairs, dermal hemorrhage
     Androgenetic alopecia: miniaturized follicles.

Labs – TSH, CBC, iron, TIBC, ferritin; consider RPR, ANA; check hormones (testosterone, DHEAS, prolactin) if irregular menses, infertility, hirsutism, severe acne, galactorrhea, or virilization.

	Hair shaft structure	Hair shaft cross section	Others
African American	Coiled, curved	Elliptical, flattened	Lowest water content, slower growth, fewer cuticular layers at minor axes (only 1–2 not 6–8), longer major axis, less dense, large follicles
Asian	Straight	Circular	Largest follicular diameter, fewer eyelashes with lower lift-up/curl-up angles and greater diameter
Caucasian	In between	In between, oval	More dermal elastic fibers anchoring hair

* Vellus hairs – true vellus hairs (small and lack melanin) and miniaturized terminal hairs are histologically identical.

Management of Acne



Thiboutot D. Acne: hormonal concepts and therapy. *Clin Dermatol* 2004; 22(5):419–28.

Aphthosis Classification and Workup

Morphologic classification

- **Minor aphthae**: single to few, shallow ulcers (<1 cm) which spontaneously heal in 1–2 weeks
- **Major aphthae** (Sutton's, periadenitis mucosa necrotica recurrens): single to few, deep ulcers (>1 cm) which heal over weeks–months and scar
- **Herpetiform aphthae**: 10–100, clustered, small ulcers (3 mm) which heal in days–weeks, may scar (not associated with HSV)

Classification by cause

- **Simple aphthae**: recurrent minor, major, or herpetiform aphthae, often in healthy, young patients
- **Complex aphthae**: >3, nearly constant, oral aphthae *or* recurrent genital and oral aphthae, *and* exclusion of Behçet and MAGIC syndromes
  - Primary: idiopathic
  - Secondary: IBD, HIV, cyclic neutropenia, FAPA (fever, aphthous stomatitis, pharyngitis, adenitis), gluten sensitivity, ulcus vulvae acutum, vitamin deficiencies (B1, B2, B6, B12, folate), iron, and zinc deficiencies, drugs (NSAIDS, alendronate, beta-blockers, nicorandil).

Work-up for complex aphthae

- HSV PCR/Cx
- CBC
- Iron, folate, vitamin B12, zinc
- Consider UA
- Consider HIV, HLA-B27, antigliadin/antiendomysial Ab
- Consider biopsy
- Consider GI, rheum, ophtho, neuro consults
- If considering dapsone, check G6PD

Local factors promoting aphthae: chemical/mechanical injury, sodium lauryl sulfate-containing dental products, inadequate saliva, cessation of tobacco.

Treatment

- Topical: anesthetics, corticosteroids (or IL), tacrolimus, retinoids, rinses (chlorhexidine, betadine, salt water, hydrogen peroxide, tetracyclines)
- Systemic: colchicine, dapsone, thalidomide (HIV)

Adapted from Letsinger JA *et al.* Complex aphthosis: a large case series with evaluation algorithm and therapeutic ladder from topicals to thalidomide. *J Am Acad Dermatol* 2005; 52(3 Pt 1):500–508.

Amyloidoses

Stains: PAS+/diastase resistant. Fluoresces with thioflavin T. Purple with crystal violet. Birefringence with Congo red (absent after treating with potassium permanganate in AA subtype).

Classification	Type	Symptoms/subtypes
Primary systemic	AL >>AH	40% have skin involvement: waxy skin colored papules (nose, eyes, mouth), alopecia, carpal tunnel, pinch purpura, shoulder pad sign. Also may deposit in heart, GI tract, tongue.
Secondary/ reactive systemic	AA	Skin NOT INVOLVED. Deposits in liver, spleen, adrenals, and kidney. Associated with chronic disease (especially TB, leprosy, Hodgkin, RA, renal cell cancer).
Primary cutaneous	AL	Nodular amyloid: nodule(s) on extremities, trunk.
	Keratin	Macular amyloid: pruritic macules interscapular region, associated with nostalgia paresthetica.
	Keratin	Lichen amyloid: discrete papules on shins.
Secondary cutaneous/ tumor associated	Keratin	Following PUVA and in neoplasms.
Familial syndromes	AA	Hereditary periodic fever syndromes: Familial Mediterranean Fever and TNF receptor-associated periodic syndromes (but not Hyper-IgD)
	AA	Cryopyrin-associated periodic syndromes: Familial cold autoinflammatory, Muckle–Wells, CINCA/NOMID

Amyloid subtype	Precursor protein	Association
AL	Ig light chain	Primary systemic, myeloma, plasmacytoma, nodular
AH	Ig heavy chain	Primary systemic, myeloma
AA	(apo) serum AA (SAA)	Reactive systemic, TRAPS, FMF, Muckle–Wells, familial cold autoinflammatory
ATTR	Transthyretin (prealbumin)	Familial amyloid polyneuropathy 1 and 2, familial amyloid cardiomyopathy, senile systemic
A β_2M	β_2-microglobulin	Hemodialysis
A β	A b Precursor protein (AbPP)	Alzheimer, Down, hereditary cerebral hemorrhage with amyloidosis (Dutch)
Keratinocyte tonofilaments		Macular and lichen, MEN IIa, secondary cutaneous (PUVA, neoplasms)

Apolipoprotein I	Familial amyloid polyneuropathy 3
Atrial natriuretic factor	Isolated atrial
Calcitonin	Medullary thyroid cancer associated
Cystatin	Hereditary cerebral hemorrhage (Icelandic)
Fibrinogen α chain	Familial fibrinogen associated
Gelsolin	Familial amyloid polyneuropathy 4 (Finnish)
Islet amyloid polypeptide	Diabetes mellitus II/insulinoma associated
Lactoferrin	Corneal lactoferrin associated
Lysozyme	Familial lysozyme associated
Medin/lactadherin	Aortic medial
Prion protein/scrapie	Creutzfeld-Jacob

Xanthomas

Type	Distribution /appearance	Associations
Xanthelasma palpebrarum	Polygonal papules esp. near medial canthus	May be associated with hyperlipidemia (50%) including any primary hyperlipoproteinemia or secondary hyperlipidemias such as cholestasis
Tuberous xanthomas	Multilobulated tumors, pressure areas, extensors	Hypercholesterolemia (esp. LDL), familial dysbetalipoproteinemia (type 3/broad beta disease), familial hypercholesterolemia (type 2), secondary hyperlipidemias (nephrotic syndrome, hypothyroidism)
Tendinous xanthomas	Subcutaneous nodules esp. extensor tendons of hands, feet, Achilles, defects, trauma	Severe hypercholesterolemia (esp. LDL), particularly type 2a, apolipoprotein B-100 secondary hyperlipidemias (esp. cholestasis, cerebrotendinous xanthomatosis, beta-sitosterolemia
Eruptive xanthomas	Crops of small papules on buttocks, shoulders, extensors, oral	Hypertriglyceridemia (esp. types 1, 4, and 5 hyperlipidemias), secondary hyperlipidemias (esp. DM2)
Plane xanthomas	Palmar creases	Familial dysbetalipoproteinemia (type 3), secondary hyperlipidemia (esp. cholestasis)
Generalized plane xanthomas	Generalized, esp. head and neck, chest, flexures	Monoclonal gammopathy, hyperlipidemia (esp. hypertriglyceridemia)
Xanthoma disseminatum	Papules, nodules, mucosa of upper aerodigestive tract	Normolipemic
Verucciform xanthomas	Solitary, oral or genital, adults	Normolipemic

Hyperlipoproteinemias: Fredrickson Classification

Type	Name	Defect, AR/AD	Lipid profile	Xanthomas	Other clinical
I	Hyperlipoproteinemia	Lipoprotein lipase, AR	↑ chylomicrons, chol, TG ↓ LDL, HDL	Eruptive xanthomas (2/3), lipemia retinalis	↑ CAD, HSM, pancreatitis
IB	Apolipoprotein C-II deficiency	APOC2 AR	Similar to Lipoprotein lipase deficiency		
IIA*	Familial hypercholesterolemia, LDL receptor disorder	LDL receptor, AD	↑ LDL, chol, TG	Tuberous, intertriginous, tendinous, planar xanthomas, xanthelasma, corneal arcus	↑ CAD
	Familial hypercholesterolemia, type B	APOB, AD	Same as IIA		
IIB	Combined hyperlipoproteinemia	Heterogeneous	↑ LDL, VLDL, chol, TG	Xanthomas rare	↑ CAD
III	Familial dysbetalipoproteinemia, broad beta-lipoproteinemia	APOE, AR	↑ chylomicron remnants/VLDL, chol, TG	Planar palmar crease, tuberous xanthomas, xanthelasma	↑ CAD, DM2
IV	Carbohydrate-inducible lipemia	AD	↑ VLDL, TG ↓ HDL	Tuberoeruptive xanthomas	↑ CAD, DM2, obesity, etoh, hypothyroidism, pancreatitis, uremia, myeloma, nephrotic, hypopituitarism, glycogen storage type I
V	Mixed hyperprebeta-lipoproteinemia and chylomicronemia	APOA5, AR/AD	↑ chylomicrons, VLDL, TG, chol ↓ LDL, HDL	Eruptive xanthomas, lipemia retinalis	Abd pain, pancreatitis, DM2, HTN, hyperuricemia, OCPs, etoh, glycogen storage type I

*Other familial hypercholesterolemia syndromes – AR Hypercholesterolemia (ARH/LDLR Adaptor Protein mutations), AD Hypercholesterolemia type 3 (PCSK9/PROPROTEIN CONVERTASE, SUBTILISIN/KEXIN-TYPE, 9 mutations)

Mallory SB. *An Illustrated Dictionary of Dermatologic Syndromes,* 2nd edition, Taylor & Francis; New York, London: 2006.

Histiocytosis

Histiocytosis	Onset	Clinical features	Associations	Pathology
Langerhans cell histiocytosis 2/3 children age 1–3 years old; 1/3 adults – usually pulmonary, often smokers. New classification by organ of involvement: 1. Restricted LCH: a. Skin only b. Monostotic lesions ± diabetes insipidus (DI), LN, rash c. Polyostotic lesions ± DI, LN, rash 2. Extensive LCH: a. Visceral organ involvement w/o dysfunction ± DI, LN, rash b. Visceral organ involvement with dysfunction ± DI, LN, rash				
Letterer–Siwe	0–2 years old	• Acute, disseminated, multisystem form • Resembles seb derm • Fever, anemia, LAN, osteolytic lesions, HSM	ALL, solid tumors	• CD1a+, S100+, Placental Alk Phos+ • Reniform, 'coffee-bean' nuclei • Birbeck granules
Hand-Schüller-Christian	2–6 years old	• Chronic, multisystem (skin lesions in 1/3) • Classic triad: bone lesions (80%, esp. cranium), DI, exophthalmos		
Eosinophilic granuloma	Older children/adults	• Localized, benign • May present with spontaneous fracture or otitis		
Hashimoto-Pritzker	Congenital	• a.k.a Congenital self-healing reticulocytosis • Widespread, red-brown papules or crusts		

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Histiocytosis	Onset	Clinical features	Associations	Pathology
Non-Langerhans cell histiocytosis without malignant features				
Juvenile xanthogranuloma	Early childhood	• Most common histiocytosis, self-limiting • Solitary lesion in 25–60% of cases • Head/neck > trunk > extremities • May be systemic (CNS, liver/spleen, lung, eye, oropharynx) • Eye = most common extracutaneous site, unilateral	• NF1 • leukemia • NF and juvenile CML	• Small histiocytes, Touton and foreign body giant cells, foam cells • CD68+, factor XIIIa+, vimentin+
Benign cephalic histiocytosis	0–3 years old	• 2–5 mm, yellow-red papules on face/neck of infant • Self-limiting • Spares mucous membranes and viscera	Probably same as JXG	a.k.a. Histiocytosis w/ Intracytoplasmic worm-like bodies (on EM)
Generalized eruptive histiocytoma	Adults>children	• Crops of small, red-brown papules. Widespread axial distribution • Spontaneous resolutions		
Indeterminate cell histiocytosis	Adults>children	• Clinically identical to generalized eruptive histiocytoma		Antigenic markers of both LCH and non-LCH
Multicentric reticulohistiocytosis	Adults (F>M) 30–50 years old	• Joints, skin, mucous membranes (50%) • Papules/nodules – head, hand, elbow, periungual 'coral beads' • Often misdiagnosed as RA • Waxes/wanes, spontaneously remits in 5–10 years	• 25% internal malignancies (gastric, breast, GU) • 6–17% autoimmune conditions • 30–60% hyperlipidemia	• Histiocytes w/ 'ground glass' appearance, oncocytic histiocytes • Multinucleate giant cells • CD45+, CD68+, CD11b+, HAM56+, vimentin+ • Usu S100−, Factor XIIIa−, CD34−

		Giant cell reticulohistiocytoma, a.k.a. solitary reticulohistiocytoma = isolated, cutaneous tumor version of MRH		
Necrobiotic xanthogranuloma	6th decade	• Usu head/neck or trunk: esp. periorbital • Scleritis, episcleritis → possible blindness • May have anemia, leukopenia, elevated ESR, 20% HSM • Often chronic, progressive	• 90% IgG paraproteinemia • 40% cryoglobulinemia	• Hyaline necrobiosis, palisaded granuloma (cholesterol cleft) • Touton and foreign body giant cells • 'Touton cell panniculitis' • CD15+, CD4+ • CD1a−, S100−
Xanthoma disseminatum	Any	• Proliferation of foamy histiocytes despite normal serum lipids • Flexors, skin folds, mucous membranes (eyes, URT, meninges → leads to DI) • Usu benign, self-limiting		• Unique scalloped histiocytes in early lesions • Histiocytes, foam cells, chronic inflammatory cells, Touton and foreign body giant cells • CD68+, Factor XIIIa+ • CD1a−, S100−
Rosai–Dorfman Dorfman a.k.a. sinus histiocytosis with massive lymphadenopathy	10–30 years old, M>F	• Generally benign, self-limiting • Painless, cervical LAN • 40% have extranodal involvement (poor prognosis) • Skin is most common extranodal site		• Expansion of LN sinuses by large foamy histiocytes, plasma cells, multinucleate giant cells • Emperipolesis • S100+, Factor XIIa+, • CD1a −
Erdheim-Chester	Middle age	• Similar to XD, but 50% mortality • Symmetric sclerosis of metaphyses/diaphyses of long bones (virtually pathognomonic) → chronic bone pain		• Histiocytes, foam cells • CD68+, Factor XIIIa+ • CD1a− • Usu S100−

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Histiocytosis	Onset	Clinical features	Associations	Pathology
		• DI, renal and retroperitoneal infiltrates, xanthoma-like skin lesions (esp. eyelids), pulmonary fibrosis, CNS		
Hemophagocytic lymphohistiocytosis	Children	• Rare, life-threatening, rapidly progressive • Dx Criteria: F, splenomegaly, cytopenia, hyperTG, hyper-fibrinogenemia, hemophagocytosis on tissue bx • Nonspecific rashes in ~60% • Median survival: 2–3 months (BM failure, sepsis) • Two Types – Primary and Familial HLH (in both cases) triggered by infection, esp. EBV	• CTD, malignancies, HIV *Familial HLH:* • FHL1 – HPLH1 • FHL2 – PRF1 (cytolytic granule content) • FHL3 – UNC13D (cytolytic granule secretion) • FHL4 – syntaxin-11 (membr-associated, SNARE family, docking/fusion)	
Sea-blue histiocytosis	Inherited	• Rare • BM, HSM – also lungs, CNS, eyes, skin • Nodular lesions; eyelid infiltration	• APOE mutations • One of the manifestations of Niemann-Pick type B • Common (<1/3) in BM bx's of MDS	Large, azure blue, cytoplasmic granules with May-Gruenwald stain (yellow-brown on H&E, dark blue with toluidine or Giemsa)
Non-Langerhans cell histiocytosis with malignant features				
Malignant histiocytosis	M>F 2:1	• Very rare, life-threatening • Liver, spleen, LN, BM • p/w painful LAN, HSM, fever, night sweats • Pancytopenia, DIC, extranodal extension • 10–15% skin involvement (esp. lower legs, buttocks).		Variable

Lupus Erythematosus

Systemic lupus erythematosus criteria (4 of 11)

Adapted from the American College of Rheumatology 1982 revised criteria

Mucocutaneous

1. Malar rash (tends to spare nasolabial folds)
2. Discoid lesions
3. Photosensitivity
4. Oral ulcers (must be observed by physician)

Systemic

5. Arthritis – nonerosive arthritis of 2+ joints
6. Serositis – pleuritis, pericarditis
7. Renal disorder – proteinuria $>$ 0.5 g/day or 3+ on dipstick
8. Neurologic – seizures or psychosis
9. Hematologic:
   - **a.** hemolytic anemia with reticulocytosis
   - **b.** leukopenia ($<$4 K) on 2 occasions
   - **c.** lymphopenia ($<$1.5 K) on 2 occasions
   - **d.** thrombocytopenia ($<$100 K)
10. Immunologic – anti-dsDNA, anti-Sm, false positive RPR
11. ANA+

Acute cutaneous lupus erythematosus

Clinical findings: transient butterfly malar rash, generalized photosensitive eruption, and/or bullous lesions on the face, neck, and upper trunk.

Associated with HLA-DR2, HLA-DR3

DIF: granular IgG/IgM (rare IgA) + complement at DEJ.

Subacute cutaneous lupus erythematosus

Clinical findings: psoriasiform or annular non-scarring plaques in a photodistribution.

Associated with:

- HLA-B8, HLA-DR3, HLA-DRw52, HLA-DQ1
- SLE, Sjögren, RA, C2 deficiency
- Medications: HCTZ, Ca+ channel blocker, ACE inhibitors, griseofulvin, terbinafine, anti-TNF, penicillamine, glyburide, spironolactone, piroxicam

DIF: granular pattern of IgG/IgM in the epidermis only (variable).

Chronic cutaneous lupus erythematosus

Discoid lupus

Clinical findings: erythematous plaques which progress to atrophic patches with follicular plugging, scarring, and alopecia on sun-exposed skin.

Progression to SLE: 5% if above the neck; 20% if above and below the neck
DIF: granular IgG/IgM (rare IgA) + complement at DEJ, more likely positive in actively inflamed lesion present × 6–8 weeks.

Lupus panniculitis

Clinical findings: deep painful erythematous plaques, nodules and ulcers involving proximal extremities and trunk. Overlying skin may have DLE changes.
Progression to SLE: 50%
DIF: rare granular deposits at the DEJ. May have deposits around dermal vessels.

Tumid lupus

Clinical findings: erythematous indurations of fat with no scale or follicular plugs.
DIF: nonspecific

Lupus band: strong continuous antibody deposits at the DEJ on nonlesional skin; found in >75% *of SLE patients on sun-exposed skin* and 50% *SLE patients on non-sun-exposed skin*

Autoantibody sensitivities and specificities

Condition	Autoantibody or target	Sensitivity (%)	Specificity (%)
SLE	ANA	93–99	57
	Histone	60–80	50
	dsDNA*	50–70	97
	U1-RNP	30–50	99
	Ribosomal-P	15–35	99
	Sm	10–40	>95
	SS-A	10–50	>85
	SS-B	10–15	
SCLE	ANA	67	
	SS-A	60–80	
	SS-B	25–50	
DLE	ANA	5–25	
	SS-A	<<10	
Drug-Induced LE	ANA	>95	
	Histone	>95	
	dsDNA		1–5
	Sm	1	

Neonatal Lupus	SS-A**	95	
	SS-B	60–80	
MCTD	ANA	100	
	U1-RNP	>95	
Localized scleroderma	Nucleosome	80	
(Morphea)	Topoisomerase II	75	
	Histone	50	
	ssDNA	50	
	ANA	45–80	
Limited SSc	ANA	90	
	Centromere	50–90	
	Scl-70	10–15	
	RNA pol III	2	
Diffuse SSc	ANA	90	
	Scl-70	20–40	
	RNA pol III	25	
	Centromere	≤5	
Sjögren	ANA	50–75	50
	SS-A	50–90	>85
	SS-B	40	>90
	RF	50	
Polymyositis (PM)	ANA	85	60 (DM/PM)
	Jo-1	25–37	
Dermatomyositis (DM)	ANA	40–80	60 (DM/PM)
Rheumatoid arthritis	CCP	65–70	90–98
	RF	50–90	>80
	ANA	20–50	55
	Histone	15–20	
Secondary Raynaud	ANA	65	40

Sensitivity and specificity for different antibodies varies depending on the assay used. The percentage reported here are estimated averages from the referenced text below.

* Correlates with SLE activity and renal disease

** Risk of neonatal lupus among babies of SS-A+ mothers: 2–6%

ANA titers of 1:80, 1:160, and 1:320 are found in 13, 5, and 3%, respectively of healthy individuals. Among healthy elderly patients, ANA titers of 1:160 may be seen in 15%.

Sheldon J. Laboratory testing in autoimmune rheumatic disease. *Best Pract Res Clin Rheumatol.* 2004 Jun; 18(3):249–69.

Lyons *et al.* Effective use of autoantibody tests in the diagnosis of systemic autoimmune disease. *Ann N Y Acad Sci.* 2005 Jun; 1050:217–28.

Kurien BT, Scofield RH. Autoantibody determination in the diagnosis of systemic lupus erythematosus. *Scand J Immunol.* 2006 Sep; 64(3):227–35.

Habash-Bseiso *et al.* Serologic testing in connective tissue diseases. *Clin Med Res.* 2005 Aug; 3(3):190–193.

Antinuclear Antibodies
(S: sensitive SP: specific)

Pattern	Antibody target	Disease	Notes
Homogenous	Histone dsDNA	**Drug-induced LE*** (>90% S), SLE (>60% S), Chronic Disease **SLE** (60% SP), **Lupus nephritis**	IC in glomeruli = nephritis, follows disease activity, test performed on *Crithidia luciliae*
Peripheral nuclear (Rim)	Nuclear Lamins Nuclear Pore	**SLE**, Linear Morphea PM	
Centromere/ true speckled	Centromere	**CREST** (50–90% S), SSc, Primary Biliary Cirrhosis (50% S), Idiopathic Raynaud, PSS	
Speckled/ particulate nuclear (ENA)	U1-RNP	**Mixed connective tissue disease** (near 100% S) **SLE** (30% S), DM/PM, SSc, Sjögren, RA	Titer > 1:1600 in 95–100% MCTD
	Smith (snRNP)	**SLE** (99% SP but only 20% S)	
	Ro/SS-A (E3 ubiquitin ligase, TROVE2)	**SCLE** (75–90% S), **Sjögren**, Neonatal LE, Congenital Heart Block, C2/C4 deficient LE	Photosensitivity work-up
	La/SS-B (binds RNA newly transcribed by RNA Pol III)	**Sjögren, SCLE**	
Nucleolar	Scl-70 (Topoisomerase I)	**SSc** (diffuse > limited)	Poor prognosis
	Fibrillarin (U3-RNP)	SSc (diffuse > limited)	
	PM-Scl	PM/SSc Overlap syndromes	Machinists hands, arthritis, Raynaud, calcinosis cutis
	RNA Pol I	SSc	Poor prognosis, renal crisis

***Drug-induced ("Dusting Pattern"):** Allopurinol, aldomet, ACE-I, chlopromazine, clonidine, danazol, dilantin, ethosuximide, griseofulvin, hydralazine, isoniazid, lithium, lovastatin, mephenytoin, mesalazine, methyldopa, MCN, OCP, *para*-amino salicylic acid, penicillamine, PCN, phenothiazine, pheylbutazone, piroxicam, practolol, procainamide, propylthiouracil, quinidine, streptomycin, sulfasalazine, sulfonamides, tegretol, TCN.

Autoantibodies in Connective Tissue Diseases

Autoantibody or target	Activity	Clinical association
LAC, β2-glycoprotein I, Prothrombin, Cardiolipin, Protein S, Annexin AV	Phospholipids	Antiphospholipid antibody syndrome*
Rheumatoid factor	Fc portion of IgG	Low level – nonspecific (SLE, SSc, MCTD, neoplasm, chronic disease) High level – associated with erosive RA
Ku	DNA end-binding repair protein complex	Overlap DM/PM, SSc, LE
U2-RNP		Overlap DM/PM, SSc
Alpha-fodrin	Actin binding protein	Specific for Sjögren
Jo-1/PL-1	Histidyl-tRNA synthetase	DM/PM** (20–40% sensitive) – increased risk of interstitial lung disease, but no increased rate of malignancy
Mi-2	Nuclear helicase	DM with malignancy, better prognosis than anti-synthetase
PDGF		SSc, cGVHD
SRP	Signal recognition protein	Anti-SRP syndrome (rapidly progressive necrotizing myopathy); association with cardiac disease not confirmed
155 K-EB antigen	Transcriptional intermediary factor-1	DM (20% sensitive in adult-onset classical form), may be associated with internal malignancy

***Antiphospholipid antibody (APA) syndrome** – Primary (50%), SLE (35%); Skin: livedo reticularis, ulcers, gangrene, splinter hemorrhages.
Diagnosis requires at least one clinical criterion:

- Clinical episode of vascular thrombosis
- Pregnancy complication: unexplained abortion after week 10, premature birth at or before week 34, or ⩾3 unexplained, consecutive SAB before week 10.

And at least one lab criterion: anticardiolipin, lupus anticoagulant, or anti-β2-glycoprotein I Abs on 2 occasions 6 weeks apart.

Adapted from Jacobe H *et al.* Autoantibodies encountered in patients with autoimmune connective diseases. In: Bolognia J, Jorizzo JL, Rapini RP. *Dermatology,* Vol. 1. London: Mosby, 2003. pp. 589–99.

****Polymyositis/dermatomyositis –** ⩾40% ANA+, 90% auto-Ab. Anti-synthetase syndrome (tRNA): interstitial lung disease, fever, arthritis, Raynaud disease, machinist hands.

Vasculitis

Initial work-up: Detailed history, physical exam, ROS, skin biopsy ± CBC, ESR, BMP, UA, consider drug-induced vasculitis.
Further testing guided by ROS and type of vasculitis suspected: CRP, SPEP, UPEP, cryo, LFT, HBV, HCV, RF, C3, C4, CH50, ANA, ANCA, ASO, CXR, guaiac, cancer screening, HIV, ENA, echo, electromyogram, nerve conduction, biopsy (nerve, respiratory tract, kidney)

Treatment of ANCA-associated vasculitis

- Induction: Cyclophosphamide 2 mg/kg/day, Prednisolone 1 mg/kg/day tapered to 0.25 mg/kg/day by 12 weeks.
- Maintenance: Azathioprine 2 mg/kg/day, Prednisolone 7.5–10 mg/day
  Frequent life severe adverse events with cyclophosphamide (Cytoxan), nitrogen mustard, alkylating agent:
  1. Hemorrhagic cystitis (10%) and risk of bladder cancer (5% at 10 years, 16% at 15 years): minimize by using copious fluids, mesna, acetylcysteine and not using h.s. dosing.
  2. Bone marrow suppression: Onset 7 days, nadir 14 days, recovery 21 days.
  3. Infection
  4. Infertility

Anti-neutrophil cytoplasmic antibody

	Wegener syndrome	Microscopic polyangiitis	Churg–Strauss syndrome
ANCA (% sensitivity)	C-ANCA (85%) > P-ANCA (10%)	P-ANCA (45–70%) > C-ANCA (45%)	P-ANCA (60%) > C-ANCA (10%)
Classic features	Upper respiratory (sinusitis, oral ulcers, rhinorrhea), glomerulonephritis (GN), saddle-nose, strawberry gingiva, ocular	Necrotizing GN (segmental and crescentic), pulmonary hemorrhage (esp. lower), neuropathy	Asthma, allergies, nasal polyps, eosinophilia, PNA, gastroenteritis, CHF, mononeuritis multiplex
Skin	Palpable purpura, SQ nodules, pyoderma gangrenosum-like lesions	Palpable purpura	Palpable purpura, SQ nodules
Pathology	Perivascular necrotizing granulomas, LCV	No granulomas, LCV with few/no immune depositis	Eosinophils, extravascular granulomas, LCV
Respiratory	Upper and lower respiratory, fixed nodular densities	Lower respiratory, alveolar hemorrhage	Patchy, transient interstitial infiltrates
Treatment	High-dose corticosteroids; Cytotoxic agents if severe (no controlled trial demonstrating benefits)	High-dose corticosteroids; Cytotoxic agents if severe (no controlled trial demonstrating benefits)	High-dose corticosteroids combined with cytotoxic agent (cyclopohsphamide) with proven benefit in survival

C-ANCA = cytoplasmic (IIF) = proteinase 3.
P-ANCA = perinuclear (IIF) = myeloperoxidase.
Other conditions which may be ANCA positive: SLE, RA, chronic infection (TB, HIV), digestive disorders (inflammatory bowel disease, sclerosing cholangitis, primary biliary cirrhosis, autoimmune hepatitis), drugs (propylthiouracil, hydralazine, methimazole, minocycline, carbimazole, penicillamine), silica/occupational solvents
Titers might indicate disease activity, relapse.

Small vessel vasculitis

Disease	Symptoms	Etiology/Associations	Treatment
Cutaneous small vessel vasculitis	Palpable purpura, lower legs/ankles/dependent areas, ± livedo reticularis, urticaria, edema, ulcers, ± pruritic, painful/burning, fever, arthralgias	Drugs, infections, CTD, neoplasms	Usually self-limited, rest, elevation, compression, NSAIDs, anti-histamines, corticosteroids, colchicine, dapsone, immunosuppressants
Henoch-Schönlein purpura	Palpable purpura on extensors and buttocks, pts 4–7 years old, polyarthralgia (75%), GI bleeding, fever, hematuria, edema, renal dysfunction, pulmonary hemorrhage, headache	1–2 weeks after respiratory infection, allergens/food, drugs; usually unknown	Primarily supportive. corticosteroids, other immunosuppressants, dapsone, factor XII
Acute hemorrhagic edema of infancy	Large, annular, purpuric plaques and edema on face, ears, extremities, usually in p<2 years old	Infections (especially respiratory), drugs, vaccines; usually unknown	Self-resolving
Urticarial vasculitis	Painful (>pruritic), lasts >24 h, post-inflammatory hyperpigmentation, ± bullae, systemic dz in hypocomplementemic version (anti-C1q precipitin, F>M, ocular, angioedema, COPD), F>M	Autoimmune/CTD (30% of Sjogren, 20% of SLE pts), drugs (serum sickness), infections (HBV, HCV, EBV), neoplasms, Schnitzler syndrome	Oral corticosteroids, anti-malarials, dapsone, colchicine, anti-histamines, NSAIDs

Hyperimmuno-globulinemia D syndrome	Periodic fever, arthralgia, GI sxs, LAN, erythematous macules/papules/nodules/urticaria on extremities, onset <10 years old, ↑ IgD and IgA levels	AR; Mevalonate kinase deficiency	NSAIDs, anti-IL-1 Ab, corticosteroids
Familial mediterranean fever	Periodic fever, arthritis, serositis, erysipelas-like rash on legs, myalgias, AA amyloidosis, renal failure, PID sxs; unlike Hyper-IgD, no LAN and nl IgD level	AR; Pyrin deficiency	Colchicine, anti-IL-1
Erythema elevatum diutinum	Yellow/brown/red papules, plaques, and nodules over joints	Hematologic diseases, HIV, IBD, CTD, streptococcal infections	Dapsone, niacinamide, topical/intralesional corticosteroids
Granuloma faciale	Brown/red plaques on face, middle-aged, M>F, Caucasian	Unknown	Treatment-resistant, intralesional steroids, dapsone, surgery
Serum sickness	Fever, LAN, arthralgias, urticaria, maculopapular, scarlatiniform, purpura, myalgias	Type III hypersensitivity, commonly following streptokinase, IVIG, Abx (cefaclor, PCN, MCN, rifampin, cefprozil)	Avoidance, anti-histamines, anti-pyretics, corticosteroids

Medium (± small) vessel vasculitis

Polyarteritis nodosa (systemic)	SQ nodules on legs, livedo reticularis, "punched-out" ulcers, digital gangrene, p-ANCA positive, universal multisystemic involvement: myocardial/GI/renal infarction, polyneuritis, CNS, arthralgias, weight loss, HTN, (renal) microaneurysms, orchitis (esp. with HBV)	Various infections/inflammatory conditions: streptococcus, HBV, HCV, CMV, HIV, SLE, IBD, hairy cell leukemia	Corticosteroids, cyclophosphamide
Polyarteritis nodosa (cutaneous)	SQ nodules, starburst pattern of livedo reticularis, mild fever, nerve and muscle involvement	As above (cPAN represents 10% but is most common form in children, more often strep)	Topical/intralesional steroids, PCN
Microscopic polyangiitis	Palpable purpura, ulcers, splinter hemorrhages, crescentic necrotizing segmental glomerulonephritis, fever, weight loss, myalgias, neuropathy, HTN, p-ANCA (60%); c-ANCA (40%)		Corticosteroids, cyclophosphamide
Wegener granulomatosis	Respiratory, renal, sinus, ocular, otologic, CNS, cardiac, joints, nasal nodules/ulcers/saddle nose, pulmonary infiltrates/ nodules, SQ nodules, c-ANCA (85%)	Unknown – distinguish from lymphomatoid granulomatosis (severe EBV+ angioinvasive B-cell lymphoma of skin and lungs)	Corticosteroids, cyclophosphamide (treat staph infection and nasal carriage to minimize relapse)
Churg–Strauss syndrome (allergic granulomatosis)	Asthma, sinusitis, allergic rhinitis, eosinophilia, arthritis, myositis, CHF, renal/HTN, mononeuritis multiplex, palpable purpura, infiltrated nodules, p-ANCA (60%)	Vaccination, leukotriene inhibitors, desensitization therapy, rapid steroid taper	Corticosteroids, cyclophosphamide

Large vessel vasculitis

Giant cell arteritis (temporal)	Tender, temporal artery, polymyalgia rheumatica, unilateral HA, jaw claudication, blindness, F>M, Northern European	Unknown	Corticosteroids
Takayasu arteritis	Constitutional sxs, pulselessness, signs/sxs of ischemia, EN-like nodules, pyoderma gangrenosum-like lesions	Associations: RA, other CTD	Corticosteroids, cyclophosphamide, surgical revascularization

Other causes of vasculitis: Infections (bacterial – meningococcemia, gonnococcemia, strep, mycobacterial; viral – HSV; fungal), Rheumatoid vasculitis, Drug-induced, Lupus, Paraneoplastic, Buerger, Mondor

Lymphocytic vasculitis: Pityriasis lichenoides, Pigmented purpuras, Gyrate erythemas, Collagen vascular disease, Degos, Perniosis, Rickettsial, TRAPS

Neutrophilic dermatoses: Sweet, Marshall (+ acquired cutis laxa), Behcet, Rheumatoid, Bowel-associated dermatosis–arthritis syndrome

Vasculo-occlusive/microangiopathies: Cryos, Anti-phospholip syndrome, Atrophic blanche/Livedoid, DIC, Purpura fulminans, Coumadin necrosis, TTP, Sneddon (livedo reticularis + cerebrovascular ischemia), Cholesterol emboli, CADASIL, Calciphylaxis, Amyloid

Cryoglobulinemia

Cryoglobulinemia type*	Monoclonal or polyclonal	Immunoglobulins	Diseases
1 ('Simple/Single')	Single monoclonal	IgM > IgG > IgA or light chain	**Associations:** Lymphoproliferative disorders: lymphoma, CLL, myeloma, Waldenstrom macroglobulinemia **Manifestations:** Retiform necrotic lesions, acrocyanosis, Raynaud phenomenon, cold urticaria, livedo reticularis, retinal hemorrhage, arterial thrombosis
2 ('Mixed')	Monoclonal and polyclonal	Monoclonal IgM (RF) complexed to polyclonal IgG	**Associations:** HCV > other autoimmune (Sjögren, SLE, RA), infections (CMV, EBV, HIV, HBV, HAV), lymphoproliferative disorders **Manifestations:** LCV with palpable purpura, arthralgias/arthritis involving PIPs, MCPs, knees and ankles, diffuse glomerulonephritis
3 ('Mixed')	Polyclonal	IgG and/or IgM	**Associations:** HCV, other autoimmune (Sjögren, SLE, RA), infections (CMV, EBV, HIV, HBV, HAV), lymphoproliferative disorders **Manifestations:** LCV with palpable purpura, arthralgias/arthritis involving PIP, MCP, knees and ankles, diffuse glomerulonephritis

Rheumatoid Factor = Antibody against Fc portion of IgG = Cryoglobulinemia Types 2 (monoclonal RF) and 3 (polyclonal RF).
Meltzer Triad = Purpura, arthralgia, weakness.
Work-up: Serum specimen must be obtained in WARM tubes. Immunoglobulins precipitate at cold temperature. Type 1 precipitates in 24 h, Type 3 may require 7 days.
Cryoglobulinemia: Immunoglobulins which reversibly precipitate on cold exposure.
Cryofibrinogen: Fibrinogen, fibrin, fibronectin which precipitate in the cold.
Cold Agglutinins: IgM antibodies which promote agglutination of RBCs on exposure to cold, triggering complement activation and lysis of RBCs.
*All 3 groups cause occlusive syndromes in the skin triggered by cold exposure.

CTCL Classification

	Relative frequency (%)	5-Year survival (%)
Indolent cutaneous T-cell and NK-cell lymphoma		
Mycosis fungoides	44	88
Follicular MF	4	80
Pagetoid reticulosis	<1	100
Granulomatous slack skin	<1	100
Cutaneous anaplastic CD30+ large cell lymphoma	8	95
Lymphomatoid papulosis	12	100
Subcutaneous panniculitis-like T-cell lymphoma	1	82
CD4+ small/medium pleomorphic T-cell lymphoma	2	75
Aggressive cutaneous T-cell and NK-cell lymphoma		
Sézary syndrome	3	24
Cutaneous aggressive CD8+ T-cell lymphoma	<1	18
Cutaneous γ/δ T-cell lymphoma	<1	–
Cutaneous peripheral T-cell lymphoma unspecified	2	16
Cutaneous NK/T-cell lymphoma, nasal-type	<1	–

Modified from: Willemze R *et al.* WHO-EORTC classification for cutaneous lymphoma. *Blood* 2005;105,3798. Based on 1905 patients with primary cutaneous lymphoma registered at the Dutch and Austrian Cutaneous Lymphoma Group 1986–2002.

Mycosis fungoides variants

Alibert-Bazin – classic type of MF

Follicular MF – 10% of MF, folliculotropic infiltrates, follicular mucinosis, favors head and neck (esp. eyebrow), alopecia, mucinorrhea, pruritic, stage as if classical tumor stage. Less responsive to skin directed

therapies due to the deep follicular localization of MF infiltrate. *Follicular Mucinosis (Alopecia Mucinosa) Classification:

- Primary localized – pediatric, H/N, upper trunk, usu resolve within several months-years
- Primary chronic, generalized – adults, concerning for malignant progression
- Secondary – benign (lupus, LSC, ALHE, drug – adalimumab, imatinib), malignant (MF, KS, Hodgkin)

Woringer-Kolopp/Pagetoid Reticulosis – $<$1% of CTCL, localized, solitary hyperkeratotic patch/plaque, slowly progressive. Good prognosis – No reports of extracutaneous dissemination or disease-related deaths.

Ketron-Goodmann – disseminated pagetoid reticulosis, aggressive

Granulomatous Slack Skin – pendulous atrophic lax skin, esp. axillae and groin. Associated with MF or Hodgkin lymphoma in 1/3 of cases. Usually indolent, very rare.

Sezary – 5% of MF cases, triad of exfoliative erythoderma, lymphadenopathy, and atypical circulating ("Sezary," "Lutzner," or "mycosis") cells. MF-like immunophenotype but characteristically CD26- and CD3+ but diminished. Change from Th1 to Th2 profile may drive progression to Sezary.

Clonality studies

- Suspected B-cell lymphomas: Flow cytometry (provides κ:λ ratio, requires fresh tissue in cell culture), immunoglobulin heavy chain gene rearrangement studies (can use paraffin-embedded tissue), immunohistochemistry for kappa or lambda restriction has low sensitivity (normally κ:λ ratio $\sim$ 3)
- Suspected T-cell lymphomas: $\alpha\,\beta$ TCR gene rearrangement studies (more sensitive than $\gamma\,\delta$ TCR gene rearrangement studies, can use paraffin-embedded tissue), flow cytometry (less useful for suspected T-cell lymphomas)
- For detecting CTCL, specificity can be increased by performing TCR rearrangement studies on biopsy specimens from $\geqslant$2 anatomic locations looking for a shared clone

MF (TNMB) staging

T (Skin)	N (Nodes)	M (Viscera)	B (Blood)
T1= Patch/plaque <10%	N0= None	M0= None	B0= <5% Sezary cells
T2= Patch/plaque >10%	N1= Palpable nodes, path (−)	M1= Visceral involvement	B1= >5% Sezary cells
T3= Tumor(s)	N2= No palpable nodes, path (+)		
T4= Erythroderma	N3= Palpable nodes, path (+)		

Stage	Clinical involvement	Clinically enlarged nodes	Histologically + nodes	TNMB	5-Year survival (%)*
IA	Patch/plaque < 10%			T1 N0 M0	96
IB	Patch/plaque > 10%			T2 N0 M0	73
IIA	Patch/plaque	+ Nodes	− Path	T1-2 N1 M0	73
IIB	Tumor(s)	± Nodes	− Path	T3 N0-1 M0	44
IIIA	Erythroderma	± Nodes	− Path	T4 N0 M0	44
IIIB	Erythroderma	+ Nodes	− Path	T4 N1 M0	
IVA		+ Nodes	+ Path	T1-4 N2-3 M0	27
IVB	Visceral involvement			T1-4 N0-3 M1	

Kim YH. Mycosis fungoides and the Sezary syndrome. *Semin Oncol*. 1999; 26: 276–89.
*Adapted from Kim YH *et al.* Long-term outcome of 525 patients with mycosis fungoides and Sezary syndrome. *Arch Dermatol*. 2003; 139: 857–66.

MF treatment algorithm

Stage	First line	Second line	Experimental
IA	SDT or no therapy		
IB, IIA	SDT PUVA, NB/BB-UVB	TSEB Radiotherapy IFN-α PUVA + IFN-α, Retinoids, or Bexarotene Low-dose MTX	Cytokines (i.e. Il-2, IL-12, IFN-γ) Pegylated Liposomal Doxorubicin Chlorodeoxyadenosine
IIB	TSEB + Superficial radiotherapy combination (2 of 3) tx w/ IFN-α, PUVA, or Retinoids	Denileukin diftitox Bexarotene IFN-α Chemotherapy Vorinostat	Autologous PBSCT, mini-allograft Zanolimumab
III	PUVA $\pm$ IFN-α or Retinoids ECP $\pm$ IFN-α MTX IFN-α	TSEB Denileukin diftitox Bexarotene Chemotherapy Alemtuzumab Vorinostat	Autologous PBSCT, mini-allograft Zanolimumab
IVA, IVB	TSEB or Radiotherapy, Chemotherapy	IFN-α Bexarotene Denileukin Diftitox Low-dose MTX Alemtuzumab Vorinostat Palliative	Autologous PBSCT, mini-allograft Zanolimumab

SDT: Skin-Directed Therapy: Emollients, Topical Steroids, Nitrogen Mustard (Mechlorethamine/HN_2, Carmustine/BCNU), Bexarotene Gel, Imiquimod, Topical-MTX
ECP: Extracorporeal Photopheresis
TSEB: Total Skin Electron Beam
PBSCT: Peripheral Blood Stem Cell Transplant
Denileukin Diftitox = IL-2/Diptheria Toxin Fusion
Bexarotene = Retinoid X Receptor Specific
Vorinostat = Suberoylanilide Hydroxamic Acid, SAHA (Histone Deacetylase Inhibitor)
Alemtuzumab = anti-CD52
Zanolimumab = HuMax-CD4

Modified from: Whittaker SJ *et al.* Joint British Association of Dermatologists and UK Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. *Br J Dermatol.* 2003 Dec; 149(6):1095–107 and Trautinger F *et al.* EORTC consensus recommendations for the treatment of mycosis Fungoides/Sézary syndrome. *Eur J Cancer.* 2006; 42:1014–30.

Cutaneous B-cell Lymphoma

Type	Clinical	Immunophenotype	5-Year survival (%)
Marginal zone	Often solitary lesions on trunk or extremities, possible Borrelia association, tattoo association	BCL2+ BCL6− CD10− IRTA1+	>95
Primary follicle center	Often solitary/ grouped plaques on scalp/forehead or trunk	BCL2− BCL6+ CD10± *	>95
Diffuse large B-cell	80% on leg of elderly patients, F>M	BCL2+ BCL6+ CD10− MUM1/ IRF4+	50

Other B-cell lymphomas – Intravascular large B-cell lymphoma, Lymphomatoid granulomatosis, CLL (ZAP-70+), Mantle cell lymphoma, Burkitt lymphoma, B-lymphoblastic lymphoma

*Secondary cutaneous follicle center lymphoma – BCL2+ BCL6+ CD10+ with t(14;18).

PREVALENCE: 20–25% of primary cutaneous lymphomas are B-cell lymphomas, each of the 3 major types representing ⩽10% of cutaneous lymphomas.

Leukemia cutis

- Affects children > adults
- Skin involvement rarely precedes systemic disease.
- Except for congenital leukemia, leukemia cutis is a poor prognostic sign, esp. with myeloid leukemia
- Frequently associated with extramedullary involvement
- Usually p/w asx papules and nodules
- Other presentations – CLL and HTLV-1-associated leukemia may be pruritic; greenish tumors = chloromas, aka granulocytic sarcomas (due to myeloperoxidase); gingival hypertrophy in AML-M4 and AML-M5; rarely leonine facies
- Histologically, often grenz zone (grenz zone DDx = granuloma faciale, lepromatous leprosy, lymphoma/leukemia/pseudolymphoma, acrodermatitis chronica atrophicans, AFX)
- Common Types:
  - AML – 10% of affected patients develop leukemia cutis (esp. AML-M4 and -M5)

- CLL and Hairy Cell Leukemia – 5–10% of affected patients develop leukemia cutis
- HTLV-1-associated leukemia – very rare type of leukemia (except in Caribbean, Japan) but 50% of patients may develop leukemia cutis (also get "infective dematitis")

Monoclonal Gammopathies

- Types of monoclonal gammopathies by frequency: monoclonal gammopathy of undetermined significance (MGUS) (65%), multiple myeloma (15%), AL amyloidosis (10%), others (10%): plasmacytoma, Waldenstrom, lymphoma
- Ig produced by monoclonal gammopathies: IgG (60%), IgM (20%), IgA (15%), extremely rarely IgD or IgE

Disease	Ig type
Direct cutaneous infiltration of cells causing monoclonal gammopathy or deposition of cell products	
Waldenstrom	IgM
AL amyloidosis	IgG
Multiple myeloma	IgG
Plasmacytoma	IgA
Cryoglobulinemia	IgM
Disorders associated with monoclonal gammopathies	
Scleromyxedema	IgG λ
Schnitzler	IgM κ
POEMS	IgA > IgG
Scleredema	IgG κ
Plane xanthoma	IgG
EED	IgA
NXG	IgG κ
Pyoderma gangrenosum	IgA
Sneddon-Wilkinson	IgA
IgA pemphigus	IgA
Sweet	IgG

Source: Daoud MS *et al.* Monoclonal gammopathies and associated skin disorders. *J Am Acad Dermatol.* 1999; 40(4):507–35.

Melanoma – Classification

T classification		
Tx	1° tumor cannot be assessed	
T0	No evidence of 1° tumor	
Tis	Melanoma *in situ*	
T1	⩽1.0 mm	a: no ulceration and Clarks level II/III b: + ulceration or Clarks level IV/V
T2	1.01–2.0 mm	a: no ulceration b: + ulceration
T3	2.01–4.0 mm	a: no ulceration b: + ulceration
T4	>4.0 mm	a: no ulceration b: + ulceration

N classification		
Nx	Nodes cannot be assessed	
N0	No regional lymphadenopathy	
N1	1 node	a: micrometastasis b: macrometastasis
N2	2–3 nodes	a: micrometastasis b: macrometastasis c: satellite or in transit metastasis *without* metastatic nodes
N3	⩾4 nodes or matted nodes, or in transit mets/satellites *and* metastatic nodes	

Micrometastases: patients without clinical or radiologic evidence of LN mets (clinically occult) but with pathologically + nodal mets after sentinel or elective lymphadenectomy

Macrometastases: patients with clinically detectable of nodal metastases confirmed by therapeutic lymphadenectomy or when nodal mets exhibit gross extracapsular extension

Adapted from Balch CM *et al.* Final version of the AJCC staging system for cutaneous melanoma. *J Clin Oncol.* 2001; 19:3635–48.

M classification	
Mx	Distant mets cannot be assessed
M0	No distant metastases
M1a	Distant skin, subcutaneous, nodal metastases
M1b	Lung metastases
M1c	Other visceral metastases or distant metastasis at any site with elevated LDH

Clark level	
Level I	Confined to the epidermis (MIS)
Level II	Invasion past basement membrane into the papillary dermis
Level III	Tumor filling papillary dermis to the junction of the superficial reticular dermis
Level IV	Invasion into the reticular dermis
Level V	Invasion into the subcutaneous tissue

Breslow depth

Breslow tumor thickness is measured in mm from the top of the granular layer of the epidermis (or the base of an ulcer) to the deepest point of tumor invasion using an ocular micrometer.

Melanoma – staging and survival

	Clinical staging			Pathologic staging			Survival (%)	
	T	N	M	T	N	M	5-Year	10-Year
IA	T1a	0	0	T1a	0	0	95	88
IB	T1b	0	0	T1b	0	0	91	83
	T2a			T2a			89	79
IIA	T2b	0	0	T2b	0	0	77	64
	T3a			T3a			79	64
IIB	T3b	0	0	T3b	0	0	63	51
	T4a			T4a			67	54
IIC	T4b	0	0	T4b	0	0	45	32
IIIA	Any T*	N1–3	0	T1-4a	N1a	0	70	63
				T1-4a	N2a		63	57
IIIB				T1-4b	N1a	0	53	38
				T1-4b	N2a		50	36
				T1-4a	N1b		59	48
				T1-4a	N2b		46	39
				T1-4a/b	N2c			
IIIC				T1-4b	N1b	0	29	24
				T1-4b	N2b		24	15
				Any T	N3		27	18
IV	Any T	Any N	Any M	Any T	Any N	M1a	19	16
						M1b	7	3
						M1c	10	6

*There are no Stage III subgroups in clinical staging.

Adapted from Balch CM *et al.* Final version of the AJCC staging system for cutaneous melanoma. *J Clin Oncol* 2001; 19:3635–648.

Melanoma – treatment guidelines

Breslow depth (mm)	Margin (cm)	SLN*	Physical exam**	Work-up***	Adjuvant Treatment
In situ	0.5	No	q6months × 1 year then yearly	• Symptom specific (CT, PET, MRI)	–
<1	1	No*	q3–12 months	• Symptom specific (CT, PET, MRI)	–
1.01–2.00	1–2	Yes	q3–6 months × 3 years, q4–12 months × 2 years, then yearly	• CXR, LDH, CBC, LFT q3–12 months (optional)	–
2.01–4.00	2	Yes		• Symptom specific (CT, PET, MRI)	• Clinical Trial • Observe
>4	2	Yes			• Clinical Trial • Observe • IFN α
Stage III SLN +, micromet	WLE (as above)	LND or clinical trial	q3–6 months × 3 years, q4–12 months × 2 years, then yearly	• CXR, LDH, CBC, LFT q3–12 months (optional) • Symptom specific (CT, PET, MRI)	• Clinical Trial • Observe • IFN α

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Breslow depth (mm)	Margin (cm)	SLN*	Physical exam**	Work-up***	Adjuvant treatment
Stage III Clinical + nodes, macromet	WLE	FNA or bx of +LN, then LND			• Clinical Trial • Observe • IFN α • $\pm$RT to nodal basin if Stage IIIC
Stage III in-transit	WLE + FNA or Bx of in-transit lesions	Yes	q3–6 months $\times$ 3 years, q4–12 months $\times$ 2 years, then yearly	• CXR, LDH, CBC, LFT q3–12 months (optional) • Symptom specific (CT, PET, MRI)	• Intralesional BCG, IL-2 • CO_2 ablation • Limb perfusion with melphalan • Clinical Trial • Radiation tx • Systemic tx
Stage IV	FNA or bx	Yes	q3–6 months $\times$ 3 years, q4–12 months $\times$ 2 years, then yearly	• Baseline CXR, Chest CT, LDH • Abd/pelvic CT, MRI brain, PET as indicated	• See NCCN Guidelines • Clinical trial • Dacarbazine • Temozolomide • High Dose IL2

*Sentinal Lymph node should be performed at time of Wide Local Excision. Consider in tumor <1mm if initial bx with Clark IV/V, ulceration, positive deep margin, or extensive regression. The yield and clinical significance of SLNBx in Stage IA is unknown.

**Follow-up: At least annual skin exam for life, educate patient in monthly self skin and lymph node exam. No evidence to support specific follow-up interval. AAD Task force recommends q3–12 months $\times$ 2 years, then q6–12 months. (Sober *et al.* AAD Guidelines: Care for primary cutaneous melanoma. *J AM Acad Dermatol* 2001; 579–86.)

***Evaluation: Strong evidence that routine CXR and blood work have limited value in patients with Stage 0/IA disease (Sober *et al.* AAD Guidelines: Care for primary cutaneous melanoma. *J Am Acad Dermatol* 2001; 579–86.) CT, PET, MRI may be performed to evaluate specific sxs.

Adapted from NCCN Practice Guideline in Oncology- v.2.2007 Melanoma.

Infectious Disease

Viruses and diseases

	Family	Examples	Replication site	Genome (+ sense; − antisense)
DNA	Poxviridae	Molluscipox: Molluscum Orthopox: Vaccinia, smallpox, cowpox Parapox: Orf, milker's nodule ("pseudo-cowpox")	Cytoplasm	dsDNA
	Papillomaviridae	Human papilloma virus	Nucleus	dsDNA
	Herpesviridae	HHV1: HSV1 HHV2: HSV2 HHV3: VZV HHV4: EBV HHV5: CMV HHV6: Roseola infantum, reactivation increases drug-induced hypersensitivity syndrome severity HHV7: ? Pityriasis rosea HHV8: Kaposi sarcoma	Nucleus	dsDNA for all
	Hepadnaviridae	HBV	Nucleus w/ RNA intermediate*	Gapped dsDNA

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	Family	Examples	Replication site	Genome (+ sense; − antisense)
	Adenoviridae	Human adenovirus	Nucleus	dsDNA
	Parvoviridae	Erythema infectiosum	Nucleus	ssDNA
RNA	Paramyxoviridae	Measles, Mumps	Nucleus	−ssRNA
	Togaviridae	Rubella, Chikungunya	Cytoplasm	+ssRNA
	Rhabdoviridae	Rabies	Nucleus	−ssRNA
	Retroviridae	HIV, HTLV	Nucleus	+ssRNA (dsDNA intermediate)
	Picornaviridae	Enterovirus (coxsackie; HAV)	Nucleus	+ssRNA
	Flaviviridae	HCV, West Nile, Yellow Fever, Dengue	Cytoplasm	+ssRNA
	Filoviridae	Ebola, Marburg	Cytoplasm	−ssRNA
	Bunyaviridae	Hantavirus, Rift valley, Congo-Crimean	Cytoplasm	−ssRNA
	Arenaviridae	Lassa	Cytoplasm	−ssRNA

*Therefore, HBV is susceptible to anti-HIV medications.

Human papillomavirus

Disease	Description	Associated HPV type
Verruca vulgaris	Common warts	1, 2, 4
Myrmecia	Large cup-shaped palmoplantar warts	1
Verruca plantaris/palmaris	Plantar warts	1, 2, 27, 57
Butcher's wart	Warty lesions from handling raw meat	2, 7
Verrucous carcinoma, foot	Epithelioma cuniculatum	2, 11, 16
Verruca planae	Flat warts	3, 10
Epidermodysplasia verruciformis	Inherited disorder of HPV infection and SCCs	3, 5, 8, 12, many others
Buschke and Löwenstein	Giant condyloma	6, 11
Condyloma acuminata	Genital warts	LOW RISK: 6, 11 HIGH RISK: 16, 18, 31 Flat condyloma: 42 Oral condyloma: 6, 11
Oral florid papillomatosis (Ackermann)	Oral/nasal, multiple lesions, smoking/ irradiation/chronic inflammation	6, 11
Recurrent respiratory papillomatosis	Laryngeal papillomas	6, 11
Heck disease (Focal epithelial hyperplasia)	Small white and pink papules in mouth	13, 32
Bowen disease	SCCIS	16, 18
Bowenoid papulosis	Genital papules and plaques resembling Bowen disease	16, 18
Cervical cancer		16, 18, 31, 33, 35, 39 Guardasil: 6, 11, 16, 18
Stucco keratoses	White hyperkeratotic plaques on legs	23b, 9, 16
Ridged wart	Wart with preserved dermatoglyphics	60

Other viral diseases

Viral disease	Description	Cause
Boston exanthem	Roseola-like morbilliform eruption on face and trunk, small oral ulcerations	Echovirus 16
Castleman disease (associated w/ POEMS and paraneoplastic pemphigus)	(Angio)lymphoid hamartoma: hyaline-vascular type, plasma cell, and multicentric/ generalized types	HHV-8
Dengue fever (virus may cause Dengue fever, Dengue hemorrhagic fever, or Dengue shock syndrome)	Rash in 50% of patients, flushing erythema within 1–2 days of symptom onset, then 3–5 days later a generalized often asx maculopapular eruption with distinct white "islands of sparing," 1/3 mucosal lesions, may be ecchymotic or petechial, incubation 3–14 days	Dengue flavivirus
Eruptive pseudoangiomatosis	Fever, transient hemangioma-like lesions, usually children, often with halo	Echovirus 25 & 32
Erythema infectiosum (Fifth disease)	Children aged 4–10 years, "slapped cheeks," reticular exanthem, usually extremities, arthropathy in adults, anemia/ hydrops in fetus, persistent in Sickle Cell	Parvovirus B19
Gianotti-Crosti syndrome (Papular acrodermatitis of childhood)	Children (often ⩽4 years old) with acute onset of often asymptomatic, lichenoid papules on face and extremities, less on trunk	Various: HBV most common worldwide, EBV most common in U.S.
Hand-foot-and-mouth	Brief mild prodrome, fever, erosive stomatitis, acral and buttock vesicles, highly contagious, mouth hurts, skin asymptomatic	Various Coxsackie viruses, Coxsackie Virus A16, Enterovirus 71
Herpangina	Fever, painful oral vesicles/ erosions, no exanthem	Coxsackie Groups A and B, various echoviruses

Viral disease	Description	Cause
Hydroa vacciniforme	Vesiculopapules, photosensitivity, pediatric with resolution by early adulthood	EBV (when severe, EBV-associated NK/T-cell lymphoproliferative disorders)
Infectious mononucleosis (Glandular fever)	2 peaks: 1–6 years old and 14–20 years old; fever, pharyngitis, (cervical) lymphadenopathy, HSM, eyelid edema, 5% rash, leukocytosis, elevated LFTs; 90% get maculopapular exanthema with ampicillin/amoxicillin	EBV (also causes nasopharyngeal carcinoma, post-transplant lymphoproliferative disorder, African Burkitt lymphoma)
Kaposi sarcoma	Vascular tumors	HHV-8
Kaposi varicelliform eruption (Eczema herpeticum)	Often generalized, crusted, vesiculopustular dermatitis; may be umbilicated*; fever, malaise, lymphadenopathy	HSV, may also occur with coxsackie, vaccinia, and other dermatitidis
Lichen planus	Purple, polygonal, planar, pruritic, papules	HCV
Measles (Rubeola)	Prodrome – cough, coryza, conjunctivitis, Koplik spots. Then maculopapular rash spreads craniocaudally. Incubation 10–14 days	Paramyxovirus
Milker's nodules	Similar to Orf From infected cows	Paravaccinia/Parapoxvirus
Molluscum contagiosum	Umbilicated papules in children and HIV, or as STD	Poxvirus; 4 MCV subtypes: MCV 1 is most common overall, MCV 2 in immunocompromised
Monkeypox	Smallpox-like but milder and lesions may appear in crops, with prominent lymphadenopathy, and without centrifugal spread	Monkeypox /Orthopoxvirus (smallpox vaccination is protective)
Oral hairy leukoplakia	Non-painful, corrugated white plaque on lateral tongue in HIV or other immunosuppressed patients, + smoking correlation	EBV

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Viral disease	Description	Cause
Orf (Ecthyma contagiosum)	Umbilicated nodule after animal contact, 6 stages; sheep, goats, reindeer; self-limiting in ~5 weeks	Orf/Parapoxvirus
Papular/Purpuric stocking-glove syndrome	Young adults, mild prodrome, enanthem, edema, erythema, petechiae, purpura, burning, pruritus on wrists/ankles	Various: Parvovirus B19, Coxsackie B6, HHV-6
Pityriasis rosea	Usually asymptomatic papulosquamous exanthem	Possibly HHV-7
Ramsey Hunt	Vesicular lesions following geniculate ganglion on external ear, tympanic membrane, with ipsilateral facial paralysis and deafness, tinnitus, vertigo, oral lesions	VZV
Roseola infantum (Exanthum subitum, sixth disease)	Infants with high fever (x3 days) followed by morbilliform rash, 15% have seizure	HHV-6B, rarely HHV-6A or HHV-7
Rubella (German measles)	Mild prodrome, tender LAN, pain with superolateral eye movements, morbilliform rash, spreads craniocaudally, petechial enanthem (Forschiemer spots), incubation 16–18 days	Togavirus
Smallpox	7–17 days incubation, 2–4 days prodrome (fever, HA, malaise), then centrifugal vesiculopustular rash, lesions are all the same stage, respiratory spread	Variola/Orthopoxvirus
STAR complex	Sore throat, elevated Temperature, Arthritis, Rash	Various: HBV, Parvovirus B19, Rubella
Unilateral laterothoracic exanthem	Age <4 years, morbilliform or eczematous, often starts in axilla, unilateral then spreads	Various: EBV, HBV, Echovirus 6

*Umblicated lesions DDx: molluscum, pox viruses, HSV, histoplasmosis, cryptococcosis, penicilliosis, perforating disorders, leprosy, GA.

Adapted from Benjamin A. Solky, MD and Jennifer L. Jones, MD. Boards' Fodder – Viruses

Mycoses

Laboratory tests

Direct Microscopy

KOH: softens keratin, clearing effect can be accelerated by gentle heating
DMSO: softens keratin more quickly than KOH alone in the absence of heat
Chlorazole Black E: chitin specific, stains hyphae green
Parker Black Ink: stains hyphae, not chitin specific
Calcofluor White: stains fungal cell wall (chitin) and fluoresces blue/white or apple/green using fluorescent microscopy
India Ink: capsule excludes ink (halo effect) – best for Cryptococcus neoformans
Gram Stain: stains blue
PAS: stains red
GMS: stains black
Mucicarmine: pink = capsule; red = yeast
AFB: + if nocardia
Lactophenol Cotton Blue: use for mounting and staining fungal colonies

Cultures

Sabouraud's Dextrose Agar: standard medium for fungal growth
+ chloramphenicol: inhibits bacteria
+ cycloheximide: use to recover dimorphic fungi and dermatophytes. Inhibits crypto, candida (*not albicans*), Prototheca, Scopulariopsis, Aspergillus
Dermatophyte Test Medium (DTM): use to recover dermatophytes
Turns medium from yellow to red (pH indicator)

Superficial mycoses

White piedra: Trichosporon. Soft mobile nodules, face, axilla, pubic, tropical.
Tx: Shave hair. Systemic antifungal if relapse.

Black piedra: Piedraia hortae. Hard non-mobile nodules, face, scalp, pubic, temperate.
Tx: Shave hair. Systemic antifungal if relapse.

Tinea nigra: Phaeoannellomyces (Hortaea) werneckii. Brown macules on the palms.
Tx: Topical iodine, azole antifungal, terbinafine for 2–4 weeks beyond resolution to prevent relapse. Resistant to griseofulvin.

Tinea versicolor: Malassezia furfur/Pityrosporum ovale. Hypo/hyperpigmented macules on trunk and extremities.

KOH: 'spaghetti and meatballs' – hyphae and spores

Tx: Topical ketoconazole cream, selenium sulfide shampoo, oral ketoconazole.

DDx superficial bacterial infection

Erythrasma: Corynebacterium minutissima (coproporphyrin III)

Trichomycosis axillaris: Corynebacterium tenuis

Pitted keratolysis: Micrococcus sedentarius

Cutaneous mycoses

Dermatophytes by sporulation characteristics

	Trichophyton	Microsporum	Epidermophyton
Macroconidia	Rare	Many	Many, grouped
Shape	Cigar/pencil	Spindled/tapered	Club/blunt
Wall	Thin/smooth	Thick/echinulate	Thin/smooth
Microconidia	Many	Few	None

Dermatophytes by mode of transmission

Zoophilic and geographic dermatophytes elicit significant inflammation

Anthrophilic	Humans	T. rubrum, T. tonsurans, E. floccosum, T. concentricum, T. mentagrophytes var. interdigitale
Zoophilic	Animals	T. mentagrophytes var. mentagrophytes, M. canis, T. Verrucosum
Geographic	Soil	M. gypseum

Most common dermatophytes

Tinea corporis, tinea cruris, tinea mannum, tinea pedis	T. rubrum, T. mentagrophytes, E. floccosum
Tinea pedis	**Moccasin:** T. rubrum, E. floccosum **Vesicular:** T. mentagrophytes var. mentagrophytes
Onychomycosis	**Distal subungual:** T. rubrum **Proximal white subungual (HIV):** T. rubrum **White superficial:** T. mentagrophytes (adults); T. rubrum (children). Also molds: Aspergillus, Cephalosporium, Fusarium, Scopulariopsis

Tinea barbae	Usually zoophilic dermatophytes (esp. T. mentagrophytes var. mentagrophytes and T. verrucosum) or T. rubrum
Tinea capitis	**US:** T. tonsurans > M. audouinii, M. canis **Europe:** M. canis, M. audouinii **Favus:** T. schoenleinii > T. violaceum, M. gypseum
Tinea imbricata/ Tokelau	T. concentricum
Majocchi granuloma	Often T. rubrum > T. violaceum, T. tonsurans

Dermatophytes invading hair

Ectothrix	Fluorescent (pteridine)	M. canis, M. audouinii, M. distortum, M. ferrugineum, M gypseum
	Non-fluorescent	T. mentagrophytes, T. rubrum, T. verrucosum, T. megninii, M. gypseum, M. nanum
Endothrix (black dot)		T. rubrum, T. tonsurans, T. violaceum, T. gourvilli, T. yaoundie, T. soudanense, T. schoenleinii (fluoresces)

M. gypseum may or may not be fluorescent; T. rubrum may be ecto- or endothrix
E. floccosum and T. concentricum do not invade scalp hair.

Subcutaneous mycoses

Disease	Etiology	*In vivo*/KOH (Tissue phase)	Culture (Mold phase)	Clinical	Tx
Sporotrichosis	*Sporothrix schenckii*	Cigar-shaped budding yeast, Splendore–Hoeppli phenomenon	Hyphae with daisy sporulation	Florist, gardener, farmer- (rose thorn, splinter), Zoonotic (cats) Sporotrichoid spread (fixed if prior exposure) Sporotrichoid DDx: leish, atypical mycobacteria, tularemia, nocardia, furunculosis	Itraconazole, SSKI
Chromoblastomycosis	*Fonsecaea* (most common), *Cladosporium, Phialophora, Rhinocladiella*	Copper pennies/Medlar bodies/sclerotic bodies		Small pink warty papule expands slowly to indurated verrucous plaques with surface black dots	Itraconazole, surgical excision
Phaeohyphomycosis	*Exophiala jeanselmei, Wangiella dermatitidis, Alternaria, Bipolaris, Curvularia, Phialophora*	Like chromo but with hyphae		Solitary subcutaneous draining abscess	Surgical excision, itraconazole
Lobomycosis (Keloidal blastomycosis)	*Loboa loboi* (*Lacazia loboi*)	Lemon-shaped cell chains with narrow intracellular bridges Maltese crosses-polarized light	Not cultured	Bottle nose dolphins and rural men in Brazil Confluent papules/verrucous nodules that ulcerate/crusts Fibrosis may resemble keloids	Surgical excision

Zygomycosis	*Conidiobolus coronatus*			Rhinofacial subcutaneous mass	
Rhinosporidiosis (protozoan)	*Rhinosporidium seeberi*	Giant sporangia (raspberries) Stains with mucicarmine	Not cultured	Stagnant water, endemic in India and Sri Lanka Nasopharyngeal polyps may obstruct breathing	Surgical excision
Prototheca (algae)	*Prototheca wickerhamii*	Morula (soccer ball)		Olecranon bursitis	
Actinomycotic mycetoma (bacterial)	*Actinomadura pelletieri* (red) *Actinomadura madur ae* (white) *Streptomyces* (yellow) *Actinomyces israeli* *Botryomycosis* *Nocardia* (white-orange)			Volcano-like ulcer and sinus tracts Sulfur grains – yellow, white, red, or brown Tissue swelling Early bone and muscle invasion	Antimicrobial
Eumycotic mycetoma (fungal)	*Pseudallescheria boydii* (most common, white-yellow) *Madurella grisea* *Madurella mycetomi* (brown-black) *Exophilia jeanselmei* *Acremonium spp.* (white-yellow)			Small ulcer with sinus tracts Sulfur grains (white or black) Tissue swelling Lytic bone changes occur late; rare muscle invasion	Antifungal rarely effective, surgical excision

Systemic mycoses

Disease	Etiology	*In vivo*/KOH (Tissue phase)	Culture (Mold phase)	Clinical	Tx
Coccidiomycosis (San Joaquin Valley fever)	*Coccidioides immitis/C. posadasii*	Large spherules, Splendore-Hoeppli phenomenon	Boxcars: barrel-shaped arthroconidia alternating with empty cells	Southwestern US, Mexico, Central America Primary pulmonary infection (60% asx) Dissemination to CNS, bone Skin lesions more verrucous. May develop EN or EM lesions	Itraconazole, fluconazole, amphoB
Paracoccidiomycosis (South American blastomycosis)	*Paracoccidioides brasiliensis*	Mariner's wheel (thin-walled yeast with multiple buds)	Oval microconidia indistinguishable from Blastomyces	South America, Central America Chronic granulomatous pulmonary disease Disseminates to liver, spleen, adrenals, GI, nodes Skin: granulomatous oral/ perioral lesions * Men >> women: estrogen may inhibit growth	Ketoconazole
Blastomycosis (Gilchrist disease, North American blastomycosis)	*Blastomyces dermatitidis*	Broad-based budding yeast with thick walls	Lollipop spores	Southeast US and Great Lakes Primary pulmonary infection Disseminates to CNS, liver, spleen, GU, long bones Skin: verrucous lesion with "stadium edge" borders	Itraconazole, amphoB
Histoplasmosis (Darling disease)	*Histoplasmosis capsulatum/H. duboisii*	Intracellular yeasts in macrophages (parasitized histiocytes, may see halo unlike Leish)	Tuberculate macroconidia	Mississippi/ Ohio river valley basin- bird/bat droppings Most common: pulmonary infection (80–95%) Dissemination to liver, BM, spleen, CNS Skin: molluscum-like lesions in AIDS	Itrazconazole, amphoB

Opportunistic mycoses

Disease	Etiology	*In vivo*/KOH (Tissue phase)	Culture (Mold phase)	Clinical
Candidiasis	*Candida albicans*	Pseudohyphae or true septate hyphae	Part of normal enteric flora Infection is due to predisposing factors: impaired epithelial barrier: burns, maceration, wounds, occlusion, foreign bodies (dentures, catheters), antibiotics Constitutional disorders: DM2, polyendocrinopathy, malnutrition Immunodeficiency: cytotoxic agents, neutropenia, agranulocytosis, HIV, chronic granulomatous disease	Topicals: nystatin, miconazole, clotrimazole Systemic: SAF
Cryptococcosis	*Cryptococcus neoformans*	Encapsulated yeasts with surrounding clear halo, "tear drop budding" Stain with mucicarmine, PAS, GMS, or India ink	Bird droppings — usually via pulmonary infection then hematogenous spread to lungs, bones, and viscera. Predilection for CNS. Skin: nasopharygeal papules/pustules, SQ ulcerated abscess	AmphoB fluconazole
Aspergillosis	*Aspergillus flavus* *A. fumigatus* *A. niger*	Phialides with chains of conidia (broom brush) Septate hyphae 45° branching	Infection from inhalation of conidia → pulmonary aspergillosis Allergic bronchopulmonary aspergillosis: hypersensitivity, no tissue invasion Invasive/ Disseminated aspergillosis: angioinvasive	Allergic: steroid Invasive: SAF
Zygomycosis/ Mucormycosis	 *Rhizopus* *Mucor* *Absidia*	Hyphae broad ribbon-like with 90° branching Rhizoid opposite sporangia No rhizoids Rhizoids between sporangia	Most commonly respiratory portal of entry → rhinocerebral infection Associated with diabetic ketoacidosis	AmphoB, surgical excision
Penicilliosis	*Penicillium marneffei*	Histo-like intracellular yeasts	Southeast Asia Umbilicated lesions, 85% of affected patients have skin lesions	AmphoB, fluconazole

SAF: Systemic Antifungal: amphoB, liposomal amphoB, fluconazole, itraconazole, voriconazole, caspofungin.

Vector-borne diseases

Disease	Cause	Vector/Transmission	Treatment
Acrodermatitis chronica atrophicans (Pick-Herxheimer disease)	*Borrelia afzelii*, *Borrelia garinii*	*Ixodes ricinus*, *Ixodes hexagonus*, *Ixodes persulcatus*	Amoxicillin, doxycycline, cefotaxime, penicillin G
African Tick-Bite fever	*Rickettsia africae*	*Amblyomma hebraeum*, *Amblyomma variegatum*	Doxycycline
African Trypanosomiasis (sleeping sickness)	*Trypanosoma brucei gambiense* (West Africa)	Tsetse fly (*Glossina morsitans*)	Pentamidine isethionate (hemolytic stage)
– Winterbottom's sign (posterior cervical LAN)			Melarsoprol or eflomithine (CNS involvement)
– Kerandel's sign (hyperesthesia)	*Trypanosoma brucei rhodesiense* (East Africa)	Tsetse fly (*Glossina morsitans*)	Suramin (hemolytic stage) Melarsoprol (CNS involvement)
Bacillary angiomatosis	*Bartonella henselae*, *Bartonella quintana*	Cat flea (*Pediculus humanus*)	Erythromycin, doxycycline
Brazilian spotted fever	*Rickettsia ricketsii*	*Amblyomma cajennense* RESERVOIR: Capybara	Doxycycline

Carrion disease (Bartonellosis, Oroya fever, Verruga peruana)	*Bartonella bacilliformis*	Sandfly (*Lutzomyia verrucarum*)	Chloramphenicol (due to frequent superinfxn with salmonella)
Cercarial Dermatitis (Swimmer's itch)	Cercariae of animal schistosomes	Snail	Topical corticosteroids
Chagas Disease (American trypanosomiasis)	*Trypanosoma cruzi*	Reduviid bug (assassin bug, kissing bug)	Benznidazole, nifurtimox
Cutaneous Larva Migrans (Creeping eruption)	*Ancylostoma brasiliense*, *Ancylostoma caninum*	Animal feces	Albendazole, ivermectin, thiabendazole topically
Cysticercosis	*Taenia solium*	Contaminated pork	Albendazole, praziquantel
Dengue fever	Flavivirus	*Aedes aegypti* or *albopticus*	Supportive Tx
Dracunculiasis	*Dracunculus medinensis* (Guinea fire worm)	Cyclops water flea ingestion	Slow extraction of worm + wound care Oral metronidazole facilitates removal
Ehrlichiosis, human monocytic (HME)	*Ehrlichia chaffeensis*	*Amblyomma americanum*	Doxycycline, rifampin (pregnancy)
Ehrlichiosis, human granulocytic (HGE) and human granulocytic anaplasmosis (HGA)	*Ehrlichia ewingii* (HGE), *Anaplasma phagocytophilum* (HGA)	*Ixodes persulcatus* and *Dermacentor variabilis*	Doxycycline, rifampin (pregnancy)

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Disease	Cause	Vector/Transmission	Treatment
Elephantiasis tropica (lymphatic filariasis)	*Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori*	*Culex*, *Aedes*, and *Anopheles* mosquitos	Diethylcarbamazine
Erysipeloid (of Rosenbach)	*Erysipelothrix rhusiopathiae*	Fish, shellfish, poultry, meat	Penicillin G, cipro, erythromycin/ rifampin
Glanders (Farcy)	*Burkholderia* (*Pseudomonas*) *mallei*	Horses, mules, donkeys	Augmentin, doxycycline, TMP-SMX
Kala-azar (visceral leishmaniasis)	*L. donovani*, *L. infantum* (Old World) *L. chagasi* (New World)	*Phlebotomus* sand fly *Lutzomyia* sand fly	Pentavalent antimony (sodium stibogluconate) or amphotericin
Leishmaniasis, New World (muco)cutaneous (Chiclero ulcer, Uta, Espundia, Bay sore)	*L. mexicana*, *L. brasiliensis*	*Lutzomyia* sand fly	Pentavalent antimony (sodium stibogluconate) or amphotericin
Leishmaniasis, Old World cutaneous (Oriental/Baghdad/Dehli sore)	*L. tropica*; *L. major*; *L. aethiopia*, *L. infantum*	*Phlebotomus* sand fly RESERVOIR: Rodents	Pentavalent antimony (sodium stibogluconate)
Loiasis (Calabar, Fugitive swelling)	*Loa loa*	*Tabanid* (horse/mango) fly, *Chrysops* (red, deer) fly	Diethylcarbamazine
Lyme disease	US: *Borrelia burgdorferi* EUROPE: *B. garinii* & *B. afzelli*	NE/GREAT LAKES: *Ixodes scapularis*/dam mini WEST US: *I. pacificus* EUROPE: *I. ricinus*	Doxycycline Amoxicillin if pregnancy or <9 years old
Mediterranean spotted fever (Boutonneuse fever)	*Rickettsia conorii*	*Rhipicephalus sanguinous* (dog tick)	Doxycycline, chloramphenicol, floroquinolone

Melioidosis (Whitmore disease)	*Burkholderia* (*Pseudomonas*) *pseudomallei*	Tropical soil, water	IV ceftazidime (high intensity phase) then TMZ-SMX and Doxycycline
Myiasis	*Dermatobia hominis* (botfly), *Cordylobia anthropophaga* (tumbu fly), *Phaenicia sericata* (green blowfly)	Mosquito (for *Dermatobia hominis*)	Removal of larvae and treatment with abx for superinfection
Onchocerciasis (River blindness)	*Onchocerca volvulus*	*Simulium* species (black fly)	Ivermectin
Plague (Bubonic)	*Yersinia pestis*	*Xenopsylla cheopis* (rat flea)	Streptomycin, gentamicin
Q Fever	*Coxiella burnetii*	Dried tick feces inhalation	Doxycycline
Rat-Bite Fever (Haverhill, Sodoku)	*Spirillium minus* (Asia/Africa), *Streptobacillus moniliformis* (US)	Rat bite, scratch, excrement, contaminated food	Penicillin
Relapsing Fever – Louse-borne	*Borrelia recurrentis* (Africa, South America)	*Pediculosis humanus*,	Doxycycline
Relapsing Fever – Tick-borne	*Borrelia duttonii*, *Borrelia hermsii* (Western US)	*Ornithodorus* genus (soft-bodied ticks)	Doxycycline
Rickettsialpox	*Rickettsia akari*	*Allodermanyssus* (*Liponyssoides*) sanguineus (house mouse mite) RESERVOIR: *Mus musculus*- domestic mouse	Doxycycline
Rift valley fever	Phlebovirus, bunyavirus	*Aedes*	Supportive Tx, ribavirin (investigational)

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Disease	Cause	Vector/Transmission	Treatment
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor andersoni*, *Dermacentor variabilis*	Doxycycline
Schistosomiasis/bilharziasis (Cercarial dermatitis, Katayama fever, late allergic dermatitis, perigenital granulomata, extragenital infiltrative)	*Schistosoma mansoni* (GI), *S. japonicum* (GI), *S. haematobium* (urinary system)	Snail	Praziquantel
Scrub typhus (Tsutsugamushi fever)	*Rickettsia/Orientia tsutsugamushi*	Larval stage of trombiculid mite (chigger, *Trombicula/Leptotrombidium akamushi*)	Doxycycline
South African tick-bite fever	*Rickettsia conorii*	*Rhipicephalus simus*, *Haemaphysalis leachii*, *Rhipicephalus mushamae*	Doxycycline
Sparganosis	*Spirometra* (dog and cat tapeworm larvae)	Application/ingestion of infected frog, snake, or fish	Surgical removal
Toxoplasmosis	*Toxoplasma gondii*	Cat feces, undercooked meat, milk	Pyrimethamine and sulfadiazine 1st trimester: spiramycin
Trench (Quintana) fever	*Bartonella quintana*	*Pediculus humanus corporis*	Doxycycline, erythromycin
Trichinosis	*Trichinella spiralis*	Undercooked pig, wild game	Steroids for severe symptoms and mebendazole or albenazole

Tularemia (deer fly fever, Ohara disease)	*Francisella tularensis*	Rabbit, *Dermacentor andersonii*, *Amblyomma americanum*, *Chrysops discalis* (deer fly), domestic cats	Streptomycin
Typhus, endemic; murine/flea-borne typhus	*Rickettsia typhi*	*Xenopsylla cheopis* (rat flea)	Doxycycline
Typhus, epidemic; Brill-Zinsser disease/ relapsing louse-borne typhus)	*Rickettsia prowazekii*	*Pediculus humanus*, squirrel fleas RESERVOIR: *Glaucomys volans*-flying squirrel	Doxycycline
Weil Disease (leptospirosis)	*Leptospira interrogans icterohaemorrhagiae*	Rat urine	Doxycycline, penicillin, ampicillin, amoxicillin
West Nile fever	Arbovirus	*Aedes*, *culex*, *anopheles*	Supportive Tx
Yellow fever	Arbovirus	*Aedes aegypti*	Supportive Tx

Adapted from Solky BA, Jones JL, Boards' Fodder – Bugs and their Vectors. Treatment adapted from *The Medical Letter.* 2004; 46:1189.

Creatures in dermatology

Creature	Scientific name	Special features
SPIDERS		
Brown Recluse spider	*Loxosceles reclusa*	• VENOM: Sphingomyelinase-D, hyaluronidase • Violin-shaped marking on back • Painless bite but with extensive necrosis • Red, white, and blue sign • Viscerocutaneous loxoscelism: fever, chills, vomit, joint pain, hemolytic anemia, shock, death • Tx: steroid, ASA, antivenom. Avoid debridement
Black Widow spider	*Latrodectus mactans*	• VENOM: A-lactotoxin • Hourglass-shaped red marking on abdomen • Painful bites but no necrosis • Neurotoxin causes chills, GI sxs, paralysis, spasm, diaphoresis, HTN, shock • Tx: IV Ca gluconate, muscle relaxant, antivenom
Jumping spider	*Phidippus formosus*	• VENOM: Hyaluronidase • Dark body hairs and various white patterns • Very aggressive spider • Painful with toxin venom but no systemic sxs
Wolf spider	*Lycosidae*	• VENOM: Histamine • Lymphangitis, eschar
Sac spider	*Chiracanthium*	• VENOM: Lipase • Yellow colored
Hobo spider	*Tegenaria agrestis*	• Herringbone-striped pattern on abdomen • Painless bite with fast onset induration then eschar • Aggressive spider • Funnel-shaped web
Green Lynx spider	*Peucetia viridans*	• Green with red spots • Painful bite with tenderness and pruritus
Tarantula	*Theraphosidae*	• Hairs cause urticaria • Ophthalmia nodosa – if hair gets into eyes → chronic granuloma formation

Creature	Scientific name	Special features
CATERPILLARS *Lepidoptera* (urticaria after contact with hairs)		
Puss/Asp	*Megalopyge opercularis*	• Brown woolly flat • Checkerboard eruption
Iomoth	*Automeris io*	• Green with lateral white strip from head to toe
Gypsy/Tent moth	*Lymantria dispar*	• Histamine in lance-like hair • Windborne can cause air-borne dermatitis
Saddleback	*Sibine stimulea*	• Bright green saddle on the back
Hylesia moth	*Hylesia metabus*	• Caparito/ Venezuela itch
Lonomia caterpillar	*Lonomia achelous/ obliqua*	• Latin America moth, fatal bleeding diathesis
FLIES		
Black fly	*Simulium*	• VECTOR: Onchocerciasis
Sand fly	*Phlebotomus* *Lutzomyia*	• VECTOR: *L. donovani*, *L. tropica*, *L. infantum*, *L. major*, *L. aethiopia* • VECTOR: *L. mexicana*, *L. braziliensis*, Bartonellosis
Tsetse fly	*Glossina*	• VECTOR: African trypanosomiasis
Deer fly	*Chrysops*	• VECTOR: Loiasis, tularemia
Botfly larvae	*Dermatobia hominis*, *Callitroga americana* (US)	• Myiasis when larvae (maggot) infest skin • Other flies whose larvae cause myiasis: *Cordylobia anthropophaga* (tumbu fly, moist clothing) and *Phaenicia sericata* (green blowfly, US)
MOSQUITOES *Culicidae*		
	Anopheles	• VECTOR: Malaria, filariasis
	Aedes	• VECTOR: Yellow fever, dengue, filariasis, chikungunya
	Culex	• VECTOR: Filariasis, West Nile
FLEAS *Siphonaptera*		
Human flea	*Pulex irritans*	• May play role in plague, affects other mammals
Cat flea	*Ctenocephalides felis*	• VECTOR: Bartonella henselae → cat scratch disease and bacillary angiomatosis • PARINAUD: oculoglandular syndrome—granulomatous conjunctivitis and preauricular LAN
Rat flea	*Xenopsylla cheopis*	• VECTOR: R. typhi → endemic typhus *Yersinia pestis* → bubonic plaque

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Creature	Scientific name	Special features
Sand /Chigoe Flea	*Tunga penetrans*	• Tungiasis • Give tetanus px when tx (surgery or ivermectin)
BEETLES		
Rove beetle	*Paederus eximius*	• Nairobi eye • TOXIN: Pederin
Blister beetle	*Lytta vesicatoria*/Spanish fly	• Source of cantharadin • Blister if squished on skin
Carpet beetle	*Attagenus megatoma* and *A. scrophulariae*	• ACD with larvae
LICE		
Pubic (crab)	*Pthirus pubis*	• Shortest and broadest body with stout claws • Maculae ceruleae (blue macules) on surrounding skin from louse saliva on blood products
Head lice	*Pediculus capitis*	• Six legs, long narrow body
Body lice	*Pediculus humanus corporis*	• Narrow, longest body • Lives in folds of clothing not directly on host • VECTORS: Bartonella quintana → trench fever Borellia recurrentis → relapsing fever Rickettsia prowazekii → epidemic typhus
MITES		
Scabies	*Sarcoptes scabiei hominis*	• Classic burrows along webspaces, folds • Skin scraping for eggs, feces, mites • Tx: Permethrin, lindane, ivermectin
Straw itch mite	*Pyemotes tritici*	• Found on grain, dried beans, hay, dried grasses • Salivary enzymes are sensitizing • May cause systemic sx: fever, diarrhea, anorexia
Demodex	*Demodicidae*	• Associated with acne rosacea, demodex folliculitis • Lives in human hair follicles
Grain mite	*Acarus siro*	• Causes baker's itch
Cheese mite	*Glyciphagus*	• Causes grocer's itch • Papular urticaria or vesicopapular eruption

Creature	Scientific name	Special features
Grocery mite	*Tyrophagus*	• Papular urticaria or vesicopapular eruption
Harvest mite (Chigger)	*Trombicula alfreddugesi*	• Intense pruritus on ankles, legs, belt line • VECTOR: *R. tsutsugamushi* → scrub typhus
Dust mite	*Dermatophagoides Euroglyphus*	• Atopy
House mouse mite	*Allodermanyssus sanguineus*	• VECTOR: *R. akari* → rickettsialpox
Walking dander	*Cheyletiella*	• Walking dandruff on dogs/cats • Pet is asx; human gets pruritic dermatitis
Fowl mite	*Ornithonyssus,*	• Bird handlers most commonly bitten
	Dermanyssus	• VECTOR: Western equine encephalitis
Copra itch	*Tyrophagus putrescentiae*	• Causes itching to dried coconut handlers • Resembles scabies on hand but no burrows
OTHERS		
Scorpions	*Centruroides sculturatus* and *C. gertschi*	• Neurotoxin causes numbness distally • Systemic: convulsion, coma, hemiplegia, hyper/hypothermia, tremor, restlessness • Arrhythmia, pulmonary edema, hypertension • Local wound care, ice packs, antihistamine
Bedbugs	*Cimex Lectularius*	• Flat with broad bodies, 4–5 mm in length
Bees, wasps, hornets, ants	*Hymenoptera*	• May cause angioedema • VENOM of honeybee: Phospholipase A
Fire ant	*Solenopsis*	• VENOM: Solenopsin D (piperidine derivative)
Reduviid bug	*Hemiptera*	• Kissing/ Assassin bugs • VECTOR: *Trypanosoma cruzi* → Chagas disease • Primary lesion: chagoma • Romana's sign: unilateral eyelid swelling • Acute: 1–2 weeks, fever, LAN, arthralgia, myalgia

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Creature	Scientific name	Special features
		• Chronic: progressive heart, megacolon
Centipedes	*Chilopoda*	• Carnivores: venomous claws cause painful bites with two black puncture wounds 1 cm apart
Millipedes	*Deplopoda*	• Vegetarians, emit toxin which burns, blister
WATER CREATURES		
Leeches		• Medicinal use associated with Aeromonas hydrophila wound infection
Sea urchin		• Foreign body reaction to spines, use hot water and vinegar for pain relief and inactivating toxins • Black sea urchin = *Diadema setosa*
Sea cucumber		• Toxin holothurin causes conjunctivitis
Dolphins		• Lobomycosis – keloidal blastomycosis, *Loboa loboi*
Schistosomes (flukes) –nonhuman host		• **Swimmer's itch/clam digger's itch** (**uncovered** skin) • Cercarial forms of flatworm penetrates skin in fresh or salt water (Northern US/Canada), causes allergic reaction • Schistosomes of ducks and fowls (nonhuman)
Schistosomes (flukes) –human host		• *S. mansonii*, *S. japonicum*, *S. hematobium* → Schistosomiasis • Cercarial forms penetrates skin and enters the portal venous system to the lungs, heart, and mesenteric vessels
Stronglyoides stercoralis (threadworm)		• **Cutaneous Larva Currens** • Serpiginous **urticarial** burrow on buttocks, groin, truck • May penetrate basement membrane to affect lungs and GI tract (chronic strongyloidiasis, Loefler's syndrome) • FAST migration (5–10 cm/h) • Tx: Ivermectin
Ancylostoma caninum, *A. braziliense* (hookworm)		• **Cutaneous Larva Migrans** • Hookworm penetrates skin on foot on sandy beaches • Cannot penetrate basement membrane (dead-end host) • Larvae deposited by dogs and cat feces • Serpiginous **vesicular** burrow • SLOW migration (2–10 mm/h) • Tx: Thiabendazole or ivermectin

- ***Cnidarian*** – Jellyfish, Portuguese man of war, sea anemone, coral, and hydroids. Stingers (nematocytes) break through skin causing pain and potential systemic symptoms. For jellyfish other than Portuguese man of war, use 3–10% acetic acid or vinegar to fix nematocytes to prevent firing and toxin release.

Box jellyfish	• Toxic stings may lead to shock
Portuguese man of war	• Painful stings may cause hemorrhagic lesions with vesicles
Sea anemone (*Edwardsiella lineate*)	• **Seabather's eruption** (pruritic papules in areas **covered** by swimwear)
Thimble jellyfish (*Linuche unguiculata*)	• Contact with **cnidarian larvae** in salt water (Southern US/Caribbean), larvae trapped beneath swimsuit

EXOTIC PETS, OTHERS

Iguana	• Salmonella, *Serratia marcescens*, Herpes-like virus
Hedgehog	• *Trichophyton mentagrophytes*, *Salmonella*, atypical mycobacteria
Cockatoo, pigeon	• Cryptococcus neoformans, avian mites
Chincilla	• *Trichophyton mentagrophytes*, *Microsporum gypseum*, *Klebsiella*, *Pseudomonas*
Fish/fish tank/swimming pool	• *Mycobacterium marinum* • Treat with TMP-SMX, clarithromycin, doxycycline
Flying squirrel	• *Rickettsia prowazekii*, *Toxoplasma gondii*, Staphylococcus
Lambs (lambing)	• Lambing ears: farmers develop blistering, itching, painful rash at pinnae (resembles juvenile spring eruption/PMLE)

Immunology

Complement

Complement type	Action
C1q	Binds antibody, activates C1r
C1r	Activates C1s
C1s	Cleaves C2 and C4
C2	Cleaves C5 and C3
C3a	Basophil and mast cell activation
C3b	Opsonin, component at which classical and alternative pathways converge
C4a	Basophil and mast cell activation
C4b	Opsonin
C5a	Basophil and mast cell activation
C5b, 6, 7, 8, 9	Membrane attack complex
C5, 6, 7	PMN chemotaxis
C5b	Basophil chemotaxis

Classical pathway: C1qrs, C1 INH, C4, C2, C3
Activated by: antibody–antigen complex
IgM > IgG (except IgG4 does not bind C1q)

Alternative pathway: C3, Properdin, factor B, D
Activated by: pathogen surfaces

Lectin pathway: Mannan-binding lectin and ficolins serve as opsonins, analogous to C1qrs. Leads to activation of the classical pathway without antibody.
Activated by: pathogen surfaces

Membrane attack complex: C5-9

C3NeF: Autoantibody that stabilizes bound C3 convertase (C3Bb). IgG isotype against Factor H inhibits its activity to also drive complement activation. Associated with mesangiocapillary glomerulonephritis and/or partial lipodystrophy.

Complement deficiencies

Most are AR, except hereditary angioneurotic edema (HAE) which is AD

Complement deficiency	Disease
Early classical pathway (C1, C4, C2)	SLE without ANA, increased infections (encapsulated organisms)
C1 esterase	HAE
Decreased C1q	SCID
C2	Most common complement deficiency, SLE (sometimes HSP, JRA)
C3	Infections, SLE, partial lipodystrophy, Leiner disease
C4	SLE with PPK
C3, C4, or C5	Leiner disease (diarrhea, wasting, seborrheic dermatitis)
C5-9	Recurrent neisseria infections

Angioedema and complement levels

	C1	C1 INH	C2	C3	C4
HAE – 1	Nl	↓	↓	Nl	↓
HAE – 2	Nl	Nl/↑ (but non-functional)	↓	Nl	↓
HAE – 3*	Nl	Nl	Nl	Nl	Nl
AAE – 1**	↓	↓	↓	Nl/↓	↓
AAE – 2***	↓	↓	↓	Nl/↓	↓
ACEI-induced	Nl	Nl	Nl	Nl	Nl

Tx: C1-INH concentrate/FFP, epi, steroids, antihistamines, androgens, antifibrinolytics (epsilon-aminocaproic acid or tranexamic acid).

*HAE-3 = estrogren-dependent form.

**AAE-1 = associated w/ B-cell lymphoproliferation.

***AAE-2 = autoimmune form, Ab against C1-INH.

Th profiles

Th Profile	Cytokines	Associated diseases
Th1	IL-2, IFN-γ, IL-12	Tuberculoid leprosy, Cutaneous leishmaniasis, Erythema nodosum, Sarcoidosis, Behcet, MF, Delayed type (IV) hypersensitivity reaction
Th2	IL-4, IL-5, IL-6, IL-10, IL-9, IL-13	Atopic dermatitis, Lepromatous leprosy, Disseminated leishmaniasis, Sezary, Pregnancy (flares Th2 diseases, helps Th1 diseases), Tissue fibrosis (i.e. SSc), Papular urticaria to fleabite
Th17*	IL-6, IL-15, IL-17, IL-21, IL-22, IL-23, TGF-β	Psoriasis, ACD, Hyper-IgE
T regulatory	IL-10 or TGF-β (also CD25+ and FOXP3+)	IPEX

*Th17 and Treg differentiation are both TGFβ dependent, but retinoic acid inhibits Th17 and promotes Treg differentiation.

Bullous Disorders

Intracorneal/subcorneal

- Impetigo – PMNs + bacteria
- SSSS – Epidermolytic/exfoliative toxins cleave Dsg 1 (160 kd) (ETA – chromosomal, ETB – plasmid-derived), strain type 71 of phage group II, organisms not usu present on bx, kids <6 years or immunosuppressed/renally insufficient adults
- Staphylococcal toxic shock – superantigens activate T-cell receptor through Vβ
- Streptococcal toxic shock – group A including (strep pyogenes), 60% have + blood cx (unlike Staphylococcal toxic shock)
- P. foliaceous – Dsg 1 (160 kd) (upper epidermis), may have dyskeratotic cells (resemble 'grains') in granular layer of older lesions
  - Endemic – fogo selvagem
  - DIF – intercellular IgG/C3
- P. erythematosus (Senear–Usher) – features of lupus + PF DIF – intercellular IgG/C3 + lupus band
- Subconeal pustular dermatosis (SPD) (Sneddon–Wilkinson) – rule-out IgA pemphigus – IgA Pemphigus has 2 variants: SPD variant (Ab's to desmocollin 1) and intraepidermal neutrophilic (IEN) variant (AB's to Dsg 1 or 3), 20% IgA monoclonal gammopathy, intercellular IgA (upper epidermis in SPD type but less restricted in IEN type)

- Infantile acropustulosis
- Erythema toxicum neonatorum – eosinophils, may be intraepidermal
- Eosinophilic pustular folliculitis
- Transient neonatal pustular melanosis – neutrophils
- AGEP – β-lactams, cephalosporins, macrolides, mercury
- Miliaria crystallina.

Intraepidermal blisters

- Palmoplantar pustulosis
- Viral blistering diseases
- Friction blister – acral, Just beneath SG
- EBS – may be suprabasilar
- Amicrobial pustulosis associated with autoimmune disease (APAD)
- Coma blisters – may be subepidermal, sweat gland necrosis (EM-like)

Suprabasilar blisters

Acantholysis – P. vulgaris, P. vegetans, Hailey-Hailey, acantholytic AK
Acantholysis + dyskeratosis – Darier, Grover, paraneoplastic pemphigus, warty dyskeratoma
Other blistering diseases with acantholysis – SSSS, P. foliaceous

- P. vulgaris – Dsg 3 (130 kd), ~50% also have Ab to Dsg 1 (160 kd), "tombstoning" with adnexal involvement unlike Hailey–Hailey, DIF: intercellular IgG/C3, IIF: 80–90% positivity, fishnet on monkey esophagus (more sensitive than guinea pig)
- P. vegetans – Dsg 3 (130 kd), Dsg 1 (160 kd), Histo: eos > pms (esp. in early pustular lesions), DIF = P. vulgaris, Two types of P. vegetans:
  - Neumann type – more common, starts erosive and vesicular, then becomes vegetating
  - Hallopeau type – starts pustular, more benign course

  Should distinguish P. vegetans from pyodermatitis–pyostomatitis vegetans – associated with IBD, DIF-
- Hailey–Hailey (Benign familial pemphigus) – dilapidated brick wall, DIF negative
- Darier – acantholytic (more than PV) dyskeratosis (less than H–H)
- Grover – 4 histo patterns: Darier-like, H–H-like, PV-like, spongiotic
- EBS
- Pemphigus-like blisters + PPK – case report with Ab to Desmocollin 3, BPAg1, LAD

Subepidermal with little inflammation

- EB
  - EBS – fragmented basal layer at base of blister, floor: BP Ag, Col IV, laminin, PAS+ BM
  - JEB – subepidermal, cell-poor, roof: BP Ag; floor: Col IV, laminin, PAS+ BM

  - DEB – subepidermal, cell-poor, roof: BP Ag, Col IV, laminin, PAS+ BM
  - EB types may also demonstrate supepidermal blisters with eos
- EBA – Ab to Col VII (290 kd), DIF: linear IgG/C3 at BMZ, EBA variant may also demonstrate subepidermal blisters with PMNs
- PCT/pseudo-PCT
- Burns and cryotherapy
- PUVA-induced
- TEN
- Suction blisters
- Bullous amyloidosis
- Kindler (now classified as major EB type with "Mixed"/Variable level of cleavage)
- Vesiculobullae over scars
- Bullous drug

Subepidermal with lymphocytes

- EM
- Paraneoplastic pemphigus – can demonstrate suprabasaliar acantholysis or subepidermal clefting, dyskeratosis, basal vacuolar change, band-like dermal infiltrate, DIF: intercellular IgG/C3 + IgG/C3 at BMZ (~P. erythematosus), IIF: intercellular staining on rat bladder
- LS&A
- LP pemphigoides
- Fixed drug
- PMLE
- Bullous tinea

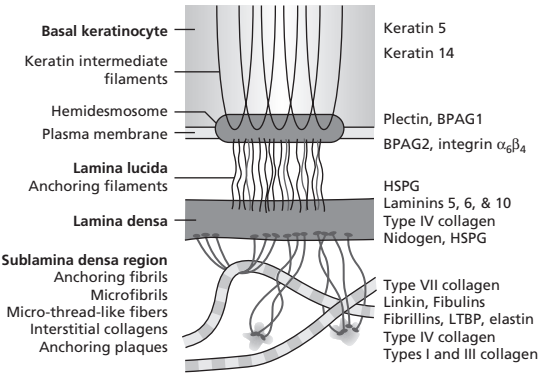
Subepidermal with eosinophils

- BP – DIF: linear BMZ IgG/C3, Abs to BPAg1 (230 kd, 80% of patients) and/or BPAg2 (180 kd, contains Col 17 and NC16A domain, 30% of patients)
- Pemphigoid gestationis (herpes gestationis) – DIF similar to BP, BPAg2 – placental matrix antigen
- Arthropod bite – esp. with chronic lymphocytic leukemia

Subepidermal with neutrophils

- DH – IgA endomysial ab, DIF: IgA at the dermal papillae (perilesional and uninvolved skin)
- Linear IgA –Various antigens including 97 kd (ladinin) or 120 kd (LAD-1) = BPAg2 degradation products (in lamina lucida form), DIF: linear IgA at BMZ (non-lesional skin)
- CP (benign mucosal pemphigoid)
  Brunsting-Perry = localized form, head/neck, w/o mucosa
- Deep lamina lucida (anti-P105) pemphigoid
- Anti-P200 pemphigoid

'Laminated' model of the epidermal basement membrane



From Yancey KB, Allen DM. The biology of the basement membrane zone, In: Bolognia JL, Jorizzo JL, Rapini RP (eds). *Dermatology*, Vol. 1. London: Mosby, 2003. p. 436, with permission from Elsevier.

- Bullous LE – Clinically, may be similar to DH or have large hemorrhagic bullae, Ab to Col VII (like EBA), Histo: like DH and often lacks vacuolar change of other forms of LE
- Sweet
- Orf – May have eos, DIF: C3/IgG at DEJ, IIF: anti-BMZ IgG (binding dermal side of SSS)

Subepidermal with mast cells

- Bullous mastocytosis

Epidermolysis bullosa

Simplex ("epidermolytic EB") – split basal layer (tonofilament clumping in basal layer on EM, 40% of EB patients, sxs worse in summer/heat, typically no scarring and not severe (except Dowling–Meara and AR forms)

Mutations: KRT5 or 14, plectin, mainly AD (99%)

IF: Col IV, laminin, BPAg on floor of blister

Localized forms:

1. Weber–Cockayne (AD) – most common, hyperhidrosis, palms/soles, usually due to KRT5 or 14 mutations, rarely may be due to ITGB4 (integrin β4) mutations
2. Kallin (AR) – anodontia/hypodontia, hair/nail anomalies
3. Autosomal Recessive EBS (AR) – KRT14

Generalized forms:

1. Koebner (AD) – mild, (−) Nikolsky, mucous membrane and nails are nl
2. Dowling-Meara (AD) – herpetiform pattern, hemorrhagic bullae, milia, oral involvement, dystrophic/absent nails, alopetic areas, confluent PPK, improves at ~10-years old and in adulthood (becomes more restricted to acral/pressure sites)
3. Ogna (AD) – hemorrhagic blister & bruising, *plectin* defect but no MD, closely linked to glutamic pyruvic transaminase
4. Mottled pigmentation (AD) – reticulated hyperpigmentation
5. Muscular dystrophy (AR) – *plectin* defect, blisters at birth with scarring, neuromuscular disease
6. Pyloric atresia (AD, AR) – *plectin* defect, may be lethal, single family reported (Pfendner E and Uitto J. Plectin gene mutations can cause epidermolysis bullosa with pyloric atresia. *J Invest Dermatol*. 2005 January 124(1):111–15).

Junctional – split lamina lucida, defect in hemidesmosome, <10% of EB patients, oral lesions, absent/dystrophic nails, dysplastic teeth, usually no scarring/milia

Mutations: Laminin 5 (=Laminin 332), $\alpha 6\beta 4$ (ITGA6, ITGB4), BPAg2, CD151/MER2, all AR except Traupe-Belter-Kolde-Voss
IF: Col IV, laminin on floor; BPAg on roof.

1. Herlitz (EB letalis or gravis) – defect: laminin 5, very severe generalized desies – may be fatal (often during infancy or childhood), manifest at birth, stereotypical stridor/cry, non-healing erosions (often large and zygomatic), GI, gallbladder, corneal, vaginal, laryngeal (>esophageal), and bronchial lesions, dystrophic/absent nails, exuberant granulation tissue and bleeding
2. Non-herlitz (non-lethal) – defect: laminin 5, moderately severe generalized disease worse pretibially, bullae smaller and healing, dystrophic nails, risk of SCC, large acquired melanocytic nevi (seen in JEB > DEB or EBS; asymmetric, irregular)
3. JEB with Pyloric Atresia – defect: $\alpha 6\beta 4$, severe mucocutaneous fragility & gastric outlet obstruction, manifest at birth, polyhydramnios during pregnancy
4. Generalized Atrophic Benign EB – defect: COL XVIIA1 (BPAg2), moderately severe generalized disease + enamel defects/oral lesions and atrophic alopecia (~ male-pattern), survive to adulthood, dystrophic nails, 'Localized Atrophic' variant also due to COL XVII mutations
5. JEB Letalis with Congenital Muscular Dystrophy – Doriguzzi C *et al.* Congenital muscular dystrophy associated with familial junctional epidermolysis bullosa letalis. *Eur Neurol.* 1993; 33(6):454–60.
6. Laryngo-Onycho-Cutaneous/laryngeal and ocular granulation tissue in children from the Indian subcontinent (LOGIC)/Shabbir – hoarse cry as newborn, erosions, and bleeding at traumatic sites, onychodystrophy,

conjunctival and laryngeal chronic granulation tissue, symblepharon, blindness, dental enamel hypoplasia, anemia
7. Pretibial EB with nephropathy and deafness – defect: CD151/MER2
8. Others: Acral, inversa, cicatricial, late-onset/progressiva

Dystrophic ("dermolytic EB") – split sublamina densa (papillary dermis), >50% of EB patients, defective anchoring fibers, scars, and milia
Mutation: Col VII*
IF: Col IV, laminin, BPAg on roof

Dominant Dystrophic EB: manifest at birth, bullae on extensor surfaces, (+) Nikolsky, (onion) scars and atrophy, milia on ears, hands, arms, and legs, mucous membrane/esophagus involved, nail dystrophy, scarring tip of tongue, improve w/time
1. Albopapuloid (Pasini, Pretibial with Lichenoid Features) – white papules on trunk not preceded by bullae, more severe, present in adolescence
2. Cockayne–Touraine – hypertrophic scars, more limited
3. Bart – aplasia cutis (legs), blisters, and nail deformities, rarely with JEB
4. Dominant transient bullous dermolysis of the newborn – vesiculobullae at birth, recover by 4 months, no scars
5. Pruriginosa – pruritis, prurigo-like lesions, nail dystrophy, and may have albopapuloid lesions, may be AR
6. EBD with subcorneal cleavage = EBS-superficialis

Recessive Dystrophic EB
1. Generalized – mitis (non-Hallopeau-Siemens) – severe blisters, generalized, esophageal strictures, ± digital cicatricial pseudosyndactyly
2. Generalized – gravis (Hallopeau-Siemens) – very severe, generalized, skin and mucous membrane bullae as newborn, high risk of SCC (primary cause of death), mitten deformity, esophageal stricture, anemia, cardiomyopathy, fatal amyloidosis (AA type)
3. Others – Inversa (axilla, groin), Centripetal, Recessive Transient Bullous Dermolysis of the Newborn

* Tumorigenesis in RDEB is increased with production/retention of Col VII containing the NC1 domain (in laminin 5-dependent process).
Non-EB genodermatoses with infantile bullae: Ichthyosis Bullosa of Siemens, BCIE, Gunther

Major bullous diseases – clinicopathologic findings

Disease	Manifestation	Antigen(s)	Size (kD)	Path	DIF	Rx
Pemphigus foliaceus	Crusted, scaly erosions, seborrheic distribution, positive Nikolsky, non-mucosal	Dsg 1 Plakoglobin	160 85	Acantholysis in upper epidermis, split in SG or right below SC	Intercellular IgG/C3, often superficial, may be throughout epidermis	Topical steroids if mild, systemics similar to PV if generalized
Pemphigus vegetans	Flaccid bullae, erosions, fungoid vegatations, intertriginous, head, mucous membrane, 2 subtypes: Neumann – severe Hallopeau – mild	Dsg 3 Dsg 1 Plakoglobin	130 160 85	Like PF	Like PF	Like PF
Pemphigus vulgaris Drug-induced (usually PF-like): penicillamine, IL-2, PCN, thiopurine, rifampin, ACE-I	Flaccid bullae, mucous membrane, + Nikolsky, + Asboe-Hansen	Dsg 3–100% Dsg 1–50% Plakoglobin	130 160 85	Suprabasilar acantholysis can follow hair, + tombstones	Intercellular IgG (also C3, IgM, IgA) throughout epidermis. Follow progression with IIF (Dsg 3) (monkey esophagus)	Prednisone, azathioprine, cyclophosphamide, mycophenolate mofetil, CSA

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Disease	Manifestation	Antigen(s)	Size (kD)	Path	DIF	Rx
IgA pemphigus	Flaccid vesicles, superficial pustules in annular/serpentine patterns, trunk (axilla, groin), proximal extremities	SPD variant – Desmocollin 1; IEN variant – Dsg 1/3	105, 115	Pustules: subcorneal or suprabasilar, no acantholysis, PMNs	IgA in upper epidermis (intercellular), no IgG	Dapsone, sulfapyridine, etretinate, UV, steroids
Pemphigus erythematosus (Senear–Usher)	Erythematous, crusted, erosions, often malar, originally PE = PV + LE	Dsg 1 Plakoglobin	160 85	Like PF	Intercellular and DEJ IgG/C3+ lupus band sometimes	Prednisone
Paraneoplastic pemphigus Associations: NHL, CLL, Castleman, sarcoma, thymoma	Bullae, erosions, EM-like, lichenoid, SJ-like in mucous membranes	Plectin Desmoplakin 1 BPAg1 Envoplakin Desmoplakin 2 Periplakin ? Dsg 1,3	500 250 230 210 210 190 170 160, 130	Suprabasilar acantholysis, dyskeratotic keratinocytes, sometimes basal layer degeneration/band-like infiltrate	Intercellular IgG/C3 in epidermis and at BMZ IIF: IgG rat bladder	Treat associated neoplasm May die from bronchiolitis obliterans
Epidermolysis bullosa acquisita Associations: myeloma, colitis, DM2, leukemia, lymphoma, amyloid, cancer	Fragile skin, blisters with trauma, atrophic scars, milia, nail dystrophy	Col VII (also an antigen in bullous LE)	290/145	Non-inflammatory subepidermal bullae, PMN>Eos	IgG/C3 linear BMZ IIF anti-BMZ Salt split skin: immunoreactants on dermal side, type IV collagen on roof	Immunosuppression, wound care

Bullous pemphigoid Drug-induced: lasix, PCN, ACE-I, sulfasalzine, nalidixic acid	Large, tense bullae on trunk and extremities	BPAg1 BPAg2 *BPAg2 worse prognosis	230 180	Subepidermal bullae, eosinophils in superficial dermis (more likely acral in infants)	Linear IgG/C3 at BMZ Salt split skin: immunoreactants on epidermal side, type IV collagen on base	Topical steroids, prednisone, MTX, mycophenolate mofetil, azathioprine, nicotinamide, TCN, sulfapyridine, dapsone
Herpes gestationis/ gestational pemphigoid Associations: HLA-DR 3,4, B8	Pruritic, urticarial plaques on trunk, starts near umbilicus, flares with delivery/OCP, increased risk of prematurity/SGA, 10% of newborns with skin lesions	BPAg1 BPAg2	230 180	Subepidermal bullae, eosinophils, perivascular infiltrate	Linear C3 ± IgG at BMZ IIF: anti-BMZ IgG by complement-added IIF.	Topical/oral steroids
Dermatitis herpetiformis	Grouped, pruritic papules and vesicles on extensors, HLA-B8, DR3, DQ2	Endomysial Ag (tissue transglutaminase) Anti-gliadin		Subepidermal bullae, PMNs in dermal papillae	Granular IgA ± C3 (tips of papillae)	Gluten-free diet, dapsone, sulfapyridine, TCN, nicotinamide, colchicine

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Disease	Manifestation	Antigen(s)	Size (kD)	Path	DIF	Rx
Linear IgA Drug-induced: vancomycin, lithium, amiodarone, ACE-I, PCN, PUVA, lasix, IL-2, oxaprozin, IFN-γ, dilantin, diclofenac, glibenclamide	DH-like vesicles (crown of jewels), BP-like bullae, 50% mucous membrane involvement, children: self-limited	Ladinin LAD-1 BPAg1 BPAg2 Col VII	97 120 230 180 290/145	Subepidermal bullae, PMNs in dermal papillae $\pm$ Eos	Linear IgA at BMZ, maybe IgG, no C3	Dapsone, steroids, TCN, nicotinamide, IVIg, colchicine
Cicatricial pemphigoid (benign mucosal pemphigoid) Drug-induced: penicillamine, clonidine	Primarily mucous membrane, vesicles, erosions, ulcers, scars, erosive gingivitis, chronic	BPAg1 BPAg2 Laminin-6 Epiligrin (Lam-5) Integrin β4	230 180 165, 220, 200 165, 140, 105 200	Like BP plus scarring in upper dermis	C3/IgG at BMZ in 80%; IIF+ in 20%, usually IgG	Topical steroids, dapsone, cyclophosphamide, oral steroids, surgery.

Glands

Glands	Apocrine	Eccrine	Sebaceous
Derivation	Ectodermal (~week 16–24)	Ectodermal (~week 14)	Ectodermal (~week 14)
Secretion	Decapitation	Merocrine	Holocrine
Innervation	Sympathetic adrenergic	Sympathetic cholinergic and cholinergic	Androgenic hormones (not innervated)
Purpose	Pheromones	Temperature regulation	Lubricate, waterproof
Locations	Axillary, breast (mammary), external ear (ceruminous), anogenital, eyelid (Moll) nevus sebaceous	Widespread (esp. soles) excluding vermilion border, labia minora, glans, nail beds, inner prepuce	Everywhere except palms and soles Associated with hair follicles except on mucosa Montgomery tubercles – nipples, areola Meibomian – deep eyelid; granuloma Glands of Zeis – superficial eyelid Tyson – foreskin, labia minora Fordyce spots – vermilion, buccal
Secretion contents	Fatty acids, cholesterol, triglycerides, squalene, androgens, ammonia, iron, carbohydrates, antimicrobial peptides	NaCl, potassium, bicarbonate, calcium, glucose, lactate, urea, pyruvate, glucose, ammonia, enzymes, cytokins, Igs	Ceramides, triglycerides, free fatty acids, squalene, sterol and wax esters, free sterols

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Glands	Apocrine	Eccrine	Sebaceous
Stains*	GCDFP, EMA, CEA, keratins	CEA, S100, EMA, keratins (CAM 5.2, AE1)	EMA, CK15, lipid stains
Non-neoplastic conditions	• Fox Fordyce (apocrine miliaria) • Apocrine chromhidrosis – ochronosis, stained undershirts • Axillary bromhidrosis – (E)-3-methyl-2-hexanoic acid, Micrococcus or Corynebacterium, M>F, post-puberty, more common than eccrine bromhidrosis except during childhood	• Neutrophilic eccrine hidradenities: chemo, palmoplantar (pediatric), pseudomonas • Syringolymphoid hyperplasia with alopecia • Miliaria • Lafora – PAS+ granules • Bromhidrosis – drugs (bromides, PCN), food, metabolic, or bacterial degradation of softened keratin • Uremia – small eccrine glands • PAS+ granules in hypothyroidism • Degeneration in lymphoma, heat stroke, coma blister • Ebola particles	• Acne • Vernix caseosa • Juxtaclavicular beaded lines • Chalazion – granuloma involving Meibomian glands • Internal hordeolum (stye) – infection/inflammation of Meibomian glands • External hordeolum (stye) – infection/inflammation of Zeiss or Moll (apocrine)

*Specificity of apocrine vs. eccrine stains is controversial.

Disorders or drugs associated with skeletal, ocular, and/or nail findings

	Ocular	Skeletal/oral	Nail
5-FU, AZT, phenophthalein, anti-malarials, hydroxyurea, MCN			Blue lunulae (also argyria, Wilson, Hgb M disease)
Acitretin			Koilonychia, onychocryptosis (ingrown/unguis incarnatus, granuloma)
Acne fulminans		Osteolytic lesions (clavicle, sternum, long bones, ilium)	
Albright hereditary osteodystrophy		Short stature, brachydactyly, subcutaneous ossifications	
Alkaptonuria	Osler sign (blue/gray slerae)	Arthritis, blue/gray ear cartilage, calcified cartilage	
Alezzandrini	Unilateral retinitis pigmentosa, retinal detachment		
Alopecia areata	Asx punctate lens opacities		Pitting, trachyonychia, red spotted lunulae
Antimalarials	Retinopathy		Blue lunulae

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	Ocular	Skeletal/oral	Nail
Apert	Hypertelorism, exophthalmos	Craniosynostosis	Brittle nails, fusion of nails
Argyria	Blue/gray sclera	Blue/gray gums	Azure lunulae
Arsenic		Garlic breath, intra-abdominal radio-opacities (acute)	Mees lines
Ataxia-telangiectasia (Louis-Bar)	Bulbar telangiectasia, strabismus, nystagmus		
Behçet	Retinal vasculitis, uveitis, hypopyon, optic disk hyperemia, macular edema	Arthritis, oral ulcers	
Buschke-Ollendorff		Osteopoikolosis	
Carbon monoxide poisoning, polycythemia, CTD, CHF,			Red lunulae
CHIME	Retinal colobomas		
Cicatricial pemphigoid	Conjunctivitis, symblepharon, synechiae, ankyloblepharon	Oral ulcers, hoarseness, dysphagia	
Cirrhosis, CHF			Terry nails
Cholesterol emboli	Hollenhorst plaque		
Cockayne	Salt and pepper retinal pigmentary degeneration, optic atrophy, cataracts, strabismus, nystagmus, sunken eyes	Dwarfism, dental caries, osteoporosis, overcrowded mouth	

Coffin-Siris	Bushy eyebrows	Hypoplastic/absent fifth distal phalanges, microcephaly	Hypoplastic/absent fifth nail
Congenital erythropoietic porphyria	Conjunctivitis, scleromalacia perforans	Erythrodontia, acro-osteolysis, osteoporosis	Nail dystrophy
Congenital syphilis	Keratitis	Osteochondritis, saddle nose, mulberry molars, Hutchinson teeth, saber shins	
Connective tissue disease, trauma		Pterygium inversum unguis	
Conradi–Hünermann syndrome	Striated cataracts, microphthalmus, optic nerve atrophy	Asymmetric limb shortening, chondrodysplasia punctata – stippled epiphyses (also in CHILD)	
Cooks syndrome		Absent/hypoplastic distal phalanges, brachydactyly fifth finger	Anonychia/onychodystrophy
Darier–White			Longitudinal red and white bands and ridging, V-shaped notches, subungual hyperkeratosis
Dermochondrocorneal dystrophy (Francois)	Corneal dystrophy, central opacities	Acral osteochondrodystrophy, contractures, subluxations, gingival hyperplasia	
Drug (azidothymidine, tetracycline), ethnicity, Laugier–Hunziker, Peutz–Jeghers			Longitudinal melanonychia
Dyskeratosis congenita	Blepharitis, conjunctivitis, epiphora	Dental caries, loss of teeth, premalignant leukoplakia, dysphagia	Longitudinal ridging, thinning, pterygium

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	Ocular	Skeletal/oral	Nail
Ehlers–Danlos VI	Fragile sclerae/cornea, keratoconus, hemorrhage, retinal detachment, blue sclerae, angioid streaks	Kyphoscoliosis	
Ehlers–Danlos VIII		Periodontitis, loss of teeth	
Ehlers–Danlos IX		Occipital horns, elbow, and wrist defects	
Endocarditis, trauma, trichinosis, cirrhosis, vasculitis			Splinter hemorrhages
Epidermal nevus syndrome	Lipodermoids, colobomas, choristomas	Kyphoscoliosis, abnormal skull shape, limb hypertrophy/asymmetry, rickets	
Fabry disease	Circular corneal opacities (cornea verticillata), tortuous vasculature, spoke-like cataracts	Oral angiokeratoma (tongue), osteoporosis	
Fanconi anemia	Strabismus, retinal hemorrhages	Radius and thumb defects	
Fever, stress, meds (chemo)			Beau lines
Gardner	Congenital hypertrophy of retinal pigmented epithelium	Osteomas, dental abnormalities	
Gaucher	Pingueculae	Erlenmeyer flask deformity, osteopenia, osteonecrosis	

Goldenhar (Facioauriculovertebral sequence)	Epibulbar choristomas, blepharoptosis or narrow palpebral fissures, eyelid colobomas, lacrimal drainage system anomalies	Ipsilateral mandibular hypoplasia, ear anomalies, vertebral anomalies	
Goltz	Retinal colobomas, microphthalmia, nystagmus, strabismus	Osteopathia striata, lobster claw deformity, cleft lip/palate, hypo/oligodontia, oral papilloma, enamel hypoplasia	
Gorlin	Cataracts, strabismus, iris colobomas	Odontogenic cysts, fused/bifid ribs, spina bifida occulta, kyphoscoliosis, calcified falx cerebri, frontal bossing	
Hallerman–Streiff syndrome	Microopthalmia, congenital cataracts, strabismus	Bird-like facies, natal teeth, hypodontia	
Hemochromatosis	Angioid streaks		Koilonychia
Homocystinuria	Ectopia lentis (downward)	Marfanoid habitus, genu valgum, osteoporosis	
Huriez		Scleroatrophy of hands, sclerodactyly, lip telangiectasia	Hypoplasia, ridging, white, clubbing
Hyperimmunoglobulin E syndrome		Osteopenia, fractures, scoliosis, hyperextensible joints, candidiasis	Chronic candidiasis
Hypoalbuminemia			Muehrcke lines

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	Ocular	Skeletal/oral	Nail
HSV, varicella	Dendritis, keratitis		
Incontinentia Pigmenti (Bloch-Sulzberger)	Strabismus, cataracts, optic nerve atrophy, retinal vascular changes, detached retina, retinal/iris colobomas	Peg/conical teeth, partial adontia, late dentition	Nail dystrophy, grooving, painful subungual dyskeratotic tumors
Iron deficiency, syphilis, thyroid disease			Koilonychia
Iso-Kikuchi		Index finger hypoplasia, brachydactyly	Hypoplastic index finger nail
JXG	Ocular JXG, hyphema, glaucoma		
KID	Keratoconjunctivitis, blepharitis, photophobia, corneal defects		Nail dystrophy
Kindler		Cicatricial pseudosyndactyly (between MCP and PIP), leukoplakia, caries	Nail dystrophy
Lamellar ichthyosis	Ectropion, corneal damage	Phalangeal reabsorption	
LCH: Hand–Schuller–Christian	Exophthalmos	Bone lesions (esp. cranium)	
LEOPARD	Hypertelorism		
Leprosy	Madarosis, lagophthalmos, keratitis, episcleritis, corneal anesthesia, blindness	Digital resorption, malaligned fractures, diaphyseal whittling, saddle nose	Longitudinal melanonychia, longitudinal ridging, subungual hyperkeratosis, rudimentary nail
Lichen planus			Pterygium
Linear morphea		Melorheostosis (of Leri; "flowing candle wax")	

Lipoid proteinosis (Urbach–Wiethe)	Eyelid beading/moniliform blepharosis	Calcifications in hippocampus (suprasellar, "bean-shaped"), thick tongue, hoarseness	
Mafucci		Enchondromas, chondrosarcoma	
Marfan	Ectopia lentis (upward)	Marfanoid habitus	
McCune–Albright		Polyostotic fibrous dysplasia	
MEN IIb	Conjunctival neuroma	Plexiform neuromas (oral mucosa, tongue), nodular lips, marfanoid habitus	
Menkes	Blue irides, strabismus, aberrant eyelashes, iris stromal hypoplasia	Wormian bones of skull, metaphyseal spurring of long bones	
Multicentric reticulohistiocytosis		Mutilating arthritis	
Myxoid cyst, verruca vulgaris			Median canaliform dystrophy
Naegeli–Franceschetti–Jadassohn	Periocular hyperpigmentation	Enamel defects, perioral hyperpigmentation	Malaligned great toenails
Nail–patella	Lester iris, heterochromia irides	Patella aplasia, posterior iliac horns, elbow arthrodysplasia	Triangular lunulae, micro/ anonychia
Necrobiotic xanthogranuloma	Scleritis, episcleritis		
NF-1	Lisch nodules, congenital glaucoma, optic glioma	Sphenoid wing dysplasia	
NF-2	Cataracts, retinal hamartomas		

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	Ocular	Skeletal/oral	Nail
Nicotine, chemotherapy, potassium permanganate, podophyllin, hydroxyurea (streaks)			Brown nails
Niemann–Pick	Cherry red spots, macular haloes		
Noonan	Hypertelorism, ptosis, epicanthic folds, downward palpebral fissures, epicanthic folds, refractive errors, strabismus, amblyopia	Pectus carinatum superiorly, pectus excavatum inferiorly, scoliosis, short stature, cubitus valgus, joint hyperextensibility	
Old age			Diminished or absent lunulae, longitudinal ridging, onychogryphosis
Olmsted	Corneal anomalies	Osteoporosis, joint laxity, leukoplakia, periorificial keratotic plaques	Nail dystrophy
Orofaciodigital 1	Colobomas	Bifid tongue, accessory frenulae, lip nodules/ pseudoclefting, supernumerary teeth, frontal bossing, syndactyly	
Osteogenesis imperfecta	Blue sclera	Brittle bones	
Pachyonychia congenita	Corneal dystrophy	Oral leukokeratosis, natal teeth	Thickened nails, pincer nails, paronychia

Papillon–Lefévre		Dural calcifications, periodonitis, gingivitis (+ acro-osteolysis and onychogryphosis in Haim–Munk)	
Phenylketonuria	Blue irides	Osteopenia	
Porphyria cutanea tarda			Photo-onycholysis
Progeria		Delayed/abnormal dentition, high-pitched voice, acro-osteolysis, short stature, osteoporosis, persistent open fontanelles	
Pseudomonas (pyocyanin)			Green nails
Psoriasis			Nail pits, oil spots
PXE (Gronblad–Strandberg)	Angioid streaks (also Paget's disease of bone, sickle cell, thalassemia, Pb poisoning, HFE, ED6)	Oral yellow papules	
Refsum	Salt and pepper retinitis pigmentosa	Epiphyseal dysplasia	
Relapsing polychondritis	Conjunctivitis, scleritis, uveitis, corneal ulceration, optic neuritis	Arthritis (truncal), aphthosis	
Renal disease			Lindsay nails
Retinoids, indinavir, estrogen		Isotretinoin – DISH-like hyperostotic changes (bones spurs, calcified tendons, ligaments)	Pyogenic granuloma

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	Ocular	Skeletal/oral	Nail
Richner–Hanhart	Pseudoherpetic keratitis	Tongue leukokeratosis	
Rothmund–Thomson	Cataracts (juvenile zonular)	Anomalies of radius and hands, hypodontia	Nail dystrophy
Rubinstein–Taybi	Long eyelashes, thick eyebrows, strabismus, cataracts	Broad thumb–great toe, clinodactyly of fourth toe and fourth to fifth fingers, short stature	Racquet nails
SAPHO		Osteomyelitis	
Schnitzler		Bone/joint pain (iliac/tibia), hyperostosis, osteosclerosis	
Schopf–Schulz–Passarge	Eyelid hidrocystomas	Hypodontia	Nail hypoplasia, dystrophy
Sjögren–Larsson	Retinitis pigmentosa, glistening dots	Short stature	
Sturge–Weber	Glaucoma, retinal malformations	Tram-track calcifications (skull x-ray)	
Sweet syndrome	Conjunctivitis, episcleritis, iridocyclitis	Arthritis, arthralgias	
Tricho-dento-osseus		Caries, periodontitis, small teeth, enamel defects, tall stature, frontal bossing	Brittle nails
Trichorhinophalangeal		Cone-shaped epiphyses, shortened phalanges and metacarpals, thin upper lip	Nail dystrophy
Trichothiodystrophy	Cataract, conjunctivitis, nystagmus	Osteosclerosis, short stature	Koiloynchia, ridging, splitting, leukonychia
Tuberous sclerosis	Retinal hamartomas (mulberry appearing), hypopigmented spots on iris	Dental pits, gingival fibromas, bone cysts, osteosclerosis	Koenen tumor

Vitamin A deficiency	Night blindness, unable to see in bright light, xerophthalmia, Bitot spots, keratomalacia	Growth retardation, excessive periosteal bone (decreased osteoclastic activity)	Brittle nails
Vitamin B2 (riboflavin) deficiency (Oral–ocular–genital)	Eye redness, burning, fatigue, sandiness, dryness, photosensitivity to light, cataracts	Cheilosis, red sore tongue	
Vitiligo	Uveitis, depigmented retina		
Von Hippel Lindau	Retinal hemangioblastoma		
Waardenburg	Dystopia canthorum, heterchromia irides	Caries, cleft lip/palate, scrotal tongue	
Werner	Cataract, glaucoma	Sclerodactyly, osteoporosis, high-pitched voice	
Wilson	Kayser–Fleischer ring		Blue lunulae
Witkop		Retained primary teeth	Nail dystrophy (toe>finger)
X-linked ichthyosis	Posterior comma-shaped corneal opacities (Descemet's membrane)		
Yellow nail syndrome			Yellow nails, thick, slowed growth (yellow lunulae – consider insecticides/weed killers (dinitro-orthocresol, diquat, and paraquat), tetracycline, smoking

Adapted from Solky BA, Jones JL. Boards' Fodder – Bones, Eyes, and Nails (http://www.aad.org/members/resident/fodder.html)

Dermatoses of Pregnancy

Condition	Frequency	Synonyms	Onset	Course	Description	Path/labs	Treatment
Polymorphic eruption of pregnancy	1:160	PUPPP, Toxic erythema/ rash of preg, Late-onset prurigo of pregnancy	Late third trimester or immediately post-partum	Often primiparous, no maternal/ fetal risk, rarely recurs, resolves 1–2 weeks post-partum	Urticarial papules/plaques in abdominal striae, spares umbilicus, spares face/palms/ soles; rapid weight gain may be risk factor	Non-specific	Topical steroids, antihistamines
Pemphigoid gestationis	1: 50,000	Herpes gestationis	Late pregnancy or immediately post-partum	Often recurs w/ subsequent preg, menstruation, and OCP, increased prematurity and SGA, $<10\%$ of neonates have skin lesions, BP2 Ag, assoc w/ Graves, resolves weeks–months post-partum	Intensely pruritic, vesiculobullous, trunk, 75% flare w/ delivery, spares face/palms/soles/ oral, HLA-DR3/DR4 associated	Subepi vesicle, perivasc lymphs/eos, DIF: linear C3 $\pm$ IgG along BMZ of perilesional skin	Systemic steroids

Atopic eruption of pregnancy	1:300	Prurigo of pregnancy, Prurigo gestationis, Early-onset prurigo, Papular derm of pregnancy, Pruritic folliculitis of pregnancy	Usu first or second trimester	No fetal/maternal risk, some have h/o atopic dermatitis, may recur w/ subsequent pregnancy, resolves weeks–months post-partum	2/3 eczematous, 1/3 papular or prurigo	Diagnosis of exclusion, non-specific path	Emollients, urea, topical steroids. If severe, systemic steroids, antihistamines, UVB
Intrahepatic cholestasis of pregnancy	1:100–1000, higher incidence with twins, + FH	Pruritus/prurigo gravidarum, Obstetric cholestasis, Jaundice of pregnancy	Third trimester	Increased rates of prematurity, fetal distress/death, and meconium staining, pruritus resolves within days post-partum, malabsorption → Vit K def, 2/3 recur w/ subsequent preg, often recurs w/ OCP	Intensely pruritic, ± jaundice, no primary lesions, UTI in 50%, sxs worse at night and on trunk and palms/soles	Increased serum bile salts, Liver US nl, Biopsy: centrilobular cholestasis	Urodeoxycholic acid, UVB, vit K
Impetigo herpetiformis	Rare	May represent acute generalized pustular psoriasis	Third trimester	Increased rates of placental insufficiency, stillbirth, fetal abnormality, hypocalcemia, vitamin D deficiency, often remits with delivery, recurs next preg	Sterile crusted pustules in flexures and inguinal, spreading centrifugally, fever, cardiac/renal failure possible	Pustular psoriasis-like path, DIF neg, hypocalcemia	Systemic steroids

Neonatal Vesiculopustular Eruptions

Condition	Population	Onset	Duration	Description	Diagnosis	Treatment
NON-INFECTIONS						
Erythema toxicum neonatorum	1/3–2/3 of Fullterm	Usu 1–2 days	1 week–1 month	Erythematous macules, papules, (subcorneal or intraepi) pustules, wheals, usu on trunk, spares palms/soles	Smear – eos	None needed
Transient neonatal pustular melanosis	4% of Black, <1% in White; Fullterm	Birth	Pustules – days; PIH – months	Fragile (subcorneal) pustules at birth → resolve with collarette of scale → PIH	Smear – PMNs	None needed
Neonatal cephalic pustulosis/ Neonatal acne	10%	Variable w/i first month	Within 6 months	Inflammatory papules/pustules on head/neck, no comedones, may scar, controversial pathogenesis – may be 2/2 hormones and/or malassezia	Smear – malassezia, PMNs	Self-limited, topical imidazole or BP/erythromycin
Miliaria crystallina	4%; high in tropics	Birth or first few weeks	Resolves w/i days when precipitants removed	Superficial clear noninflammatory vesicles; forehead, upper trunk (sub/intra-corneal eccrine duct obstruction)	Smear – negative	Avoid overheating and swaddling
Miliaria rubra	4%; high in tropics	Usu after first week	Resolves w/i days when precipitants removed	Pruritic, erythematous papules and pustules usu on forehead, upper trunk (eccrine duct obstruction at malpighian layer)	Smear – negative	Avoid overheating and swaddling

Infantile acropustulosis	<1%, increased in Black males	Up to 18 months, usu 3–6 months	Until 2–3 years	Pruritic acral (subcorneal) pustules/vesicles in crops (q2–4 weeks), eosinophilia, no burrows	Smear – eos (early), PMNs (late); Scabies prep neg	Midpotency topical steroids, antihistamines
Eosinophilic pustular folliculitis/Ofuji's	M>F	Birth or first few weeks	Several years	Pruritic, crusted, erythematous follicular papules/pustules/ vesicles in crops (q2–4 weeks), mainly on scalp, eosinophilia	Smear – eos	Topical steroids, systemic abx
Congenital self-healing langerhans/Hashimoto–Pritzker	Unknown, likely underreported	Birth or days	Weeks–months	Widespread red-brown nodules, skin-limited	Bx – CD1a+, S100+	None needed
Incontinentia pigmenti/ Block–Sulzberger	1:300,000, XLD	Birth or days	Linear and whorled; Stages: Vesicular/Bullous (birth – 1 year) → Verrucous (months – 3 years) → Hyperpigmented (1–20 years) → Hypopigmented/Atrophic (adulthood)		Bx: Bullous – eos spong; Verrucous – eos dysk; Hyperpig – dermal melanin; Hypopig – epi atrophy, no appendages	Referrals: ophtho, audiology, neuro, dental

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Condition	Population	Onset	Duration	Description	Diagnosis	Treatment
VIRAL						
HSV – congenital/ intrauterine	5% of newborn HSV	Birth		Generalized vesicles, pustules, scars, erosions, microcephaly, choriotretinitis, hydranencephaly, microphthalmia	Tzank – multinucleated giant cells; DFA, PCR, Cx, IgG serology	IV acyclovir
HSV – primary neonatal	95% of newborn HSV (usu peri- not postnatal infxn); ~1:3200 deliveries	Birth (30%) to several weeks	30–50% mortality if disseminated	40% Skin–Eye–Mucosal disease, 35% CNS, 25% disseminated (sepsis, hepatitis, resp, coag); Primary maternal infxn has 10× the risk of perinatal infxn vs. recurrent maternal infxn	Tzank – multinucleated giant cells; DFA, PCR, Cx, IgG serology	IV acyclovir
VZV – congenital	~10% risk with exposure (<20 weeks gestation)	Birth		LBW, scars, limb hypoplasia, microcephaly encephalitis, cortical atrophy, optho, MSK, GI, GU	Tzank – multinucleated giant cells; DFA, Cx	VZIG/acyclovir w/i 5 days to exposed mom

VZV – neonatal	20–60% risk with maternal exposure 5 days before or 2 days post-partum	Birth to 2 weeks	30% mortality	Pustules, vesicles → may ulcerate, necrose; pneumonitis, encephalitis, hepatitis	Tzank – multinucleated giant cells; DFA, Cx	VZIG/acyclovir w/i 5 days to exposed mom and to neonate
VZV – infantile zoster	2% of patients w/ intrauterine exposure by 20 weeks gestation	First year		Dermatomal papules, vesicles	Tzank – multinucleated giant cells; DFA, Cx	Consider iv acyclovir
FUNGAL						
Candidiasis – congenital/ intrauterine	<1%	Birth	Several weeks	Widespread erythematous papules/pustules, thrush, rarely systemic; Risk factors – prematurity, cervical/uterine foreign bodies	KOH: budding yeast, pseudohyphae	Topical nystatin or imidazole unless severe or disseminated
Candidiasis – neonatal	5%	Few days or weeks	Several weeks	Red plaques, satellite papules/pustules, more common and may disseminate in LBW babies	KOH: budding yeast, pseudohyphae	IV fluconazole if preterm/LBW
Aspergillosis	Premature/LBW/ immunodef	Days or weeks		Necrotic papules, pustules, ulcers	Bx: branching hyphae at 45°; Cx	Debridement, ampho

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Condition	Population	Onset	Duration	Description	Diagnosis	Treatment
Parasites						
Scabies	Rare in neonates			Excoriated vesicles, pustules, papules, nodules, burrows	KOH/Mineral oil – mites, feces/ scybala, eggs	Permethrin 5% 1 week apart, treat linens/family; sulfur; lindane contraindicated
BACTERIAL						
Impetigo neonatorum		Anytime		Erythematous pustules, vesicles, tense bullae, honey-colored crust, oozing, glazed, central clearing, satellite lesions, fever, adenopathy, diarrhea	Gram stain and cx; Staph – Gram + cocci in clusters; Strep – Gram + cocci in chains	Mupirocin, oral abx, nursery isolation
Rare, life-threatening bacterial infxns: *Listeria monocytogenes, Chlamydia trachomatis, E. coli, H. influenzae, Pseudomonas*		Onset: Birth, days, or weeks			Systemic involvement; Risk factors: prematurity, LBW, immunodef, maternal fever	Gram – rods: *Pseudomonas, H. influenzae, E. coli* Gram + rods: *Listeria monocytogenes*

Other neonatal vesiculopustular eruptions: Pustular leukemoid rxn in Down syndrome, Hyper IgE, Neonatal Behcet, Pustular Psoriasis, Zygomycetes, Syphilis.

Adapted from Van Praag MC *et al.* Diagnosis and treatment of pustular disorders in the neonate. *Pediatr. Dermatol.* 1997 March–April; 14(2):131–43; Johr RH and Schachner LA. Neonatal dermatologic challenges. *Pediatrics in Review.* 1997; 18:86–94. Pauporte M and Frieden I. Vesiculobullous and erosive diseases in the newborn, In: Bolognia Jorizzo JL, Rapini RP. *Dermatology*, Vol. 1. London: Mosby, 2003.

Genital Ulcers

Infection	Organism	Incubation	Presentation	Treatment	Notes
Chancroid	*Haemophilus ducreyi*	3–10 days	Painful, soft, ragged edges; tender and unilateral LAN	Azithromycin, ceftriaxone, ciprofloxacin, erythromycin	"School of fish" Gram stain
Primary syphilis (chancre)	*Treponema pallidum*	2–4 weeks	Painless, indurated, sharp and raised edges; bilateral and nontender LAN	Penicillin	Rubbery, "ham-colored base"
Genital HSV	HSV	3–7 days	Painful, grouped	Antivirals	
Lymphogranuloma venereum	*Chlamydia trachomatis* serovars L1-3	3–12 days	Painless, soft; tender LAN	Doxycycline	"Groove sign" – tender nodes around Poupart's ligament
Donovanosis/granuloma inguinale	*Calymmatobacterium/ Klebsiella granulomatis*	2–12 weeks	Non- or mildly painful, beefy red, bleeding	TMP-SMX, doxycycline, erythromycin, ciprofloxacin	"Safety pin" Donovan bodies

Other infectious causes of genital ulcers: EBV, Amebiasis, Candida, TB, Leishmaniasis.
Non-Infectious causes of genital ulcers: Behcet/Apthous, Crohn, Lichen Planus, Tumor, Lichen Sclerosis, Contact, Trauma, Factitial, Fixed Drug (NSAIDs, metronidazole, sulfonamide, acetaminophen, TCN, phenytoin, OCPs, phenolphthalein, barbiturates), Other Meds (all-trans-retinoic acid, foscarnet), MAGIC Syndrome, Cicatricial/Bullous Pemphigoid, Hemangioma, EM/SJS/TEN.

Common Contact Allergens

Allergen	Uses/products/cross reactions (X-RXN)	Test
METAL		
Nickel	• Jewelry, watches, coins, buckles, eyelash curlers, kitchen utensils, canned food	Dimethylglyoxime – to detect nickel; TRUE test #1
Gold	• Jewelry, dentistry, electronics X-RXN: nickel, cobalt	
Chromates/potassium dichromate	• Tanned leather, cement, mortar, matches, anti-rust products, paint, plaster, GREEN dyes/tattoos (pool/card table felt) X-RXN: nickel, cobalt	TRUE test #4
Cobalt	USES: mixed with metals for strength • Cement, cosmetics, vitamin B12 injections, pigment in porcelain, paint, crayon, glass, pottery X-RXN: nickel, chromates	TRUE test #12
RESIN		
p-tert-Butylphenol (PTBP) formaldehyde resin	USES: Resin for adhesive • Glues, shoes/watchband/handbag (glued leather products), plywood, disinfectants, rubber, varnish, printer inks, fiberglass; depigmenting	TRUE test #13
Epoxy resin (bisphenol A)	USES: Resin for adhesive Allergens: bisphenol A, epichlorohydrin • Glues, plastics, adhesives, PVC products, electrical insulation	TRUE test #14
Rosin (colophony, abietic acid)	Adhesives, cosmetics, epilation wax, polish, paint, chewing gum, paper products; from conifer	TRUE test #7
RUBBER COMPOUND		
Carba mix	USES: Rubber stabilizer • Elastic bands, condoms, shoes, cements X-RXN: thiurams	TRUE test #15
Black rubber mix	USES: Rubber stabilizer Isopropyl PPD, cyclohexyl PPD, diphenyl PPD • Black and gray rubber products: tires, rubber boots, eyelash curlers, scuba suits, balls	TRUE test #16

Allergen	Uses/products/cross reactions (X-RXN)	Test
Thiuram mix	USES: Rubber additives • Gloves, adhesive, latex, condoms, fungi- and pesticides, disulfiram	TRUE test #24
Mercapto mix	USES: Rubber accelerator MOR: morpholinyl mercapto-benzothiazole CBS: *N*-cyclohexyl-2-benzothiazyl sulfenamide MBTS: dibenzothiazyl disulfide • Rubber products: gloves, makeup sponges, undergarments, tires	TRUE test #22
Mercapto-benzothiazole (MBT)	USES: Rubber accelerator • Rubber shoes, tires, undergarments, shoes	TRUE test #19
MEDICAMENTS		
Lanolin/wool alcohol	USES: Emulsifier From: sheep sebum (wool wax/alcohol/fat) • Cosmetics, soaps, adhesives, topical agents X-RXN: Aquaphor, Eucerin (cetyl or stearyl alcohols)	TRUE test #2 (wool alcohols)
Neomycin sulfate	Aminoglycoside group • Topical creams, ear/eye drops X-RXN: aminoglycosides Co-sensitivity: bacitracin	TRUE test #3
Benzocaine/tetracaine	PABA derivative, ester anesthetic X-RXN: procaine, cocaine, PABA, sulfa meds, thiazide, PPD	TRUE test #5: Caine mix
Dibucaine	Amide anesthetic X-RXN: lidocaine, bupivicaine	TRUE test #5: Caine mix
Corticosteroids	Four classes based on structure: A – HC/Prednisone B – TMC acetonide C – Betamethasone D – Hydrocortisone-17-butyrate and clobetasone-17-butyrate Tixocortol pivalate – test for class A; Budesonide – test for classes B and D	
Ethylenediamine	Stabilizer • Topical antibiotic/steroid creams (Mycolog cream); dye, rubber, resin, waxes X-RXN: hydroxyzine, aminophylline, phenothiazine	TRUE test #11

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Allergen	Uses/products/cross reactions (X-RXN)	Test
Propylene glycol	Dimer alcohol to increase drug solubility • Vehicle base in topical meds, valium, lubricant jelly; brake fluid, antifreeze	
Bacitracin Clioquinol	Risk groups: leg ulcers, post-op, chronic otitis externa Topical antibacterials and antifungals	
FRAGRANCES		
Fragrance mix (8 fragrances)	α-amyl cinnamic aldehyde, cinnamic alcohol, cinnamic aldehyde (toothpaste, gum, lipstick) hydroxycitronellal – synthetic, floral isoeugenol, eugenol – clove oak moss absolute – lichen extract, cologne geraniol – geranium X-RXN: colophony, wood tars, turpentine, propolis, benzoin, storax	TRUE test #6
Balsam of peru (myroxylon pereirae)	Cinnamic acid, cinnamyl cinnamate, benzyl benzoate, benzoic acid, vanillin • Fragrances, spices (cloves, cinnamon, Jamaican pepper), flavoring agent (wine, tobacco, vermouth, cola), mild antimicrobial properties X-RXN: Colophony, turpentine, benzoin, wood tar	TRUE test #10
PRESERVATIVES		
Formaldehyde	• Ubiquitous – fabric finishes (waterproof, anti-wrinkle), cosmetics, cleansers, paper products, paint Formaldehyde-releasing preservatives: quaternium-15, imidazolidinyl urea, diazolidinyl urea, DMDM-hydantoin	TRUE test #21
Quaternium-15 (Dowicil 200)	Formaldehyde-releasing preservative Sensitivity may be to formaldehyde • Soaps, shampoos, moisturizers	TRUE test #18
Methyl-choloro-isothiazinolone (Kathon CG)	Cosmetics, hair/skin products (Eucerin), household products (toilet paper), permanent waves, latex emulsions	TRUE test #17
Paraben mix	USES: preservatives • Topical pharmaceutical products, cosmetics X-RXN: PABA, PPD	TRUE test #8
Thimerosal (Merthiolate)	Preservative/antiseptic/vaccine/eye drops Two components: thiosalicylic acid and ethyl mercuric chloride X-RXN: piroxicam, mercury	TRUE test #23

Allergen	Uses/products/cross reactions (X-RXN)	Test
Imidazolidinyl urea (Germall 115, Tristat)	Formaldehyde-releasing preservatives • Cosmetics, skin/hair products, adhesive, latex emulsions	
OTHERS		
Paraphenylenediamine (PPD)	Blue-black aniline dye • Permanent hair dyes, tattoos, photography solutions, printer inks, oils, gasoline X-RXN: pro/benzocaine, PABA, azo- and aniline dyes, sulfas, para-aminosalicylic acid	TRUE test #20
Ammonium persulfate	Bleaching agent • Hair bleach, flour Contact urticaria, anaphylactoid rxn	
Disperse blue dyes	Fabrics; waistbands, thighs, axillae	
Glyceryl monothioglycolate	Acidic perming solutions Chemical remains in hair shaft for months	
Latex	Sap from the rubber tree *Hevae brasiliensis* • Gloves, condom, balloon High risk: children with spina bifida, health care workers X-RXN: avocado, banana, chestnut, kiwi, papaya	RAST test, prick test
Cocamidopropyl betaine	Nonionic surfactant from coconut oil Antigens: amidoamine, DMAPA, CAPB • Shampoo, liquid soaps Usually facial pattern rash	
Ethyl cyanoacrylate	"Superglue" • Artificial nails glue, liquid bandage	
Methyl methacrylate	• Artificial nails, dental work, glue for surgical prostheses	
Gluteraldehyde	Cold sterilizing solution Health care workers, embalming fluid, electron microscopy, hand cleansers	
Limonene	• Citrus peels, fragrance additive, sanitizers, cleansers, degreasers	
Propolis	Dimethylallyl ester of caffeic acid • Bee glue, lipstick, ointments, mascara	

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Allergen	Uses/products/cross reactions (X-RXN)	Test
Thioureas	Rubber antioxidant • Wet suits, shoe insoles, adhesives, copy paper, photography	
Euxyl K-400	Methyldibromo glutaronitrile phenoxyethanol • Cosmetic/personal care products	
Toluene-sulfonamide (tosylamide) formaldehyde resin	Nail lacquer/ hardener: eyelid, face, neck, finger dermatitis	
Benzyl alcohol	Solvent, preservative, anesthetic • Plants, essential oils, foods, cosmetics, medications, paints/ lacquers	

Features suggestive of specific irritant/toxin

Acne/folliculitis	Arsenic, oils, glass fibers, asphalt, tar, chlorinated naphthalenes, polyhalogenated biphenyls
Miliaria	Occlusion, aluminum chloride, UV, infrared
Alopecia	Borax, chloroprene dimers
Granulomatous	Silica, beryllium, keratin, talc, cotton

Plants and dermatoses

Plants causing non-immunologic contact urticaria

Urticaceae family (nettle):
- *Urtica* spp. (dioica) – stinging nettle
- *Dendrocnide* spp. – Australian stinging nettle, may be fatal

Euphorbiaceae family (spurge):
- *Acidoton* and *Cnidosculus* spp.
- Croton plant

Hydrophyllaceae family (water-leaf)

Plants causing mechanical irritant dermatitis

Hedera helix – Araliaceae – common ivy
Opuntia spp. – Cactaceae – prickly pear
Tulipa spp. – Liliaceae – tulip
Ficus and *Morus* spp. – Moraceae – fig, mulberry
Carduus and *Cirsium* spp. – Asteraceae – thistle
Bidens tripartite – Asteraceae – bur marigold
Other Asteraceae – dandelion, lettuce, chicory (irritant latex)

Plants causing chemical irritant dermatitis

Chemical	Plant	Scientific name
Calcium oxalate	Daffodil	*Narcissus* spp. (Amaryllidaceae)
	Century plant	*Agave americana* (Agavaceae)
	Dumb cane	*Dieffenbachia picta* and *Philodendron* spp. (Araceae)
	Philodendron	
	Pineapple	*Ananas cosmosus* (Bromeliaceae)
	Hyacinth	*Hyacinthus orientalis* (Liliaceae)
	Rhubarb	*Rheum rhaponticum* (Polygonaceae)
Thiocyanates	Garlic	*Allium sativum* (Alliaceae)
	Black mustard	*Brassica nigra* (Brassicaceae)
	Radish	*Raphanus sativus* (Brassicaceae)
Cashew nut shell oil	Cashew tree	*Anacardium occidentale* (Anacardiaceae)
Bromelin	Pineapple	*Ananas comosus* (Bromeliaceae)
Phorbol esters, diterpenes (latex)	Poinsettia	*Euphorbia pulcherrima* (Euphorbiaceae)
Protoanemonin	Buttercup	*Ranunculus* spp. (Ranunculaceae)
Capsaicin	Chili pepper	*Capsicum anuum* (Salanaceae)

Phytophotodermatoses

Apiaceae: hogweed (*Heracleum sphondylium*), celery (*Apium gaveolens*), parsley (*Petroselinum*), parsnips, fennel (*Foeniculum vulgare*)
Rutaceae: lime, orange, lemon, garden rue, Hawaiian lei, gas plant/burning bush
Moraceae: mulberry, fig tree
Fabaceae/Leguminosae: bavachee/scurf-pea (vitiligo tx)

Plant allergic contact dermatitis

Allergen	Family	Plant (scientific name)
Urushiol	Anacardiaceae	Poison ivy/oak/sumac (*Toxicodendron vernix*)
		Cashew nut tree (*Anacardium occidentale*)
		Mango (*Mangifera indica*)
	Cross-reactions: *Ginko biloba*, *Grevillea*	Brazilian pepper tree (*Schinus terebinthifolius, Florida Holly*)
		Indian marking tree nut (*Semecarpus anacardium*)
		Japanese lacquer tree (*Toxicodendron verniciflua*)

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Allergen	Family	Plant (scientific name)
		Rengas tree (*Gluta* spp.) Poisonwood tree (*Metopium toxiferum*)
Sesquiterpene lactones	Asteraceae (Compositae)	Feverfew (*Tanacetum parthenium*)
		Chrysanthemum (*X Dendranthema*) Dandelion (*Taraxacum officinale*) Sunflower (*Helianthus annuus*) Scourge of India (*Parthenium hysterophorus, wild feverfew*) Daisy (*Leucanthemum* spp.) Ragweed (*Ambrosia* spp.) Marigold (*Tagetes* spp.) Artichoke (*Cynara scolymus*) Lettuce (*Lactuca sativa*) Endive (*Cichorium endiva*) Chicory (*Cichorium intybus*) Chamomile, mugwort (*Artemisia* spp.) Yarrow (*Achillea millefolium*)
Diallyl disulfide	Alliaceae	Onion (*A. cepa*) Garlic (*A. sativum*) Leek (*A. porrum*) Chive
Tuliposide A	Alstromeriaceae and Lillaceae	Tulip, Peruvian lily (*A. auriantiaca and A. ligtu*)
Primin	Primulaceae	Primrose (*Primula obconica*)
	Lamiaceae	Peppermint (*menthol*), spearmint (*carvone*), lavender, thyme
d-limonene	Myrtaceae	Tea tree (*Melaleuca* spp.)
Colophony and turpentine/ carene	Pinaceae	Pine tree (*Pinus* spp.) Spruce tree (*Picea* spp.)
Ricin	Castor bean	*Ricinus communis*
Abrin	Jequirity bean	*Abrus precatorius*
Usnic acid, evenic acid, atronorin	Lichens	

Vitamin Deficiencies/Hypervitaminoses

Vitamin A
Vitamin A supplementation helpful in rubeola
Deficiency = Phrynoderma (toadskin)

- Due to fat malabsorption, diet; found in animal fat, liver, milk
- Night blindness, poor acuity in bright light, Bitot spots, keratomalacia, xerophthalmia, xerosis, follicular hyperkeratosis, fragile hair, apathy, mental and growth retardation

Hypervitaminosis A

- Similar to medical retinoid treatment: dry lips, arthralgias, cheilitis, alopecia, onychodystrophy/clubbing, hyperpigmentation, impaired bone growth, hyperostosis, pseudotumor cerebri, lethargy, anorexia

Vitamin B1 – Thiamine
Deficiency = Beriberi

- Due to diet (polished rice), pregnancy, alcoholism, GI disease
- Glossitis, edema, glossodynia, neuropathy, Wernicke-Korsakoff, CHF

Vitamin B2 – Riboflavin
Deficiency

- Alcoholics, malabsorption, neonatal phototherapy, chlorpromazine
- Oral-ocular-genital syndrome: cheilits, seborrheic dermatitis-like rash, tongue atrophy, belpharitis, conjunctivitis, photophobia, genital and peri-nasal dermatitis, anemia

Vitamin B3 – Niacin/Nicotinic Acid
Deficiency = Pellagra

- May be due to precursor (tryptophan, Hartnup) deficiency, alcoholism, carcinoid tumor, INH, 5-FU, azathioprine, GI disorders, anorexia
- Casal necklace eruption, photosensitivity, shellac-like appearance, acral fissures, perineal rash, cheilitis, diarrhea, dementia
- Below granular layer (stratum malpighii): vacuolar changes

Vitamin B6 – Pyridoxine
Deficiency

- Due to cirrhosis, uremia, isoniazid, hydralazine, OCP, phenelzine, penicillamine
- Rash resembling seborrheic dermatitis, intertrigo, cheilitis, glossitis, conjunctivitis, fatigue, neuropathy, disorientation, N/V

Vitamin B12– Cyanocobalamin
Deficiency

- Due to diet (found in animal products), pernicious anemia, malabsorption
- Glossitis, hyperpigmentation, canities, neurologic symptoms

Vitamin C
Deficiency = Scurvy

- Alcoholics, diet
- Water-soluble, fruits/vegetables
- Perifollicular hyperkeratosis and petechiae, corkscrew hairs, hemorrhagic gingivitis, epistaxis, hypochondriasis, subperiosteal hemorrhage (pseudoparalysis), soft teeth, gingivitis, hematologic changes, weakness

Vitamin D
Physiology

- Vit D_2 and D_3 in the diet are transported to the liver in chylomicrons and Vit D_3 from the skin and Vit D_2 and D_3 from fat cell stores are bound to Vit D-binding protein for transport to the liver
- In the liver, Vit D-25-hydroxylase turns Vit D into 25-hydroxyvitamin D, or 25(OH)D, the main circulating form of Vit D
- 25(OH)D is biologically inactive until it is converted to 1,25-dihydroxyvitamin D, or $1,25(OH)_2D$, by 25-hydroxyvitamin D-1α-hydroxylase in the kidneys
- $1,25(OH)_2D$ is inactivated by 25-hydroxyvitamin D-24-hydroxylase and turned into calcitroic acid, which is excreted in the bile
- In osteoblasts, $1,25(OH)_2D$ increases RANKL which bind RANK on preosteoclasts, leading to activation
  In intestinal cells, $1,25(OH)_2D$ binds VDR-RXR, leading to increased calcium channel TRPV6 and calcium binding protein calbindin 9K
- Calcium-phosphate product: saturation product = 60 mg^2/dl^2; between 42 and 52 mg^2/dl^2 is desirable in the ESRD population 60 mg^2/dl^2; between 42 and 52 mg^2/dl^2 is desirable in the ESRD population.

Deficiency

- Poor diet (Vit D is fat soluble – found in oily fish, eggs, butter, liver, cod-liver oil), insufficient sun (need UVB to convert 7-dehydrocholesterol to previtamin D_3, which is quickly turned into vitamin D_3), anticonvulsants, fat malabsorption, old age, chronic kidney disease, breastfeeding (human milk has low Vit D)
- Requirements: controversial, ~800 IU/day of vitamin D3
- Alopecia, rickets/osteomalacia, osteoporosis, cancer (colon, breast, prostate, hematologic), autoimmune disease, muscle weakness

Hypervitaminosis D

- Hypercalcemia, calcinosis, anorexia, headache, N/V

Vitamin K

Deficiency

- Due to diet (fat-soluble, meat, green leafy vegetables; GI flora produces 50% of requirements), anorexia, CF, liver disease, malabsorption, coumadin, cephalosporins, salicylates, cholestyramine
- Hemorrhage

Zinc deficiency

- Due to AR genetic defect, diet (low zinc, excess fiber), malabsorption, CRF, alcoholism, TPN, cancer
- Typically when wean breastfeeding but zinc in human breastmilk does have lower bioavailability than cowmilk and may sometimes be low; premature infants have reduced zinc stores, poor GI absorbance, and higher zinc needs
- Acrodermatitis enteropathica (acral, periorificial, periungual, cheilitis), diarrhea, alopecia, candida/staph superinfection, paronychia, irritable, photophobia, blepharitis, failure to thrive
- Resembles biotin deficiency, essential fatty acid deficiency, CF, Crohn, necrolytic migratory erythema
- Low alkaline phosphatase
- Histo: epidermal pallor $\pm$ psoriasiform hyperplasia, necrosis, subcorneal/intraepidermal vesicle (similar to necrolytic migratory erythema, necrolytic acral erythema, genetic deficiency of M subunit of LDH)
- Zinc-responsive diseases: necrolytic acral erythema, amicrobial pustulosis of the flexures and scalp

Biotin deficiency

- Due to short gut (gut bacteria make biotin), malabsorption, avidin (raw egg white) consumption, biotinidase deficiency (infantile), multiple carboxylase synthetase or holocarboxylase synthetase defects (neonatal)
- Rash like zinc deficiency, alopecia, conjunctivitis, fatigue, paresthesias

Essential fatty acid deficiency

- Due to GI abnormalities/surgery, diet, chronic TPN
- Rash resembling biotin and zinc deficiencies, alopecia, leathery skin, intertrigo
- Eicosatrienoic acid: Arachidonic acid ratio > 4

Copper

- Deficiency in Menkes, Wilson
- Local, exogenous excess – green hair (copper in water)

Selenium deficiency

- Component of glutathione peroxidase
- Due to TPN, low soil content
- Weakness, cardiomyopathy, elevated transaminases and CK, hypopigmentation (skin/hair), leukonychia

Lycopenemia

- Excess consumption of red fruits/vegetables (tomatoes, papaya) → reddish skin

Carotenemia

- Carotene-containing foods: carrots, squash, oranges, spinach, corn, beans, eggs, butter, pumpkins, papaya, baby foods
- Yellow soles/palms, central face (sebaceous area)

Kwashiorkor

- Protein deficiency
- Due to diet, GI surgery, HIV
- Dyschromia, pallor, flaky paint desquamation, sparse, hypopigmented hair, flag sign, potbelly, edema, moon facies, cheilitis, soft nails, irritable, infections

Marasmus

- Protein and caloric deficiency
- Due to diet neglect, anorexia, malabsorption, HIV, liver/kidney failure
- Xerotic, lax, thin skin, follicular hyperkeratosis, broken lanugo-like hair, monkey/aged facies, no edema/hypoproteinemia

Genodermatoses

Gene list

Disease	Gene	Protein		Comment
Acral peeling skin syndrome	TGM5	Transglutaminase-5	AR	
Acrodermatitis enteropathica	SLC39A4	Intestinal zinc–specific transporter	AR	Defective zinc absorption from the gut
Acrokeratosis verruciformis of hopf	ATP2A2	ATPase, Ca^{2+} transporting	AD	Allelic to darier
AEC	P63	P63	AD	Tumor suppressor; Allelic to EEC, Rapp–Hodgkin, limb-mammary syndrome, split-hand and split-foot malformation type 4, and acro-dermatoungual-lacrimal-tooth (ADULT)
Albright hereditary osteodystrophy	GNAS1	G protein, alpha stimulating	AD	G protein subunit of adenylate cyclase; Allelic to McCune–Albright and progressive osseus heteroplasia
Alagille	JAG1	Jagged-1 NOTCH2	AD	Jagged-1 is a ligand for NOTCH
Alkaptonuria	HGO	Homogentisate 1,2-dioxygenase	AR	Deficient homogentisic acid oxidase causes homogentisic acid to accumulate in tissues
Alport	COL4A3 COL4A4 COL4A5	Collagen 4	AR AR XL	XL form may be associated with leiomyomatosis (esophageal, tracheo-bronchial, female genital)

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Disease	Gene	Protein		Comment
Anhidrotic ectodermal dysplasia (Christ–Siemens–Touraine; hypohidrotic)	EDA	Ectodysplasin-A	XLR	Similar to AD form due to ectodysplasin anhidrotic receptor (EDAR) mutation; Similar to AR form due to either EDAR or EDAR-associated death domain (EDARADD) mutations
Anhidrotic ectodermal dysplasia with immune deficiency ± osteoporosis and lymphedema	NEMO	NF–κB essential modulator/IKK-gamma	XLR	Allelic to IP
Anonychia congenita	RSPO4	R-spondin 4	AR	Wnt/β-catenin signaling pathway (no bone hypoplasia unlike Cooks)
Apert	FGFR2	Fibroblast growth factor receptor 2	AD	Allelic to Beare–Stevenson and Crouzon
Argininosuccinic aciduria	ASL	Argininosuccinate lyase	AR	Urea cycle defect
Arrhythmogenic right ventricular dysplasia/ cardiomyopathy	DSP PLK2 DSG2 DSC2	Desmoplakin Plakophilin-2 Desmoglein-2 Desmocollin-2	AR	
Atrichia with papular lesions	HR	Hairless	AR	Zinc finger protein
Ataxia–telangiectasia	ATM	Ataxia telangiectasia mutated	AR	Phosphatidyl inositol 3 kinase-like domain
Autoimmune polyendocrinopathyI	AIRE	Autoimmune regulator	AD AR	Candidiasis, ectodermal dysplasia
Bannayan–Riley–Ruvalcaba	PTEN	Phosphatase and tensin homolog	AD	Tumor suppressor; Allelic to Cowden and Lhermitte–Duclos

Bart–Pumphrey	GJB2	Connexin 26	AD	Knuckle pads, leukonychia, and sensorineural deafness; Allelic to KID and classic Vohwinkel
Basal cell nevus syndrome (Gorlin)	PTCH1	Patched	AD	Tumor suppressor, SHH transmembrane receptor, inhibits SMOH
Beare–Stevenson Cutis Gyrata	FGFR2	Fibroblast growth factor receptor 2	AD	Allelic to Apert and Crouzon
Beckwith–Wiedemann	CDKN1C/ KIP2/P57; NSD1; 11p15 imprinting	Cyclin-dependent kinase inhibitor 1C	Sp > AD	Deregulation of imprinted growth regulatory genes; 11p15 imprinting region also involved in Russell-Silver
Birt–Hogg–Dube	FLCN	Folliculin	AD	Interacts with AMPK and FNIP1 in mTOR signaling
Bloom	RECQL3	RecQ protein-like 3	AR	DNA helicase
Brooke–Spiegler	CYLD	Cylindromatosis	AD	Tumor suppressor
Bruton agammaglobulinemia	BTK	Bruton agammaglobulinemia tyrosine kinase	XLR	Tyrosine kinase
Bullous congenital ichthyosiform Erythroderma (epidermolytic hyperkeratosis)	KRT 1, 10	Keratin 1, 10	AD	Intermediate filaments
Buschke–Ollendorff	LEMD3/MAN1	LEM domain-containing protein 3	AD	Inner nuclear membrane protein; Allelic to familial cutaneous collagenoma syndrome
Capillary malformation-arteriovenous malformation	RASA1	RAS family, GTPase activating protein	AD	

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Disease	Gene	Protein		Comment
Caridiofaciocutaneous	KRAS BRAF MEK1 MEK2	Kirsten rat sarcoma virus oncogene homolog	Sp	All proteins in RAS-ERK pathway
Carney complex (NAME, LAMB)	PRKAR1A	Protein kinase A regulatory subunit 1α	AD	
Carney complex with distal arthrogryposis	MYH8	Myosin heavy chain 8	AD	Variant associated with trismus and pseudocamptodactyly
Cartilage hair hypoplasia	RMRP	Mitochondrial RNA-processing endoribonuclease	AR	
Carvajal	DSP	Desmoplakin	AR	Dilated cardiomyopathy with woolly hair and keratoderma; Allelic to keratosis palmaris striata II, lethal acantholytic EB, skin fragility-wooly hair syndrome
CEDNIK (cerebral dysgenesis, neuropathy, ichthyosis, PPK)	SNAP29	Synaptosomal-associated protein 29	AR	
Cerebral capillary malformations, familial	CCM1/KRIT1	Krev-interaction trapped 1	AD	Hyperkeratotic AVMs
Cerebrotendinous xanthomatosis	CYP27	Cytochrome p450, subfamily 27A, polypeptide 1 (sterol-27-hydroxylase)	AR	
Chèdiak–Higashi	LYST	Lysosomal trafficking regulator	AR	Lysosomal transport – transfer of melanosomes

CHILD	NSDHL	NADP steroid dehydrogenase-like	XLD	Cholesterol biosynthesis (aka 3β-hydroxysteroid dehydrogenase)
Chondrodysplasia punctata 1	ARSE	Arylsulfatase E	XLR	
Chondrodysplasia punctata 2 (Conradi–Hünermann)	EBP	Emopamil-binding protein	XLD	Sterol isomerase – cholesterol biosynthesis
Chondrodysplasia punctata, rhizomelic, type 1	PEX7	Peroxisomal type 2 targeting signal receptor (PTS2)	AR	Allelic to refsum
Chondrodysplasia punctata, rhizomelic, type 2	DHAPAT	Acyl-CoA:dihydroxyacetone phosphate acyltransferase	AR	
Chronic granulomatous disease Cytochrome, X-linked	CYBB	p91-Phagocyte oxidase (cytochrome b-245 beta subunit)	XLR	Cytochrome b is part of NADPH oxidase – need oxidative burst to kill catalase+ bacteria
Chronic granulomatous disease Cytochrome b-negative	CYBA	p22-Phagocyte oxidase	AR	
Chronic granulomatous disease Cytochrome b-positive type 1	NCF1	p47-Phagocyte oxidase	AR	
Chronic granulomatous disease Cytochrome b-positive type 2	NCF2	p67-Phagocyte oxidase	AR	
Cleft lip-Palate with ectodermal dysplasia	PVRL1	Poliovirus receptor-like 1	AR	Cell adhesion molecule/herpes virus receptor; Margarita Island ED, Rosselli–Giulienetti, Zlotogora–Ogur

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Disease	Gene	Protein		Comment
Cockayne	ERCC6 ERCC8	Excision repair cross–complementing group 6 or 8	AR	
Congenital adrenal hyperplasia	CYP21A2 CYP11B1 CYP17A1 STAR	21-hydroxylase 11-β-hydroxylase 17-α-hydroxylase Steroidogenic acute regulatory protein	AR	21-hydroxylase = most common; STAR = lipoid variant, most severe
Congenital contractural arachnodactyly (Beals)	FBN2	Fibrillin 2	AD	Similar to Marfan syndrome
Congenital generalized lipodystrophy (Berardinelli–Seip)	AGPAT2 BSCL2	1-acylglycerol-3-phosphate O-acyltransferase-2 (Lysophosphatidic acid cyltransferase) Seipin	AR	
Congenital ichthyosiform erythroderma (nonbullous)	TGM1 ALOXE3 ALOX12B CGI58/ABHD5	Transglutaminase-1 Lipoxygenase-3 12R-Lipoxygenase Abhydrolase domain-containing 5 (Dorfman–Chanarin)	AR	Allelic variants of TGM1 include lamellar ichthyosis and self-healing collodion baby
Corneal dystrophy of Meesmann	KRT3 KRT12	Keratin 3 Keratin 12	AD	
Cornelia de Lange	NIPBL SMC1A (X-linked) SMC3	Nipped-β-like structural maintenance of chromosomes 1A and 3	Sp > AD	Components of cohesin complex

Costello	HRAS KRAS	Harvey and Kirsten rat sarcoma virus oncogene homolog	Unk	
Cowden	PTEN	Phosphatase and tensin homolog	AD	Tumor suppressor; Allelic to Bannayan–Riley–Ruvalcaba and Lhermitte–Duclos
Crohn's disease susceptibility	CARD15/NOD2	Caspase recruitment domain-containing protein 15 Nucleotide-binding oliogmerization domain protein 2	Cplx	CED4/APAF family of apoptosis regulators Allelic to Blau syndrome and early-onset sarcoidosis
Crouzon	FGFR2	Fibroblast growth factor 2	AD	Allelic to Apert and Beare–Stevenson
Crouzon with acanthosis nigricans	FGFR3	Fibroblast growth factor 3	AD	Allelic to severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN)
Cutaneomucosal venous malformation	TIE2/TEK, VMCM1	Tyrosine kinase, endothelial	AD	Endothelial cell-specific receptor tyrosine kinase
Cutis Laxa (X-linked variant = Ehlers–Danlos 9, Occipital Horn Syndrome)	FBLN5 FBLN4 ELN ATP7A	Fibulin 5 Fibulin 4 Elastin ATP7A	AR, AD AR AD XLR	Copper ion-binding ATPase ATP7A allelic to Menkes
Darier	ATP2A2	SERCA2 – Sarcoendoplasmic reticulum Ca^{2+} ATPase isoform 2	AD	Ca^{2+} ATPase; allelic to acrokeratosis verruciformis
Dowling–Degos–Kitamura	KRT5	Keratin 5	AD	Allelic to EBS

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Disease	Gene	Protein		Comment
Drug hypersensitivity (anticonvulsant hypersensitivity syndrome)	EPHX	Epoxide hydrolase	?	
Dyschromatosis symmetrica hereditaria	DSRAD	Double-stranded RNA-specific adenosine deaminase	AD	
Dyskeratosis congenita	DKC1 TERC	Dyskerin telomerase RNA candidate 3	XLRAD	Ribosomal assembly chaperone
Ectodermal dysplasia, skin fragility	PKP1	Plakophilin 1	AD	Desmosomal component
Epidermolysis Bullosa (EB), dominant dystrophic (Cockayne–Touraine)	COL7A1	Collagen 7	AD	290 kDa, Anchoring fibrils
EB, recessive dystrophic (Hallopeau–Siemens)	COL7A1	Collagen 7	AR	290 kDa, Anchoring fibrils
EB simplex	KRT5, 14	Keratin 5, 14	AD	Intermediate filaments
EB simplex, Koebner type	KRT5	Keratin 5	AD	Allelic to Dowling–Degos–Kitamura
EBS with muscular dystrophy, Also EBS ogna variant	PLEC1	Plectin	AR	In hemidesmosomes, intermediate filament binding protein
GABEB (generalized atrophic benign epidermolysis bullosa) – junctional	COL17A1 LAMA3 LAMB3 LAMC2	Collagen 17 Laminin A3 Laminin B3 Laminin C2	AR	Structural protein – BP Ag 2 Laminin subunits
Junctional EB – Herlitz type	LAMA3 LAMB3 LAMC2	Laminin 5 subunits	AR	In lamina lucida, anchoring filaments

Junctional EB – Non-Herlitz	LAM5 COL17A1	Laminin 5 Collagen 17	AR	Laminin 5 or type 17 collagen
Junctional EB with pyloric atresia	ITGA6 ITGB4	Alpha 6 Beta 4 Integrin	AR	Hemidesmosome transmembrane protein complex
Junctional EB with nephropathy and deafness	CD151	RBC antigen MER2	AR	Resembles Alport (nephropathy + deafness)
Ectodermal dysplasia, skin fragility	PKP1	Plakophilin 1	AR	Desmosomal plaque protein
Ehlers–Danlos, severe classic/Gravis 1	COL5A1 COL5A2 COL1A1	Collagen 5α1 Collagen 5α2 Collagen 1α1	AD	Allelic to Ehlers–Danlos 2 (COL5A1/2) Allelic to Ehlers–Danlos 7 and osteogenesis imperfecta (COL1A1)
Ehlers–Danlos, mild classic/Mitis 2	COL5A1 COL5A2	Collagen 5α1 Collagen 5α2	AD	Allelic to Ehlers–Danlos 1
Ehlers–Danlos, hypermobility 3	COL3A1 TNXB	Collagen 3α1 Tenascin XB	AD	Allelic to Ehlers-Danlos 4 TNXB = extracellular membrane protein
Ehlers–Danlos, vascular 4	COL3A1	Collagen 3A1	AD, AR	Allelic to Ehlers–Danlos 3
Ehlers–Danlos, X-linked 5	Unknown		XLR	
Ehlers–Danlos, kyphoscoliosis/Ocular 6	PLOD	Lysyl hydroxylase	AR	
Ehlers–Danlos arthrochalasis 7a, 7b	COL1A1 COL1A2	Collagen 1α1 Collagen 1α2	AD	Defective conversion of procollagen into type I collagen
Ehlers–Danlos dermatosparaxis 7c	ADAMTS-2	Procollagen *N*-peptidase	AR	

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Disease	Gene	Protein		Comment
Ehlers–Danlos, periodontosis 8	Unknown		AD	
Ehlers–Danlos, occipital horn 9	ATP7A	ATP7A	XLR	X-linked cutis laxa; Allelic to Menkes; copper transporter
Ehlers–Danlos, Fibronectin-deficient 10	Fibronectin		AR	
Ellis–Van Creveld–Weyers acrodental dysostosis complex (chondroectodermal dysplasia)	EVC1 EVC2	Ellis–Van Creveld 1, 2	EVC=AR WAD=AD	EVC2 = Limbin
Epidermodysplasia verruciformis	EVER1 EVER2	Epidermodysplasia verruciformis 1, 2	AR	Susceptible to HPV 3, 5, 8
Erythrokeratoderma variabilis (Mendes de Costa)	GJB3 GJB4	Connexin 31 Connexin 30.3	AD	GAP junction protein
Erythromelalgia	SCN9A/Nav1.7	Sodium channel, voltage-gated, type 9, subunit α	AD	
Fabry	GLA	α-galactosidase A	XLR	Lysosomal hydrolase; build up of glycosphingolipids in the body – ceramide trihexose
Familial dysautonomia (Riley-Day)	IKBKAP	Inhibitor of kappa light polypeptide gene enhancer in B cells, kinase complex-associated protein	AR	Ashkenazi Jews
Familial GIST with hyperpigmentation	C-KIT	= Mast cell growth/stem cell factor	AD	± mastocytosis; Activating mutations unlike piebaldism
Familial mediterranean fever	MEFV	Pyrin	AR	PMN inhibitor

Familial partial lipodystrophy 1 (Kobberling)	Unknown			
Familial partial lipodystrophy 2 (Dunnigan)	LMNA	Nuclear lamins A/C	AD	
Familial partial lipodystrophy 3	PPARG	Peroxisome proliferator-activated receptor-gamma		
Farber lipogranulomatosis	AC/ASAH	Acid ceramidase/*N*-acylsphingosine amidohydrolase	AR	Ceramide accumulates
Gardner	APC	Adenomatous polyposis coli	AD	Tumor suppressor, cleaves β-catenin
Gaucher	GBA	Acid-β-glucosidase	AR	Decreased glucocerebrosidase activity
Giant axonal neuropathy with curly hair	GAN1	Gigaxonin	AR	Protein degradation, neuronal survival
Glomuvenous malformations	GLMN	Glomulin	AD	
Griscelli 1	MYO5A	Myosin 5A	AR	Melanosome transport to keratinocytes
Griscelli 2	RAB27A	RAB27A	AR	Ras-related GTP-binding protein
Griscelli 3	MLPH MYO5A	Melanophilin Myosin 5A	AR	
Hailey–Hailey	ATP2C1	ATPase, Ca^{2+} transporting	AD	Calcium ATPase
Haim–Munk	CTSC	Cathepsin C	AR	Allelic to Papillon–Lefévre
Harlequin ichthyosis	ABCA12	ATP-binding cassette, subfamily A, member 12	AR	ABC transporter superfamily; Allelic to lamellar ichthyosis 2

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Disease	Gene	Protein		Comment
Hartnup	SLC6A19	System B(0) neutral amino acid transporter-1	AR	Failure to transport tryptophan; Pellagra-like photosensitive rash, cerebellar ataxia, emotional instability, and aminoaciduria
Hemochromatosis 1	HFE	Hemochromatosis	AR	Increased intestinal Fe absorption
Hemochromatosis 2A	HJV	Hemojuvelin	AR	Juvenile type
Hemochromatosis 2B	HAMP	Hepcidin antimicrobial peptide	AR	Juvenile type
Hemochromatosis 3	TFR2	Transferrin receptor 2	AR	
Hemochromatosis 4	SLC40A1	Ferroportin	AD	
Hereditary angioedema 1, 2	C1INH	C1 esterase inhibitor	AD	
Hereditary angioedema 3	F12	Coagulation factor 12	AD	
Hereditary hemorrhagic telangiectasia 1 (Osler–Weber–Rendu)	ENG	Endoglin	AD	TGF β-binding protein
Hereditary hemorrhagic telangiectasia 2	ALK1/ACVRL1	Activin receptor-like kinase	AD	TGF β receptor–like
Hereditary hemorrhagic telangiectasia with juvenile polyposis	SMAD4	Mothers against decapentaplegic, drosophila, homolog of, 4	AD	Tumor suppressor, intracellular TGFb receptor signal transducer
Hereditary lymphedema 1 (Nonne–Milroy)	FLT4	Vascular endothelial growth factor receptor 3 (VEGFR–3)	AD	Gene is FMS-like tyrosine kinase
Hereditary lymphedema 2 (Meige, late-onset, praecox)	MFH1/FOXC2	Forkhead box C2	AD	Transcription factor; allelic to lymphedema-distichiasis, lymphedema and ptosis, and lymphedema and yellow nail syndrome

Hermansky–Pudlak syndrome 1	HPS1, 3-8	Hermansky–Pudlak	AR	Lysosome, melanosome, and platelet dense body formation; HPS7=DTNBP1, HPS8=BLOC1S3
Hermansky–Pudlak syndrome 2	AP3B1	Adaptin β-3a subunit	AR	Type 2 has immunodeficiency
Hidrotic ectodermal dysplasia (Clouston)	GJB6	Connexin 30	AD	
Holt–Oram Syndrome (Heart–Hand)	TBX5	T-box 5	AD	Thumb anomaly and atrial septal defect
Homocystinuria	CBS	Cystathionine β-synthetase	AR	Condensation of homocystine and serine; homocystine builds up
Howel–evans syndrome (tylosis with esophageal cancer)	TOC	Tylosis with esophageal cancer	AD	
Hypereosinophilic syndrome	FIP1L1-PDGFRA fusion	Fusion of FIP1-like-1 and PDGF receptor-α		4q12 deletion; constitutively activated tyrosine kinase
Hyper-IgD	MVK	Mevalonate kinase	AR	Allelic to mevalonic aciduria
Hyper-IgE	STAT3 TYK2	Signal transducer and activator of transcription 3 Tyrosin kinase 2	AD	Downstream target of IL-6
Hyperlipoproteinemia Type 1A	LPL	Lipoprotein lipase	AR	Increased chylomicrons
Hyperlipoproteinemia Type 1B	APOC2	Apolipoprotein C2	AR	Increased chylomicrons
Hyperlipoproteinemia Type 2A	LDLR	Low-density lipoprotein receptor	AD	Familial hypercholesterolemia High LDL and cholesterol

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Disease	Gene	Protein		Comment
Hyperlipoproteinemia Type 2B	APOB	Apolipoprotein B-100	AD	Mutation in LDL receptor binding domain of this apoliprotein
Hyperlipoproteinemia Type 3 (dysbetalipoproteinemia)	APOE	Apolipoprotein E2	AR	Defective clearing of intermediate density lipoproteins and chylomicrons
Hypotrichosis with juvenile macular dystrophy	PCAD/CDH3	P-cadherin	AR	Membrane glycoprotein, calcium-dependent cell–cell adhesion; Allelic to ectodermal dysplasia, ectrodactyly, macular dystrophy, monilethrix-like
Hypotrichosis, localized, AR	DSG4 LIPH	Desmoglein 4 Lipase H	AR	Overlap with AR monilethrix
Hypotrichosis–lymphedema–telangiectasia	SOX18	SRY-box 18	AD, AR	HMG box-containing transcription factor
Hypotrichosis simplex	CDSN	Corneodesmosin	AD	Corneodesmosome component (desquamation of corneocytes), psoriasis susceptibility gene
Ichthyosis bullosa of Siemens	KRT2A	Keratin 2A (2e)	AD	Expressed in upper spinous layer with keratin 9
Ichthyosis hystrix Curth–Macklin	KRT1	Keratin 1	AD	Tonofibril defect, resembles EHK
Ichthyosis, lamellar 1	TGM1	Transglutaminase 1	AR	Abnormal epidermal cross-linking; Allelic to NCIE and self-healing collodion baby
Ichthyosis, lamellar 2	ABCA12	ATP-binding cassette, subfamily A, member 12	AR	ABC transporter superfamily; Allelic to harlequin ichthyosis

Ichthyosis vulgaris	FLG	Filaggrin	AD	
Ichthyosis, X–linked	STS	Aryl sulfatase C	XLR	Steroid sulfatase
Incontinentia pigmenti	NEMO	NF-κB essential modulator/IKK-gamma	XLD	Allelic to AED with immune deficiency ± osteoporosis and lymphedema
Immunodysregulation, polyendocrinopathy, and enteropathy, X-linked	FOXP3	Forkhead box P3	XLR	Forkhead family transcription factor
Insensitivity to pain, congenital, with anhidrosis	NTRK1	Neurotrophic tyrosine kinase receptor 1	AR	Signal transduction of nerve growth factor
Juvenile hyaline fibromatosis (systemic juvenile hyalinosis)	CMG2/ANTXR2	Capillary morphogenesis protein-2/ anthrax toxin receptor 2	AR	
Kallman 1	KAL1	Anosmin	XLR	
Kallman 2	KAL2 (FGFR1)	Fibroblast growth factor receptor 1	AD	
Keratosis palmoplantaris striata type 1 (Brunauer–Fohs–Siemens)	DSG1	Desmoglein 1	AD	Calcium-binding transmembrane desmosomal glycoprotein; PF antigen
Keratosis palmoplantaris striata type 2	DSP	Desmoplakin	AD	Desmosomal plaque protein, allelic to Carvajal, skin fragility–woolly hair, and lethal acantholytic EB
Keratosis palmoplantaris striata type 3	KRT1	Keratin 1	AD	Suprabasal expression

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Disease	Gene	Protein		Comment
KID syndrome (Keratitis–Ichthyosis–Deafness)	GJB2	Connexin 26	AD or AR	Allelic to Bart–Pumphrey and Classic Vohwinkel
Kindler	KIND1	Kindlin-1	AR	Focal contact for keratinocyte
Klippel–Trenaunay–Weber	VG5Q (AGGF1)	Angiogenic factor with G patch and FHA domains 1	Sp	This defect in some cases only
Leiomyomata, multiple cutaneous and uterine	FH	Fumarate hydratase	AD	Enzyme in Krebs cycle Defect also causes hereditary leiomyomatosis and renal cell ca
LEOPARD-1	PTPN11	Protein–tyrosine phosphatase, nonreceptor	AD	Same gene as Noonan-1
Leprechaunism	INSR	Insulin receptor	AR	Allelic to Rabson–Mendenhall
Lesch–Nyhan	HGPRT	Hypoxanthine guanine phosphoribosyltransferase	XLR	Purine salvage pathway
Lhermitte–Duclos	PTEN	Phosphatase and tensin homolog gene	AR	Allelic to Bannayan–Riley–Ruvalcaba and Cowden
Lipoid proteinosis	ECM1	Extracellular matrix protein 1	AR	Anti-ECM1 antibodies in lichen sclerosis
Loeys–Dietz	TGFβ R1,2	TGFβ receptors 1 and 2	AD	Marfan-like but short-arterial aneurysms and tortuosity, hypertelorism, bifid uvula, cleft palate
Lymphedema and ptosis, lymphedema-distichiasis, hereditary lymphedema 2	FOXC2 (MSH1)	Forkhead box C2	AD	Transcription factor

Mal de Meleda	SLURP1	Ly6/uPar-related protein 1	AR	Keratoderma palmoplantaris transgrediens
Marfan	FBN1	Fibrillin 1	AD	Elastic fibers fragmented
Marinesco–Sjögren	SIL1	BIP-associated protein (BAP)	AR, AD	Endoplasmic reticulum glycoprotein, interacts with BIP, involved in nucleotide exchange
McCune–Albright	GNAS1	Guanine nucleotide-binding protein alpha subunit	Som	Stimulates G protein, increases cAMP by regulating adenylate cyclase
Melanoma	CDKN2A CDK4 MC1R	Cyclin-dependent kinase inhibitor 2a Cyclin-dependent kinase 4 Melanocortin 1 receptor	AD	Hereditary melanoma; Defective MC1R cannot convert eumelanin to pheomelanin
Menkes Kinky hair syndrome	ATP7A	ATPase, Cu2+ transporting, alpha subunit	XLR	Allelic to occipital horn syndrome and X-linked cutis laxa Wilson disease = ATP7B
MIDAS	HCCS	Holocytochrome C synthase	XLD	Mitochondrial
Monilethrix	KRTHB1 KRTHB3 KRTHB6 DSG4	Keratin hair, basic 1, 3, and 6 Desmoglein-4	AD AR	Intermediate filaments; human hair keratins Hair shaft "blebs"
Muckle–Wells	CIAS1	Cryopyrin	AD	Allelic to chronic infantile neurologic cutaneous and artciular (CINCA) syndrome and familial cold autoinflammatory syndrome

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Disease	Gene	Protein		Comment
Mucopolysaccharidosis 1 (Hurler syndrome)	IDUA	α-L-iduronidase	AR	Build up of glycosaminoglycans due to lack of degradation
Mucopolysaccharidosis 2 (Hunter syndrome)	IDS	Iduronate 2-sulfatase	XLR	Build up of glycosaminoglycans due to lack of degradation
Muir–Torre	MLH1 MSH2	MutL homolog 1, colon cancer, nonpolyposis type 2 MutS homolog 2, colon cancer, nonpolyposis type 1	AD	DNA mismatch repair genes; also seen in Lynch cancer family syndrome (hereditary nonpolyposis colorectal cancer)
Multiple carboxylase deficiency	BTD HLCS	Biotinidase Holocarboxylase synthetase	AR	Decreased free serum biotin; metabolic acidosis
Multiple cutaneous and uterine leiomyomas	FH	Fumarate hydratase	AD	Krebs cycle enzyme
Multiple endocrine neoplasia 1 (Wermer)	MEN1	Menin	AD	Binds nuclear GUND
Multiple endocrine neoplasia 2a (Sipple), 2b	RET	Receptor tyrosine kinase	AD	Protooncogene, encodes a tyrosine kinase receptor
Multiple familial trichoepithelioma	CYLD	Cylindromatosis	AD	Same gene as Brooke–Spiegler tumor suppressor
Naegeli–Franceschetti–Jadassohn	K14	Keratin 14	AD	Allelic to EBS and dermatopathia pigmentosa reticularis; NFJ/DPR – mutations in nonhelical head (E1/V1) domain EBS – mutations in central alpha-helical rod domain
Nail–Patella	LMX1B	LIM homeobox transcription factor 1β	AD	

Naxos	JUP	Junction plakoglobin	AR	PPK with woolly hair and RV cardiomyopathy
Netherton	SPINK5 (LEKT1)	Serine protease inhibitor, Kazal-type 5	AR	Serine protease inhibitor
Neurofibromatosis 1	NF1	Neurofibromin	AD	Inhibits Ras; Allelic to NF-1-Noonan overlap syndrome, similar to NF1-like syndrome due to SPRED1 defects
Neurofibromatosis 2	NF2	Neurofibromin 2 (schwannomin, merlin)	AD	
Niemann–Pick disease A, B	SMPD–1	Sphingomyelin phosphodiesterase-1	AR	Sphingomyelinase deficiency
Niemann–Pick disease C1, D	NPC1	Niemann–Pick C1	AR	Cholesterol esterification
Niemann–Pick disease C2	NPC2/HE1	Niemann–Pick C2	Ar	Cholesterol binding
Noonan 1	PTPN11 (SHP2)	Protein tyrosine phosphatase, non-receptor type 11	AD, Sp	Allelic to LEOPARD-1
Noonan 3	KRAS	Kirsten rat sarcoma virus oncogene homolog	AD	Allelic to CFC and Costello
Noonan 4	SOS1	Son of sevenless, drosophila homolog		Guanine nucleotide exchange factor; Allelic to gingival fibromatosis
Noonan 5	RAF1	V-RAF-1 murine leukemia viral oncogen homolog 1	AD	Serine–threonine kinase, activates MEK1/2; Allelic to LEOPARD-2
Oculocutaneous albinism 1	TYR	Tyrosinase	AR	Melanin pathway

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Disease	Gene	Protein		Comment
Oculocutaneous albinism 2	P gene	Mouse pink-eyed dilution gene	AR	Regulation of melanosome pH
Oculocutaneous albinism, rufous and OCA 3	TYPR1	Tyrosinase-related protein 1	AR	Stabilizes tyrosinase
Omenn syndrome	RAG1 RAG2 DCLRE1C	Recombinase activating Artemis	AR	Omenn = SCID with hypereosinophilia; RAG1 and RAG2 mutations may also cause a more severe T-B-NK+ SCID; DCLRE1C mutations may also cause SCID with sensitivity to ionizing radiation
Orofaciodigital 1 (Papillon–Leage)	CXORF5	Chromosome X open reading frame 5	XLD	
Osteogenesis imperfecta I–IV	COL1A1 COL1A2	Collagen 1α1 Collagen 1α2	AD or AR	Allelic to Ehlers–Danlos 7
Pachyonychia congenita 1 (Jadassohn–Lewandowsky)	KRT6A KRT16	Keratin 6a Keratin 16	AD	Intermediate filaments; KRT16 mutations also associated with non-epidermolytic palmoplantar keratoderma (non-epidermolytic Unna–Thost)
Pachyonychia congenita 2 (Jackson–Lawler)	KRT6B KRT17	Keratin 6b Keratin 17	AD	Intermediate filaments; KRT17 version allelic to SCM
Palmoplantar keratoderma, epidermolytic (Vömer)	KRT9	Keratin 9	AD	Expressed in upper spinous layer
Palmoplantar keratoderma, non-epidermolytic (Unna–Thost)	KRT1 KRT16	Keratin 1 Keratin 16	AD	KRT1 mutations also associated with epidermolytic hyperkeratosis, BCIE, ichthyosis hystrix; KRT16 mutations also associated with PC1
Papillon–Lefèvre	CTSC	Cathepsin C	AR	Lysosomal protease; Allelic to Haim–Munk

Peutz–Jeghers	STK11	Serine threonine kinase 11	AD	Tumor suppressor
Phenylketonuria	PAH	Phenylalanine hydroxylase	AR	Phenylalanine and metabolites build up
Piebaldism	KIT SNAI2	C-KIT Snail, drosophila homolog of, 2	AD	Inactivating mutations; Protooncogene, tyrosine kinase Neural crest transcription factor
Popliteal pterygium	IRF6	Interferon regulatory factor 6	AD	Allelic to Van der Woude
Porphyria, acute intermittent	PBGD	Porphobilinogen deaminase	AD	PBGD also referred to as hydroxymethylbilane synthase (HMBS)
Porphyria, congenital erythropoietic (Gunther)	UROS	Uroporphyrinogen III synthase	AR	UROS also referred to as hydroxymethylbilane hydrolyase
Porphyria, hepatoerythropoietic	UROD	Uroporphyrinogen decarboxylase	AD	Cytosolic
Hereditary coproporphyria	CPOX	Coproporphyrinogen oxidase	AD	Mitochondrial gene
Erythropoietc protoporphyria	FECH	Ferrochelatase	AD/R	Mitochondrial gene
Porphyria cutanea tarda	UROD	Uroporphyrinogen decarboxylase	AD	Increased skin uroporphyrin causes photosensitivity to light at 400–410 nm
Porphyria, variegate	PPOX	Protoporphyrinogen oxidase	AD	Mitochondrial gene
Progeria (Hutchinson–Gilford)	LMNA	Lamin A	AD	Nuclear envelope

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Disease	Gene	Protein		Comment
Progressive Symmetric ErythroKeratodermia (PSEK)	LOR	Loricrin	AD	Allelic to Vohwinkel and EKV
Prolidase deficiency	PEPD	Peptidase D	AR	Splits iminodipeptides
Pseudofolliculitis barbae	K6hf	Keratin 6, hair follicle		Susceptibility gene
Pseudoxanthoma elasticum	ABCC6	ATP-binding cassette subfamily C, member 6	AR AD	Transmembrane transporter gene
Psoriasis	HLA-Cw6, IL-15, SLC12A8, IL-23/IL-23R, HLA-B17			Susceptibility genes
PXE-like syndrome	GGCX	Gamma-glutamyl carboxylase	AD/AR	Gamma-carboxylation of gla-proteins; associated with cutis laxa and coagulation defects
Pyogenic Arthritis–Pyoderma Gangrenosum–Acne (PAPA)	PSTPIP1	Protein–serine–threonine phosphatase-interacting protein 1	AD	
Refsum	PAHX PEX7	Phytanoyl Co-A Hydroxylase peroxin-7	AR > AD	Phytanic acid builds up Receptor targets enzymes to peroxisomes
Refsum, infantile form	PEX1 PEX2 PEX6	Peroxin-1, 2, and 6	AR	Deficient and impaired peroxisomes, severe defects cause Zellweger syndrome
Restrictive dermopathy	ZMPSTE24 (FACE-1) LMNA	Zinc metalloproteinase STE24, Lamin A	AR	
Richner–Hanhart (Tyrosinemia II)	TAT	Tyrosine aminotransferase	AR	Tyrosine accumulates in all tissues

Rothmund–Thomson (poikiloderma congenita)	RECQL4	RecQ protein-like 4	AR	DNA helicase
Rubinstein–Taybi	CREBBP EP300	CREB-binding protein E1A-binding protein, 300 kd	AD	CREB = cAMP response element-binding protein Transcriptional coactivators
SCID, X-linked	IL2Rγ	IL-2 receptor γ chain	XLR	T-B+NK-
SCID, autosomal recessive	ADA JAK3 IL7Rα CD3δ CD3ε CD3ζ CD45 ZAP-70	Adenosine deaminase Janus kinase 3	AR	T-B-NK- T-B+NK- T-B+NK+ T-B+NK+ T-B+NK+ T-B+NK+ T-B+NK+ T-B+NK+
SCID with sensitivity to ionizing radiation	DCLRE1C	DNA cross-link repair 1C (Artemis)	AR	T-B-NK+ Allelic to Omenn
SCID, T-B-NK+	RAG1 RAG2	Recombinase-activating gene	AR	Allelic to Omenn
Self-healing collodion baby	TGM1	Transglutaminase	AR	Allelic to lamellar ichthyosis 1 and NBCIE
Sjögren–Larssen	ALDH3A2	Fatty aldehyde dehydrogenase	AR	
Steatocystoma multiplex	KRT17	Keratin 17	AD	In pachyonychia congenita 2
Systemic sclerosis	CTGF	Connective tissue growth factor	AR	Polymorphism in promoter region

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Disease	Gene	Protein		Comment
T-cell immunodeficiency, congenital alopecia, and nail dystrophy	FOXN1 (WHN)	Forkhead box N1	AR	Transcription factor
Takahara (Acatalasemia)	CAT	Catalase	AR	
Tangier	ABCA1/CERP	ATP-binding cassette A1/Cholesterol efflux regulatory protein	AR	Allelic to familial HDL deficiency (which may also result from apolipoprotein A-1 mutations)
Thrombotic thrombocytopenic purpura, congenital (Schulman–Upshaw)	ADAMTS13/ VWFCP	von Willebrand factor-cleaving protease	AR	
Tietz (Albinism–Deafness)	MITF	Microphthalmia-associated transcription factor	AD	Allelic to Waardenberg 2A
TNF Receptor-Associated Periodic fever (TRAPS)	TNFRSF1A	TNF receptor 1	AD	
Trichodentoosseous	DLX3	Distal-less homeobox 3	AD	
Trichorhinophalangeal 1 and 3	TRPS1	Trichorhinophalangeal syndrome 1	AD	Putative transcription factor
Trichorhinophalangeal 2	Continuous TRPS1 and EXT1 deletion	TRP1 and Exostosin	AD	TRP1 with multiple exostoses
Trichothiodystrophy (PIBIDS)	ERCC2 (XPD) ERCC3 (XPB)	Excision repair cross-complementing rodent repair deficiency, complementation groups 2 and 4	AR	ERCC2 same as XP group D; DNA helicase; most cases caused by mutations in XPD, a subunit of transcription factor IIH
TTD, non-photosensitive 1 (TTDN1/BIDS)	TTDN1/ C7ORF11	Chromosome 7 open reading frame 11	AR	

Ullrich, congenital scleroatonic muscular dystrophy	COL6A1/2/3	Collagen VI	AR	
Tuberous sclerosis	TSC1 TSC2	Hamartin Tuberin	AD	GTPase-activating protein domain
Van de Woude	IRF6	Interferon regulatory factor 6	AD	Allelic to popliteal pterygium
Vitiligo, associated autoimmune/inflammatory conditions	NALP1	NACHT leucine-rich-repeat protein 1	AD	Regulator of the innate immune system; SNPs related to susceptibility
Vohwinkel syndrome, variant form (mutilating keratoderma with ichthyosis)	LOR	Loricrin	AD	Cornified cell envelope component; Allelic to PSEK
Vohwinkel syndrome, classic, with deafness	GJB2	Connexin 26	AD	Allelic to Bart–Pumphrey and KID
Von–Hippel Lindau Syndrome	VHL	von Hippel–Lindau	AD	Tumor suppressor gene
Waardenburg 1	PAX3	Paired box gene 3	AD	Transcription factor, activates MITF promoter; dystopia
Waardenburg 2A	MITF	Microphthalmia-associated transcription factor		Transactivates tyrosinase gene, no dystopia; Allelic to Tietz (Waardenburg 2D is due to SNAI2)
Waardenburg 3 (Klein–Waardenburg)	PAX3	Paired box gene 3	AD, AR	
Waardenburg 4 (Waardenburg–Shah)	EDNRB EDN3 SOX10	Endothelin receptor B Endothelin 3 SOX10	AD	Involved in neural crest cell migration; Endothelin 3 is a ligand for endothelin B receptor; SOX 10 is a transcription factor, activates MITF promoter

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Disease	Gene	Protein		Comment
Watson	NF-1	Neurofibromin	AD	Café-au-lait macules with pulmonic stenosis, ~ to NF-1
Werner	RECQL2 LMNA	RecQ protein-like 2 Nuclear lamin A/C	AR	DNA helicase enzyme Lamin defect – severe phenotype
White sponge nevus (Cannon)	KRT4 KRT13	Keratin 4 Keratin 13	AD	
Wilson	ATP7B	ATPase, Cu2+ transporting, beta subunit	AR	Defect in copper transport and biliary excretion of copper
Wiskott–Aldrich	WAS	Wiskott Aldrich syndrome protein	XLR	Binds GTPase and actin
Witkop	MSX1	Muscle segment, homeobox, drosophila, homolog of, 1	AD	
Xeroderma pigmentosum		XPA-DDB1 (DNA damage binding protein) XPB-ERCC3 (excision repair cross-complementing) XPC-Endonuclease XPD-ERCC2 XPE-DDB2 XPF-ERCC4 XPG-Endonuclease XPV-Polymerase	AR	

X-linked dominant: Incontinentia Pigmenti, Goltz, CHILD, MIDAS, OFD–1, Conradi-Hunermann, Bazex

X-linked recessive: Chad's Kinky Wife

CGD, Hunter, Anhidrotic Ectodermal Dysplasia, Dyskeratosis Congenita, SCID, Kinky (Menkes, Cutis Laxa, Occipital Horn), Wiskott-Aldrich, Ichythosis X-linked, Fabry, Ehlers–Danlos 5,9; Also: Bruton's Agammaglobulinemia, Chondrodysplasia Punctata 1, Kallman 1, Lesch-Nyhan, X-linked SCID (IL2Rγ).

Chromosome abnormalities

Syndrome	Chromosome
Cri du Chat	5p-
Down	Trisomy 21
Edwards	Trisomy 18
Hypomelanosis of Ito	Various
Klinefelter	X aneuploidy – i.e., XXY
Pallister–Killian	Mosaic tetrasomy 12p
Patau	Trisomy 13 (Phyloid pigmentation = mosaic trisomy 13)
Turner	XO monosomy
Warkany	Mosaic Trisomy 8 (nail/patella dysplasia)

Tumors

Tumor	Gene	Protein	Comment
Anaplastic large cell lymphoma, primary systemic	NPM-ALK fustion	Nucleophosmin-anaplastic lymphoma kinase fusion protein	T(2:5)(p23;q35); ALK+ systemic anaplastic large cell lymphomas have better prognosis than ALK neg systemic large cell lymphomas (primary cutaneous cases are ALK neg)
Basal cell carcinoma	PTCH2	Patched	Somatic and BCNS
Clear cell sarcoma	EWS-ATF1	Fusion of Ewing sarcoma and activating transcription factor 1	a.k.a. "malignant melanoma of the soft parts"
Dermatofibrosarcoma protuberans	COL1A PDGF	Collagen 1A Platelet-derived growth factor	t(17;22)(q22;q13), may have supernumerary ring chromosome
Hypereosinophilia syndrome	FIP1L1-PDGFRA	F/P fusion	~chronic eosinophilic leukemia
Mantle cell lymphoma	T(11;14)	Fusion of Bcl-1/Cyclin D1 and immunoglobulin heavy chain	
Mastocytosis	KIT	C-kit	Adult but not childhood forms
Melanoma*	CDKN2A/p16-INK4A/p14-ARF, BRAF, KIT, NRAS, MITF, PTEN, AKT, MC1R, APAF-1		BRAF often mutated in melanoma and benign melanocytic nevi but unusual in Spitz nevi (similar to NRAS but reverse w/ HRAS); BRAF and NRAS mutations are reciprocal; BRAF phosphorylates ERKs/MAPKs; MC1R mutations impair cAMP synthesis; p16-INK4A inhibits Rb; p14-ARF inhibits p53 degradation

Merkel cell carcinoma	Trisomy 6		
Mycosis fungoides	CDKN2A, TNFRSF6 (Fas), JUNB		
Pilomatricoma	CTNNB1	B-catenin	Activating mutation; wnt signaling pathway
Seborrheic keratosis	FGFR3, PIK3CA	FGF receptor 3, phosphatidylinositol kinase 3, catalytic, alpha	Same genes as epidermal nevi
Spitz nevi	11p amplifications	HRAS	Minority of Spitz have HRAS mutations, but much more often than in melanoma

* Melanomas from skin *without* chronic photodamage – BRAF and NRAS mutations but nl CDK4 and CCND1 vs. melanomas from skin *with* chronic photodamage – increase in number of CDK4 and CCND1 but nl BRAF and NRAS vs. melanomas from *non-sun-exposed* skin (acral, mucosal) – KIT mutations but nl BRAF and NRAS; Acral MMs have higher degrees of chromosomal aberrations; p53 mutations uncommon in MM except LMM or MM associated with XP-C or Li-Fraumeni.

Genodermatoses

Disorders of cornification

Ichthyosis

Ichthyosis vulgaris: Onset: infancy, gray-brown, erythematous scales, may spare flexures and face, atopy, KP, hyperlinear palms, decreased stratum granulosum. AD, Filaggrin defects. (Mutated filaggrin is also a risk factor for atopic dermatitis and associated with disease severity. Among patients with atopic dermatitis, mutated filaggrin is associated with asthma, allergic rhinitis, and allergic sensitization. However, mutated filaggrin is not independently associated with asthma. Mutated filaggrin is not associated with psoriasis or KP. Among patients with alopecia areata, filaggrin mutations predict more severe courses.)

X-linked ichthyosis: Onset: third to sixth month (never collodion baby!), widespread, dirty, brown scales, dirty face, may spare flexures, delayed parturition, comma-shaped/flower-like (pre-Descemet) corneal opacities in posterior capsule, cryptorchidism, if broad deletion → hypogonadotropic hypogonadism with anosmia (Kallman) or chondrodysplasia punctata, neither hyperlinear palms nor KP, low maternal serum unconjugated estriol during pregnancy screening. XLR, steroid sulfatase defects.

Lamellar ichthyosis: Collodion baby, ectropion, eclabion, everted ears, plate-like scale, PPK, erythroderma, phalangeal reabsorption, rickets in severe cases. AR, TGM1, ABCA12, FLJ39501/CYP4F2 defects.

Congenital ichthyosiform erythroderma/nonbullous CIE: Subtype of lamellar ichthyosis. AR, TGM1, ALOXE3, ALOX12B, CGI58/ABHD5, Ichthyin defects.

Bullous CIE/epidermolytic hyperkeratosis: Rapidly resolving collodion baby → diffuse erythema, scale, bullae, erosions, acantholysis, "gothic church" hyperkeratosis. AD, KRT1 or 10 defects.

Icthyosis bullosa of Seimens: Collodion-like → superficial, rippled hyperkeratosis, erosions, bullae in early childhood, PPK, mauserung = oval desquamation, minimal erythema. AD, KRT2e defects.

Harlequin fetus: Massive hyperkeratosis, deep fissures, ectropion, eclabium, necrotic phalanges, absent lamellar granules, fatal without high-dose retinoids. AR, ABCA12 defects.

Netherton: Collodion baby, erythroderma, ichthyosis linearis circumflexa (serpiginous, double-edged, migratory erythema), atopy, trichorrhexis invaginata, asthenia. AR, SPINK5/LEKT1 defects.

Refsum: IV-like ichthyosis, retinitis pigmentosa, peripheral neuropathy, cerebellar ataxia, nerve deafness, ECG abnormalities/arrhythmias, yellow nevi, increased tissue and plasma phytanic acid, Tx: eliminate dietary chlorophyll (animal fat/phytol, green vegetables/phytanic acid) and avoid rapid loss of weight (releases phytanic acid). AR, PAHX or PEX7 defects.

Rud: Ichthyosis, hypogonadism, short stature, MR, epilepsy, retinitis pigmentosa.
Sjögren–Larsson: Onset: birth or early infancy, generalized, pruritic ichthyosis, spastic paralysis, MR, szs, degenerative retinitis, maculopathy (white macular dots), AR, FALDH defects.
CHILD: Congenital hemidysplasia, icthyosiform erythroderma, Limb Defects, >2/3 in females, cardiovascular (main cause of death), CNS and renal defects, 2/3 right-sided involvement. XLD, NSDHL defects.
Conradi–Hunerman/XLD chondrodysplasia punctata: Collodion-like presentation, large scale, ichthyosiform erythroderma in Blaschko lines → follicular atrophoderma ± hypo/hyperpigmentation, flat face, linear alopecia, stippled epiphyses, asymmetric limb shortening, scoliosis, hip dysplasia, eye abnormalities. XLD, EBP defects.
KID: Keratitis, ichthyosis, deafness, spiny hyperkeratosis, sparse hair, absent eyelashes, follicular plugging, onychodystrophy, hypohidrosis, limbal stem cell deficiency, SCC. AD, GJB2/Connexin 26 defects.
Erythrokeratoderma variabilis/Mendes de Costa: Erythematous, hyperkeratotic, well-demarcated plaques in bizarre geographic, figurate distributions with daily variations. AD, defects: GJB3/Connexin 31 and GJB4/Connexin 30.3.
Icthyosis follicularis with atrichia and photophobia: Alopecia, non-erythematous, follicular keratoses, atopy, epilepsy, recurrent respiratory infections, corneal vascularization, blindness, retinal vascular tortuosity.
Lipoid proteinosis: Skin and mucous membrane infiltrated with hyaline-like material, weak cry/hoarseness as infant, bullae, pustules, crusts, pitted scars, verrucous plaques on elbows and knees, sickle/bean-shaped calcification of temporal lobes, szs. AR, ECM1 defects.
Dorfman–Chanarin/neutral lipid storage disease with ichthyosis: Lamellar ichthyosis, MR, cataracts, lipid vacuoles in circulating leukocytes (Jordans' anomaly). AR, CGI58/ABHD5 defects.
Acquired ichthyosis: Neoplastic (Hodgkins, multiple myeloma, MF), autoimmune (sarcoid, dermatomyositis, GVHD, SLE), drugs (nicotinic acid, corticosteroids), infections (HIV, leprosy), endocrine (hypothyroidism, hyperparathyroidism), metabolic (chronic liver or kidney disease).
Ichthyosis hystrix – Curth Macklin: AD, KRT1 defects.
Epidermal nevus syndrome: Sporadic, linear whorled verrucous plaques, MR, szs, hemiparesis, deafness, ocular defects (lipodermoids, colobomas, corneal opacities), scoliosis, rickets, syringocystadenoma papilliferum, Wilm's tumor, astrocytoma.
Pityriasis rotunda: Circular, hypopigmented, hyperkeratotic plaques, confluent and geometric, AD, South Africa, Sardinia, Japan, Type 1: Asians, Blacks, hyperpigmented, older, malignancies (hepatic), Type 2: Whites, hypopigmented, younger.
Multiple minute digitate hyperkeratosis: Minute keratotic spikes on extremities and trunk.

Ulerythema ophryogenes/KP atrophicans facei: Erythematous, follicular papules with scarring alopecia, KP, atopy, woolly hair, AD, loss of lateral 1/3 eyebrows, seen in: Noonan, CFC, IFAP.
Atrophoderma vermiculatum: Reticular atrophy on cheeks, AD, may be seen in: Rombo, Nicolau–Balus (+ eruptive syringoma and milia) (atrophoderma vermiculatum is similar to atrophia maculosa varioliformis cutis of Tuzun).
Self-healing collodion baby: AR, TGM1 defects.
Collodion baby: Most often: lamellar or NBCIE; others: Sjögren–Larsson, Dorfman–Chanarin, EHK, self-healing, TTD, Netherton, ectodermal dysplasias.

Keratodermas

Inherited Keratoderma

Transgrediens	Clouston, Mal de Meleda, Olmsted, Papillon–LeFevre, Greither
Non-transgrediens	Unna–Thost, Vorner, Howel–Evans

Unna–Thost/non-epidermolytic PPK: Thick, yellow, well-demarcated PPK, non-transgrediens, hyperhidrosis. AD, KRT1 or 16 defects.
Vorner/epidermolytic PPK: Resembles Unna–Thost, non-transgrediens, may blister, EH on histopath. AD, KRT9 defects.
Olmsted: Periorificial plaques, thick, transgrediens PPK, mutilating, pseudoainhum, leukokeratosis.
Papillon-LeFevre: Transgrediens PPK, periodontitis, can involve knees/elbows, calcified dura mater and falx cerebri, pyogenic liver abscesses. AR, Cathepsin C defects.
Haim–Munk: PPK, periodontitis, onychogryphosis, arachnodactyly. AR, Cathepsin C defects.
Vohwinkel: Honeycomb hyperkeratosis, pseudoainhum, starfish keratoses, scarring alopecia. AD, GJB2/Connexin 26 (Classic with Deafness) or Loricrin (Mutilating Variant with Ichthyosis) defects.
Bart–Pumphrey: Knuckle pads, leukonychia, deafness. AD, GJB2/Connexin 26.
Mal de Meleda: Glove and sock PPK, transgradiens, hyperhidrosis, pseudoainhum, onychodystrophy, high-arched palate. AR, SLURP1 defect.
Acrokeratoelastoidosis of Costa: Asymptomatic, firm, translucent papules on lateral acral margins, starts at puberty, uncommon and controversial association with scleroderma, AD but F>M, if elastorrhexis is absent on biopsy then dx = focal acral hyperkeratosis, DDx includes keratoelastoidosis marginalis (due to chronic sun exposure and trauma).
Howel–Evans: Tylosis, blotchy PPK, non-transgrediens, esophageal CA, soles>palms. AD, TOC defects.
Carvajal: PPK, woolly hair, LV cardiomyopathy. AR, Desmoplakin defects.
Naxos: PPK, woolly hair, RV cardiomyopathy. AR, Plakogobin defects.
Richner–Hanhart: Tyrosinemia Type 2, painful PPK, weight bearing surfaces, plaques on elbows/knees, leukokeratosis, MR, corneal ulceration. AR, tyrosine aminotransferase defects.

Symmetric progressive erythrokeratoderma/Gottron: Non-migratory, hyperkeratotic, erythematous plaques, favors extremities and buttocks, PPK, pseudoainhum. AD, Loricrin defects.
Huriez: Scleroatrophy, sclerodactyly, PPK, nail hypoplasia, nasal poikiloderma, lip telangiectasia, hypohidrosis, fifth finger contractures, SCC, bowel cancer, AD.
Punctate palmoplantar keratoderma/Buschke–Fischer–Brauer: Keratotic plugs, may be limited to palmar creases, AD.
Disseminated superficial actinic porokeratosis (DSAP): 3rd–4th decade, F>M, lowest risk of malignant transformation among the porokeratosis syndromes (except punctate variety which has no risk; linear and long-standing lesions have the greatest risks). AD, SART3 defects.

Acquired Keratoderma

Keratoderma climactericum: Pressure bearing acral area, peri-menopausal, may represent psoriasis.
Porokeratosis plantaris discreta: Painful, sharply marginated, rubbery nodules on weight bearing surface, adult females, SCC.

Acantholytic Disorders

Darier: Dirty, malodorous papules on face, trunk, flexural, punctate keratosis on palms/soles, V-shaped nicking, red/white nail bands, mucosal cobblestoning, guttate leukoderma, schizophrenia, MR. AD, ATP2A2/SERCA2 defects.
Acrokeratosis verruciformis of Hopf: Verrucous papules on dorsal hands/feet, punctate pits on palms/soles, onychodystrophy. AD, ATP2A2 defects.
Hailey–Hailey/benign familial chronic pemphigus: Vesicles, crust, erosions in intertriginous areas, begins in adolescence. AD, ATP2C1 defects.
Peeling skin syndrome/keratolysis exfoliativa congenita: Exfoliation and scale ± erythema and pruritus, esp. palms/soles, AR.

Disorder of hair, nail, ectoderm

Hair

Trichothiodystrophy: Sulfur (cystine, cysteine)-deficient brittle hair, tiger-tail polarizing, trichoschisis, absent cuticle, immunodeficiency, osteosclerosis; PIBIDS: Photosensitivity, ichthyosis, brittle hair, decreased intellect, decreased fertility, short. AR, defects in ERCC2/XPD, ERCC3/XPB, TFB5 – all TFIIH subunits – and TTDN1/C7ORF11 (non-photosensitive TTD).
Marinesco–Sjögren: TTD + neonatal hypotonia, cerebellar ataxia, congenital cataracts, MR, thin brittle nails, short, hypogonadism, myopathy, chewing difficulties. AR, SIL1 defects.
Hallermann–Streiff: Beaked nose, microphthalmia, micrognathia, mandibular hypoplasia, dental abnormalities, congenital cataracts, hypotrichosis (following cranial sutures), dwarfism.
Klippel–Feil: Low posterior hairline, short webbed neck, fused cervical vertebra, scoliosis, renal anomalies, hearing impairment, torticollis, cardiac septal defects, cleft palate, increased in females, AD or AR.

Pili Torti: Twisting, brittle hair, AD, syndromes: Menkes, Bjornstad, Crandall, TTD, hypohidrotic ED, Bazex, anorexia nervosa, Laron.
Bjornstad: Deafness, pili torti. AD, BCS1L defects.
Crandall: Deafness, hypogonadism, pili torti.
Citrullinemia: Pili torti, periorificial dermatitis. AR, defects: Argininosuccinate synthetase or SLC25A13.
Menkes: Steel wool-like hair, pili torti, monilethrix, trichorrexis nodosa, epilepsy, hypothermia, decreased copper and ceruloplasmin. XLR, ATP7A defects.
Uncombable hair: AR, spun glass hair, longitudinal groove, pili canaliculati et trianguli.
Monilethrix: Beaded hairs, dry, fragile, sparse, KP, brittle nails. AD or AR: type 2 hair keratins KRTHB1, 3, or 6 defects (AD), Desmoglein-4 (AR).
Trichorrexis nodosa: Arginosuccinic aciduria (red fluorescence of hair), citrullinemia, Menkes, TTD, Netherton, isotretinoin, hypothyroidism, physical/chemical trauma, proximal in Blacks and genetic forms vs. distal in Whites and Asians.
Trichorrexis invaginata: Bamboo hair, Netherton.
Pili annulati: Ringed hair, spangled, alternating bands (light bands to the naked eye = dark bands on light microscopy = air-filled cavities within the cortex of the hair shaft), associated with alopecia areata, AD.
Woolly hair: Onset: birth, "Afro in a non-African," Associations: KP, PPK, facial dysmorphism, skin fragility, neuropathy, osteoma cutis, diarrhea, ulerythema ophryogenes; DDx: Noonan, CFC, Trichodento-osseous, CHANDS, woolly hair nevus, Carvajal, Naxos.
Acquired progressive kinking of the hair (APKH): Rapid, adolescent onset, curly, lusterless, frizzy hair, frontotemporal and vertex, may evolve into androgenetic alopecia.
Localized hypertrichosis: Becker nevi, casts, POEMS, pretibial myxedema, cubiti, auricle.
Generalized congenital hypertrichosis/hypertrichosis lanuginosa: "Werewolf," curly hairs, sparing palms/soles and mucosa, X-linked.
Congenital temporal triangular alopecia: Onset: birth to 6 years old, uni- or bilateral, nl number of follicles but all vellus AD.
Kinky hair: Menkes, woolly hair syndromes, woolly hair nevus, pili torti syndromes, pseudomonilethrix, uncombable hair, APKH, Tricho-Dento-Osseous, oral retinoids.
GAPO: Growth retardation, alopecia, pseudoanodontia, optic atrophy, cranial defects, frontal bossing, umbilical hernia, muscular appearance, renal abnormalities.
Cantu: Congenital hypertrichosis, osteochondrodysplasia, cardiomegaly, MR, short stature, macrocranium, hypertelorism, cutis laxa, wrinkled palms and soles, joint hyperextensibility, AD.

Keratosis Follicularis Spinulosa Decalvans: Corneal dystrophy, photophobia, KP (becomes atrophicans), cicatricial alopecia (scalp, eyebrows), PPK, atopy, aminoaciduria, XLR.
Atrichia with Papular Lesions: Atrichia, milia, hypopigmented scalp streaks. AR, Hairless defects (Hereditary Vitamin D-dependent Rickets may be identical + hypocalcemia, hyperparathyroidism, osteomalacia, rickets).

Hair color

PKU: Blonde hair.
Homocystinuria: Bleached hair.
Menkes: Light hair.
Chediak–Higashi, Griscelli, Elajalde: Silvery hair.
Fe deficiency: Segmental heterochromia (Canities segmentata sideropaenica).
Early graying: Familial, Hutchinson–Gilford, Werner, Book syndrome (premolar aplasia, hyperhidrosis, and canities premature).
Gray patches: Piebaldism, Vitiligo, Vogt–Koyanagi–Harada, NF1, Tietze, Alezzandrini, TS.

Nail and oral disorders

Pachyonychia congenita: Type 1 (Jadassohn–Lewandowsky): Thickened nails, yellow, pincer nails, PPK, follicular keratosis on elbows/knees, oral leukokeratosis, Type 2 (Jackson–Sertoli): 1 + steatocystoma multiplex, PPK may blister, hyperhidrosis, natal teeth, Type 3: 1 + 2 + ocular lesions, cheilosis, Type 4: 1 + 2 + 3 + thin, sparse hair, MR, laryngeal involvement. AD, Defects: KRT6A and 16 (Type 1), KRT6B and 17 (Type 2).
Dyskeratosis congenita/Zinsser–Cole–Engman: Nail thinning, longitudinal ridging, oral leukokeratosis (premalignant), neck – poikiloderma vasculare atrophicans, thin hair, hands/feet: dorsal atrophy/ventral hyperkeratosis, epiphora, aplastic anemia, caries, defects: DKC1 (XLR), TERC (AD) (**Hoyeraal–Hreidarsson** – DC + cerebellar hypoplasia)
Nail-patella: Hypo- or anonychia, triangular lunula, absent/hypoplastic patella, luxation, posterior iliac horns, renal dysplasia, GU anomalies, Lester iris. AD, LMX1B defects.
Iso–Kikuchi/COIF: Congenital Onychodysplasia of the Index Finger, brachydactyly, short hands, inguinal hernia, digital artery stenosis, AD.
Yellow nail: Yellow nails, lymphedema, pleural effusions, bronchiectasis. AD, FOXC2/MFH1 defects.
Naegeli–Franceschetti–Jadassohn: Hyperkeratotic nails with congenital malalignment, reticulate pigmentation (axillae, neck), punctate PPK, enamel hypoplasia, hypohidrosis abnormal dermatoglyphics. AD, KRT14 defects.
Cannon: White sponge nevus, not premalignant. AD, KRT4 and 13 defects.

Oral–facial–digital-1/Papillon–League: Bifid tongue, accessory frenulae, cleft palate/lip, lip nodules, milia, alopecia, dystopia canthorum, syndactyly, brachydactyly, CNS anomalies, polycystic kidneys. XLD, CXORF5/OFD1 defects.
Rubinstein–Taybi: MR, broad thumbs/great toes, hypertrichosis, high-arched palate, crowded teeth, beak nose, heavy eyebrows, capillary malformations, keloids, pilomatricomas (multiple pilomatricomas also reported with Steinert myotonic dystrophy, Turner, sarcoidosis), cardiac abnormalities. AD or AR, CREBBP or EP300 defects.
Cooks: Anoncyhia-onychodystrophy (fingers and toes) absent or hypoplastic distal phalanges, AD.

Ectodermal dysplasia

Hidrotic ectodermal dysplasia/Clouston: Hypotrichosis, nail dystrophy, keratoderma, normal teeth, normal sweating. AD, GJB6/Connexin 30 defects.
Hypohidrotic/anhidrotic ectodermal dysplasia/Christ–Siemens–Touraine: Heat intolerance 2/2 decreased or absent sweating, hypodontia, fine sparse hair, brittle nails, thick lips, saddle nose, sunken cheeks, frontal bossing, depressed cell mediated immunity, elevated IgE, rhinitis, no smell or taste, salivary abnormalities, decreased pulmonary/GI secretions, xerosis, eczema. XLR: EDA, AD: EDAR, AR: EDAR, EDARADD.
Hypohidrotic ectodermal dysplasia with immunodeficiency ± osteoporosis and lymphedema: AR, NEMO defects.
Witkop/tooth-and-nail: Onychodystrophy, toenails > fingernails, retained primary dentition. AD, MSX1 defects.
Tricho-Dento-Osseous: Whitish, curly hair, brittle nails, xerosis, dental pitting, taurodontism, tall. AD, DLX3 defects.
Ellis–Van Creveld–Weyers/acrodental dysostosis: Hypoplastic nails, sparse hair, dwarfism (short distal extremities), cone-shaped epiphyses (hand), natal teeth, septal heart defects.
P63 complex: EEC, AEC, Rapp-Hodgkin, Limb-Mammary type 4, ADULT, all are AR.
Ectrodactyly–ectodermal dysplasia–clefting/EEC: Lobster claw deformity, ectodermal dysplasia, sparse wiry blond hair, peg-shaped teeth, dystrophic nails, cleft lip, lacrimal duct defects.
Ankyloblepharon–ectodermal dysplasia–clefting/AEC: Ankyloblepharon, ectodermal dysplasia, clefting, chronic erosive dermatitis – esp. scalp, patchy alopecia, hypotrichosis, lacrimal duct defects, hypospadias, includes CHAND syndrome.
Rapp–Hodgkin: Ectodermal dysplasia, clefting, onychodysplasia, dry wiry hair, hypodontia, hypospadias.
Limb–Mammary Type 4: Aplastic nipples/mammary glands, limb defects, onychodysplasia, MR, hair defects.
Acral–dermato–ungual–lacrimal–tooth/ADULT: Ectrodactyly, freckling, onychodysplasia, lacrimal duct defects, hypodontia.

Ectomesodermal dysplasia

Goltz: Cribiform fat herniations in Blaschko lines, perinasal red papules, papillomas in genital and folds, mosaic hypohidrosis, onychodysplasia, scarring alopecia, syndactyly, eye defects, delayed dentition, osteopathia striata, coloboma. XLD, PORCN defects.

MIDAS: Microphthalmia, dermal aplasia, sclerocornea, linear atrophic Blaschkonian plaques, MR, coloboma, strabismus, CNS lesions, cardiac defects. XLD, Holocytochrome C Synthase/HCCS defects.

Phakomatosis

TS: Angiofibromas, angiomyolipomas, shagreen patch, Koenen tumors, ash leaf macules, CALM, lymphangioleiomyomatosis, dental pitting, cardiac rhabdomyomas, phalangeal cysts, retinal gliomas, szs, gingival fibromas, brain calcifications, molluscum pendulum. AD, TSC-1 (Hamartin) and TSC-2 (Tuberin) defects.

NF1: Diagnosis – At least 2 of: >6 CALM, >2 neurofibromas or 1 plexiform neurofibroma, axillary/inguinal freckling, optic glioma, first degree relative, Lisch nodules, winged sphenoid, pheochromocytoma (1% of pts). AD, Neurofibromin defects.

NF2: Neurofibromas, bilateral acoustic neuromas, schwannomas, posterior supcapsular lenticular opacity. AD, Merlin defects.

NF-Noonan overlap: AD, Neurofibromin defects.

SPRED1 NF-1-like syndrome: Axillary freckling, CALM, macrocephaly, Noonan-like appearance. AD, SPRED1 defects.

Craniofacial abnormalities

Treacher Collins: Mandibulofacial dysostosis, downward eyes, lid coloboma, ear anomalies, NL intelligence. AD, TCOF1 defects.

Beare–Stevenson cutis gyrata: Craniosynostosis, cutis gyrata, AN, ear anomalies, anogenital anomalies, acrochordons, prominent umbilical stump. AD, FGFR2 defects.

Apert: Craniosynostosis, craniofacial anomalies, severe syndactyly, acneiform lesions, hyperhidrosis, 10% cardiac defects, 10% GU anomalies. Sporadic, FGFR2 defects.

Crouzon: Craniosynostosis, hypertelorism, parrot nose, exophthalmos. AD, FGFR2 defects.

Crouzon with acanthosis nigricans: AD, FGFR3 defects.

Cornelia/Brachmann de Lange: Synophrys, hirsutism, low hairline, MR, heart defects, thin lips, small nose, low-set ears, livedo reticularis/cutis marmorata, small hands and feet, cryptorchidism/hypospadias. Defects: NIPBL (AD), SMC1L1 (XL), or SMC3 (mild, AD) – all in cohesin complex.

Costello: Cutis laxa-like skin, verruca-like papillomas (face, anus, axillae), acrochordons, AN, PPK, coarse facies, macroglossia, hypertelorism, broad nasal root, thick lips, onychodystrophy, hyperextensible fingers, short

stature, malignancies (bladder, neuroblastoma, rhabdomyosarcoma), nevi, must distinguish from Noonan and CFC. AR, HRAS or KRAS defects.
Trichorhinophalangeal: Sparse brittle hair, pear-shaped nose, long philtrum, brachyphalangia, cone-shaped digital epiphysis, crooked fingers, short, brittle nails, short, loose skin, cartilaginous exostoses. AD, defects: Types 1 and 3: TRPS1; Type 2: continuous TRPS1 and EXT1 deletion.
Goldenhar/oculoauriculovertebral dysplasia/hemifacial microsomia: Extraauricular appendage, choristoma, eyelid coloboma, cervical vertebral abnormalities, cardiac defects.
Nevus sebaceous syndrome: Linear NS, szs, CNS abnormalities, coloboma, skeletal defects.
Noonan: Mimics Turner, acral lymphedema, nevi, hypertelorism, low-set ears, coarse curly hair, low posterior hairline, broad/webbed neck, KP atrophicans, ulerythema ophryogenes, short stature, chest deformities, heart defects, bleeding diathesis. AD, PTPN11/SHP2, KRAS, SOS1 defects.
Cardio-facio-cutaneous: Sparse/absent eyelashes, KP, low posterior hairline, ichthyosis, palmoplantar hyperkeratosis, sparse curly hair, short neck, pulmonary stenosis, AV septal defects, short stature, similar to Noonan. AD, KRAS, BRAF, MEK1, MEK2 defects.
Fanconi anemia: Pancytopenia, diffuse hypo/hyperpigmentation, CALMs, absent thumbs and radius (~40%), retinal hemorrhage, strabismus, short stature, GU anomalies. AR, defects in Fanconi anemia complementation group genes A–N.

Tumor syndromes

Cowden: Tricholemmomas, oral mucosal papillomatosis/cobblestoning, acral keratoses, lipomas, sclerotic fibromas, thyroid gland lesions (2/3) (esp. adenomatous goiter or follicular adenomas), fibrocystic breast lesions, breast cancer (3/4 of F), GI polyposis, GU lesions (1/2 of F, endometrial cancer), adenoid facies, high-arched palate, lingua plicata, acral papular neuromatosis, inverted follicular keratoses. AD, PTEN defects.
Gardner: Epidermal cysts (pilomatricoma-like), desmoid tumors, fibromas (esp. back/paraspinal/nuchal), osteomas, lipomas, leiomyomas, neurofibromas, supernumerary teeth, GI polyps (frequent malignant transformation), CHRPE, dental anomalies, adrenal adenomas, hepatoblastoma, CNS tumors (Turcot), thyroid carcinoma. AD, APC defects.
MEN I: Parathyroid, pituitary, pancreas, adrenal, thyroid tumors, lipomas, inclusion cysts, angiofibromas, collagenomas, CALMs, gingival macules. AD, Menin defects.
MEN IIa: Medullary thyroid CA, phaeochromocytoma, parathyroid adenomas, macular and lichen amyloidosis. AD, RET defects.
MEN IIb: Medullary thyroid CA, pheochromocytoma, mucosal neuromas, large lips, lordosis, genu valgum, kyphosis, CALMs, lentigines, marfanoid habitus, synophrys, megacolon/ganglioneuromatosis. AD, RET defects.

Von Hippel–Lindau: Retinal angioma, cerebellar medullary angioblastic tumor, pancreatic cysts, RCC, pheochromocytoma, polycythemia, AD.
Brooke–Spiegler: Trichoepitheliomas, cylindromas, spiradenomas, milia. AD, CYLD defects.
Multiple familial trichoepithelioma/epithelioma adenoides cysticum of Brooke: Trichoepitheliomas, milia. AD, maps to 9p21 (distinct from Brooke–Spiegler).
Birt–Hogg–Dube: Fibrofolliculomas, trichodiscomas, acrochordons, lipomas, collagenomas, RCC (50% chromophobe/oncocytic hybrid), PTX/lung cysts, hypercalcemia, colon polyps. AD, FLCN defects.
Schopf–Schulz–Passarge: Eyelid hydrocytomas, hypodontia, hypotrichosis, nail defects, PPK, eccrine syringofibroadenoma, AR.
Multiple cutaneous and uterine leiomyomata (fibromas): 15–60% develop renal duct or papillary renal type II cancer, rarely cerebral cavernomas. AD, Fumarate Hydratase defects (homozygous mutations cause severe mitochondrial encephalopathy, fumaric aciduria).
Li–Fraumeni: Diverse malignancies – breast, leukemia, brain, soft tissue/bone sarcomas, adrenal, melanoma.

KA syndromes

Muir–Torre: KA, sebaceous carcinoma, sebaceous adenomas, colorectal cancer (50%), GU neoplasms (25%), breast/lung neoplasms. AD, MSH2, MLH1, or MSH6 defects.
Ferguson–Smith: Multiple self-healing KAs, onset: 2nd decade, usually sun-exposed areas, scar, singly or in crops. AD, 9q31 (near PTCH1).
Grzybowski: Numerous small eruptive (2–3 mm), adult onset, oral mucosa and larynx may be involved, pruritus.
Witten and Zak: Combo of Ferguson–Smith and Grzybowski.
Keratoacanthoma centrifugum marginatum: Large with peripheral growth and central healing, non-involuting, dorsal hand or leg.
Others: Subungual, KA dyskeratoticum and segregans, and KAs occurring post-UV, post-surgery, post-aldara, or post-laser resurfacing.

BCC syndromes

Rombo: BCC, trichoepitheliomas, hypotrichosis, atrophoderma vermiculata, milia, cyanosis of lips/hands/feet, telangiectasia, AD.
Bazex–Dupre–Christol: BCC, follicular atrophoderma, pili torti, milia, ulerythema ophryogenes, scrotal tongue, spiny hyperkeratoses, neuropsychiatric, XLD.
Gorlin/basal cell nevus/nevoid BCC: BCC, palmoplantar pits, odontogenic jaw cysts, hypertelorism, frontal bossing, ovarian CA/fibroma, medulloblastomas, milia, lipomas, epidermal cysts, calcification of falx, fused/bifid ribs, eye anomalies, hypogonadism. AD, PTCH1 defects.

Disorders of connective tissue

Pachydermoperiostosis/Touraine–Solente–Gole: Thickening of skin, folds and creases on face, scalp, and extremities, clubbing, AD.
Aplasia cutis congenita (ACC): Group 1: solitary scalp ACC, Group 2: scalp ACC + limb defects, Group 3: scalp ACC + epidermal/sebaceous nevus, Group 4: scalp ACC overlying embryologic defect, Group 5: ACC + fetus papyraceous (linear/stellate, trunk or limb), Group 6: ACC + EB, Group 7: localized ACC on extremities, Group 8: ACC due to HSV, VZV, methimazole (imperforate anus), Group 9: ACC in trisomy 13 (Patau, large membranous scalp defects), 4p- (Wolf-Hirschhorn), Setleis, Johanson-Blizzard, Goltz, amniotic band, Delleman, Xp22 (Reticulolinear).
Adams–Oliver: Aplasia cutis, cutis marmorata, heart defects, limb hypoplasia, AD.
Bart: Aplasia cutis (esp. legs), DDEB>JEB.
Setleis: Bitemporal forcep-like lesions, leonine facies, absent eyelashes, low frontal hairline, periorbital swelling, flat nasal bridge, upslanting eyebrows, large lips, bulbous nose (Brauer syndrome – isolated temporal lesions), AD or AR.
Pseudoxanthoma elasticum/PXE/Gronblad–Strandberg: Calcification/clumping/fragmentation of elastic fibers, "plucked chicken" skin, angoid streaks, tears in Bruch's membrane, ocular hemorrhage, retinal pigmentary changes, claudication, CAD/MI, GI hemorrhage, HTN, EPS. AR, ABCC6 defects.
PXE-like: PXE-like phenotype + cutis laxa, vitamin K-dependent clotting factor deficiency, cerebral aneurysms, minimal ocular sxs. AR, GGCX defects (PXE-like syndrome can be seen in sickle cell or beta-thalasemia).
Goltz/focal dermal hypoplasia: Cribiform fat herniations in Blaschko lines, papillomas (genital, anal, face), osteopathia striata, syndactyly, oligodactyly, colobomas. XLD, PORCN defects.
Buschke–Ollendorff: Osteopoikilosis, disseminated lenticular CT nevus, sclerotic bone foci. AD, LEMD3 defects.
Marfan: Hyperextensible joints, arachnodactyly, aortic aneurysms, dissection/insufficiency, MVP, downward ectopia lentis, PTX, striae, xerosis, EPS, tall stature, long facies, pectus excavatum. AD, Fibrillin-1 defects (Fibrillin-2 defects = Beals, Congenital Contractural Arachnodactyly – "crumpled ears").
Osteogenesis imperfecta: Brittle bones, thin translucent skin, EPS, bruising, hyperextensible joints, wormian bones, hearing loss, normal teeth, ~normal stature, hernias, arcus senilis, respiratory failure 2/2 kyphoscoliosis, Tx: bisphosphonates, Type 1: blue sclerae, Type 2: perinatal lethal/congenital, Type 3: progressively deforming with normal sclerae, Type 4: normal sclerae, Genetic basis – Type 1, 2A, 3, 4: AD defects in COL1A1 or COL1A2; Type 2B, 7: AR defects in CRTAP.
Cutis laxa: Elastolysis, sagging skin, hound dog appearance, deep voice, emphysema, diverticuli, hernia, hook nose, oligohydramnios, CV anomalies. AR (FBLN4 or 5, or ATP6V0A2), AD (Elastin or FBLN5), XL (ATP7A – EDS9 and Menkes).

Ehlers–Danlos

	Type	Inhr	Defect	Characteristics
I	**Gravis**	AD	COL 5A1,2	Skin fragility, joint/skin hyperextensibility, bruising, "cigarette paper" scars, prematurity of newborn, molluscoid pseudotumors (at scars), SQ spheroids
II	**Mitis**	AD	COL 5A1	Similar to Gravis but less severe
III	**Hypermobile**	AD	COL 3A1, Tenascin-XB	Marked small and large joint hypermobility and dislocation, *minimal* skin changes, MSK pain
IV	**Vascular/ecchymotic/sack**	AD	COL 3A1	*Arterial, bowel, and uterine rupture*, bruising, thin, translucent skin with visible/*varicose* veins, only mild small joint hyperextensibility, tendon/muscle rupture, EPS, facies – thin nose, hollow cheeks, staring eyes
V	**X-linked**	XLR		Similar to Mitis, bruising/skin hyperextensibility > skin fragility
VI	**Kyphoscoliotc/ocular-scoliotic**	AR	Lysyl hydroxylase, PLOD1	Skin/joint laxity, *corneal/scleral fragility*, keratoconus, ocular hemorrhage, *muscle hypotonia* (neonatal), kyphoscoliosis, arterial rupture, reduced urinary pyridinium cross-links
VII A,B	**Arthrochalasia multiplex**	AD	COL 1A1,2	*Congenital hip dislocation*, severe joint hypermobility, soft skin, abnormal scars, short, micrognathia
VII C	**Dermatosparaxis**	AR	ProCOL I N-proteinase/ ADAMST2	Skin fragility (dermatosparaxis = "*skin tearing*"), *sagging and redundant* skin, joint/skin hyperextensibility, bruising, short, micrognathia
VIII	**Periodontal**	AD		Similar to types I/II + prominent *periodontal* disease, pretibial hyperpigmented (NLD-like) scars
IX	**Occipital horn/cutis laxa**	XLR	ATP7A	Occipital exostoses, abnormal clavicles, abnormal copper transport, joint hypermobility, GU abnormalities, malabsorption, allelic to Menkes
X	**Fibronectin**	AR	Fibronectin	Bruising, abnormal clotting, defective platelet aggregation, skin laxity, joint hypermobility
XI	**Large joint hypermobile**	AD		

Progeria/Hutchinson–Gilford: Atrophic, sclerodermoid, poikilodermatous skin, prominent veins, alopecia, bird facies, failure to thrive, premature graying, short stature, coax valga, flexural contractures, abnormal dentition, early death from atherosclerotic heart disease. AR, LMNA defects.
Acrogeria: May be a spectrum of Vascular EDS, atrophic acral skin, mottled pigmentation, nail dystrophy, micrognathia, atrophic tip of nose.
Werner/adult progeria: Short, high-pitched voice, beaked nose, cataracts, DM2, muscle atrophy, osteoporosis, sclerodermoid changes, painful callosities, severe atherosclerosis, progressive alopecia, canities, hyperkeratosis at elbows/knees/palms/soles, ischemic ulcers, reduced fertility, sarcomas, thyroid carcinoma. AR, RECQL2 defects.
Rothmund–Thomson/hereditary congenital poikiloderma: Photosensitivity, poikiloderma, dorsal hand keratoses (25% SCC transformation), sparse hair, loss of eyebrows/eyelashes, short, bone defects (radius and hands), juvenile zonular cataracts (50% blind), MR, hypodontia, EPS, osteosarcomas, hypogonadism. AR, RECQL4 defects.
Cockayne: Premature graying, cachetic dwarfism, retinal atrophy, deafness, sunken eyes, beaked nose, large ears, photosensitivity, telangiectasia, dementia, premature aging, loss of subcutaneous fat, thin hair, flexion contractures, severe MR, salt and pepper retina. AR, CSA – ERCC8 defects, CSB – ERCC6 defects.
Juvenile systemic fibromatosis/infantile systemic hyalinosis: Nodules on H/N (ears/nose/scalp) and fingers, gingival hypertrophy, joint contractures, osteopenia, short stature, myopathy. AR, Capillary Morphogenesis Protein-2 (CMG2/ANTXR2) defects.
Francois/dermochondrocorneal dystrophy: Papulonodules on dorsal hands, nose, ears, gingival hyperplasia, osteochondrodystrophy, corneal dystrophy, AR.
Restrictive dermopathy: Taut, translucent skin, open mouth, joint contractures, arthrogryposis, pulmonary insufficiency. AR, LMNA or ZMPSTE24 defects.
Whistling face/Freeman-Sheldon: Contractures (hands, feet, neck), microstomia, deep-set eyes, strabismus, colobomas, scoliosis, cryptochordism.

Collagen types

Type	Distribution	Diseases
I	Skin (85% of adult dermis), bone, tendon, ECMs	Arthrochalasia multiplex, Osteogenesis imperfecta
II	Vitreous humor, cartilage	Stickler arthro-ophthalmopathy, Kneist dysplasia, Spondyloepiphysela dysplasia, Achondrogenesis, Avascular necrosis of femoral head, Antibodies: Relapsing polychondritis

III	Skin (10% of adult dermis), fetal skin, GI/lung, vasculature	Vascular > Hypermobile
IV	Basement membranes	Goodpasture, Alport, Benign familial hematuria, Porencephaly, Diffuse leiomyomatosis
V	Ubiquitous	Gravis/Mitis
VI	Cartilage, skin, aorta, placenta, others	Ullrich muscular dystrophy, Bethlem myopathy
VII	Anchoring fibrils, skin, cornea, mucous membranes, amnion	DEB, Isolated toenail dystrophy, Transient bullous disease of the newborn, EB pruriginosa, Antibodies: CP and BLE
VIII	Endothelial cells, skin, Descemet's membrane	Fuchs corneal dystrophy
IX	Cartilage	Stickler arthro-ophthalmopathy, Multiple epiphyseal dysplasia ± myopathy, Intervertebral disc disease susceptibility
X	Cartilage (hypertrophic)	Metaphyseal chondrodysplasia
XI	Hyaline cartilage	Stickler arthro-ophthalmopathy, Marshall skeletal dysplasia, Familial deafness, Otospondylomegaepiphyseal dysplasia
XVII	Skin hemidesmosomes	JEB, Generalized atrophic EB, Antibodies: BP

Fibril-forming: I, II, III, IV, V, XI.
Fibril-associated collagens with interrupted triple helices: IX, XII, XIV, XVI, XIX, XX, XXI.
Microfibrillar: VI.
Network-forming: VIII, X.
Transmembrane domains: XIII, XVII.
Lysyl oxidase – cross-linking of collagen; cofactors – vitamin C, B6, copper.
Cystathionine synthase – cross-linking of collagen; homocytinuria.
Tenascin-XB – EDS3 and EDS-like syndrome.

Disorders of metabolism

Enzymatic deficiencies

PKU: MR, szs, pigmentary dilution, atopic dermatitis. AR, phenylalanine hydroxylase or dihydropteridine reductase defects.

Homocystinuria: Marfanoid, premature heart disease, low IQ, szs, osteoporosis, codfish vertebrae with collapse, livedo on legs, fine sparse hair, pigmentary dilution, upward ectopia lentis. AR, cystathione β-synthase or MTHFR defects.

Alkaptonuria: Dark urine/sweat, arthritis, discolored cartilage, kyphoscoliosis, joint destruction, tendon rupture, deafness, vs. exogenous ochronosis due to hydroxyquinone, phenol, or picric acid. AR, homogentisic acid oxidase/homogentisate 1,2-dioxygenase defects.

Lesch–Nyhan: HGPRT deficiency, hyperuricemia, self-mutilation, MR, spastic CP, tophi. XLR, HPRT defects.

Niemann–Pick: Classical infantile form (A, Ashkenazi), visceral form (B, adults, non-neuropathic), subacute/juvenile form (C), Nova Scotia form (D), adult form (E), HSM, lymphadenopathy, MR, cherry red macula, yellow skin, dark macules in mouth. AR, Sphingomyelinase or NPC1 defects.
Gaucher: Glucosylceramide/GlcCer/glucosylcerebroside accumulates in the brain, liver, spleen, marrow, Type 1: "nonneuronopathic," HSM, bronze skin, pinguecula of sclera, adults; Type 2: "acute neuronopathic," infant, may be preceded by ichthyosis; Type 3: "subacute neuronopathic," juvenile, chronic neuro sxs; Type 3C: with CV calcifications. AR, acid β-glucosidase defects (except atypical Gaucher – PSAP/Saposin C defect).
Fabry: Angiokeratoma corporis diffusum, whorl-like corneal opacities, "maltese cross" in urine, painful paresthesias, ceramide accumulates in heart, autonomic nervous system, and kidneys (main cause of mortality), CVA/MI (second most cause of mortality), autoantibodies (esp. LAC and antiphospholipid), thrombosis. XLR, α-Galactosidase A.

Angiokeratoma

Solitary Papular: usu extremity, preceding trauma
Circumscriptum: large single Blaschkonian plaque, extremity
Corporis Diffusum: Fabry, Fucosidosis
Mibelli: Fingers and toes, adolescence, cold-provoked
Fordyce: Scrotum, vulva, middle-aged
Caviar Spot: Tongue

Fucosidosis: Angiokeratoma corporis diffusum, coarse thick skin, MR, szs, spasticity, dysostosis multiplex, visceromegaly, growth retardation, respiratory infections. AR, α-L-Fucosidase.
Hartnup: Error in tryptophan secretion, pellagra-like rash, psychiatric changes. AR, SLC6A19 defects.
Hurler: HSM, BM failure, thick lips, large tongue, MR, corneal opacities, broad hands with claw-like fingers, dried urine with toluidine blue turns purple, dermatan sulfate and heparan sulfate in urine. AR, α-L-Iduronidase defects.
Hunter: Like Hurler but milder, pebbly lesions. XLR, iduronate sulfatase defects.
Oxalosis: Livedo, nephrocalcinosis, cardiomyopathy. AR, Type 1 – alanine-glyoxylate aminotransferase (AGXT) defects, glyoxylate reductase/hydroxypyruvate reductase (GRHPR) defects.
Tangier: Alpha lipoprotein deficiency, orange-yellow striations on large tonsils, splenomegaly, neuropathy, decreased cholesterol. AR, ATP-binding cassette-1 (ABC1) defects.
Lipogranulomatosis/Farber: SQ masses over wrists/ankles, arthritis, hoarse, involves larynx, liver, spleen, kidneys, CNS. AR, Acid Ceramidase (also called *N*-acylsphingosine amidohydrolase – ASAH) defects.

Lipomatosis

Madelung/Launois–Bensaude/familial symmetrical lipomatosis: Alcoholism, liver disease, DM2, gout, hyperlipidemia, massive symmetrical lipomas around neck and upper trunk, "body-builder" appearance.
Dercum/Adiposa dolorosa: Psychiatric issues, obese women, multiple painful lipomas, asthenia, AD.
Familial multiple lipomatosis: AD, spares shoulders and neck.

Total lipodystrophies

Bernadelli–Seip: Congenital total/generalized lipodystrophy, increased appetite, increased height velocity, AN, hyperpigmentation, thick curly hair, mild MR, DM2, CAD, hypertriglyceridemia, hepatic steatosis. AR, Type 1 – 1-acylglycerol-3-phosphate *O*-acyltransferase-2 (AGPAT2) defects, Type 2 – Seipin (BSCL2) defects.
Seip–Lawrence: Acquired total lipodystrophy, begins before age 15, preceded by infxn or CTD, DM2, AN, liver involvement is worse and commonly fatal, muscle wasting, growth retardation.

Partial lipodystrophies

Kobberling–Dunnigan: At puberty, loss of SQ fat from extremities, buttocks, and lower trunk, gain fat on face, neck, back, and axilla, AN, hirsutism, PCOS, DM2, increased TG. AD or XLD, Type 1 – unknown genetic defect, Type 2 – LMNA defects, Type 3 – PPARG defects.
Barraquer–Simons: Acquired progressive lipodystrophy, first and second decade onset after viral illness, begins in face and progresses downward to iliac crests/buttocks, increased C3 nephritic factor, glomerulonephritis, third trimester abortions, DM2, LMNB2 defects.
Insulinopenic partial lipodystrophy w/Rieger anomaly/SHORT: In infancy, loss of fat on face and buttocks, retarded growth, bone age, and dentition, DM2 with low insulin, NO AN, Rieger anomaly = eye and tooth anomalies, S = stature; H = hyperextensibility of joints or hernia; O = ocular depression; R = Rieger anomaly; T = teething delay.

Porphyria

Pseudoporphyria	–	2/2 NSAIDS, tetracycline, hemodialysis, tanning booths, thiazide, furosemide	Normal urine, blood, feces PCT-like, photosensitive blistering and skin fragility;no hypertrichosis/hyperpigmentation/ sclerodermoid changes
PCT	AD	Uroporphyrinogen decarboxylase	U/B: uroporphyrin 3× > coproporphyrin Stool: Isocoproporphyrin Photosensitive blistering, skin fragility, hypertrichosis, sclerodermoid changes Tx: phlebotomy, anti-malarials. Check Fe, HCV, hemochromatosis
Hepatoerythropoietic porphyria (Homozygous PCT)	AR	Uroporphyrinogen decarboxylase	Similar U/B/Stool as PCT, plus elevated protoporphyrins in RBCs Similar to CEP – photosensitive blistering in infancy, hypertrichosis, hyperpigmentation, neurologic changes, anemia, dark urine, erythrodontia
Variegate porphyria	AD	Protoporphyrinogen oxidase	U: dALA, PBG (during attack); coproporphyrin > uroporphyrin (unlike PCT) B: 626 nm fluorescence Stool: elevated coproporphyrins > protoporphyrins Most often asx; may have PCT-like skin, AIP-like neurologic and GI sx Avoid precipitating factors
Acute intermittent porphyria	AD	Porphobilinogen deaminase	U: PBG, dALA B: dALA Abdominal pain, muscle weakness, psychiatric sx, no skin findings/photosensitivity, risk of liver cancer

Hereditary coproporphyria	AD	Coproporphyrinogen oxidase	U: coproporphyrin, dALA, PBG (during attack) Stool: coproporphyrin (always) PCT-like skin, AIP-like neurologic and GI sxneuron
Congenital erythropoietic porphyria	AR	Uroporphyrinogen-III synthase	U/Stool/RBC: uroporphyrin and coproporphyrin
(Gunther)			Severe photosensitivity, erythrodontia, mutilating scars, hypertrichosis, madarosis, scleromalacia perforans, red urine, anemia, gallstones Tx: Transfuse to keep Hct 33% (turn off porphyrin production)
Erythropoietic protoporphyria	AD AR	Ferrochelatase	U: nl B/RBC/stool: protoporphyrin Severe photosensitivity (elevated protoporphyrin IX), purpura, erosions/scars, waxy/"weather beate" thickening (nose, knuckles), gallstones, anemia, liver dysfunction Tx: β-carotene, antihistamine, NBUVB to induce UV tolerance

U: Urine B: Blood

Disorders of pigmentation

Carney complex: NAME (Nevi, Atrial myxoma, Myxomatous neurofibromata, Ephelids), **LAMB** (Lentigines, Atrial myxoma, Myxoid tumors, Blue nevi), Sertoli cell tumors, psammomatous melanotic schwannomas, mammary neoplasia, CVA from cardiac emboli, pigmentary nodular adrenal tumors, pituitary adenomas. AD, PRKAR1A defects.

LEOPARD/Moynahan: Lentigines, EKG abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, growth Retardation, Deafness. AD, PTPN11 defects.

Peutz–Jeghers: 90% small bowel involved, colic pain, bleeding, intussusception, rectal prolapse, 20–40% malignant transformation of GI polyps, cancer (breast, ovary, testes, uterus, pancreas, lungs), sertoli cell tumors, oral lentigines (also facial, hands/soles, genital, perianal), longitudinal melanonychia, presents before or in early puberty. AD, STK11 defects (vs. **Laugier–Hunziker:** Non-familial orolabial pigmented macules similar to P–J without GI involvement, Caucasians presenting between ages 20 and 40 years).

Familial GI stromal tumors (GISTs) with hyperpigmentation: GISTs, perineal hyperpigmentation, hyperpigmented macules (perioral, axillae, hands, perineal – not oral/lips), ± urticaria pigmentosum. AD, C-KIT defects (activating mutations).

Bannayan–Riley–Revalcaba/Bannayan–Zonana: Macrocephaly, genital lentigines, MR, hamartomas (GI polyps), lipomas, hemangiomas. AD, PTEN defects.

Russell–Silver: Growth retardation, feeding difficulties, triangular facies, downturned lips, blue sclerae, limb asymmetries, clinodactyly of fifth digit, CALM, urologic abnormalities, 10% demonstrate maternal uniparental disomy of chromosome 7.

McCune–Albright: "Coast of Maine" CALM, precocious puberty, polyostotic fibrous dysplasia (fractures, asymmetry, pseudocystic radiographic lesions), endocrinopathies (hyperthyroidism, Cushing, hypersomatotropism, hyperprolactinemia, hyperparathyroidism). Mosaic activating GNAS1 defects.

Albright hereditary osteodystrophy: Pseudo or pseudopseudo-hyperparathyroidism, short fourth and fifth digits, osteoma cutis, short stature, dimpling over knuckles, MR. Maternally inherited GNAS1 mutations.

Pallister–Killian: Hyperpigmentation in Blaschko lines, coarse facies, temporal hypotrichosis, CV anomalies, MR. Mosaic tetrasomy 12p.

OCA1A, 1B/tyrosine negative albinism (OCA = oculocutaneous albinism): 1A: No Tyrosinase activity, strabismus, photophobia, reduced acuity, 1B: Slightly more tyrosinase activity. AR, Tyrosinase defects (if temperature sensitive mutation → "Siamese cat" pattern).

OCA2: Tyrosinase +, increased in Blacks/South Africa, 1% of Prader-Willi and Angelman patients have OCA2. AR, P gene defects.
OCA3: Blacks, copper/ginger hair, light tan skin, ± eye involvement. AR, TYRP1 defects.
Rufous oculocutaneous albinism/ROCA: Copper-red skin/hair, iris color diluted, South Africa. AR, TYRP1 defects.
OCA4: AR, MATP/SLC45A2 defects.
Cross–McKusick/oculocerebral syndrome with hypopigmentation: Albinism, MR, szs, spastic di/quadriplegia, silvery-gray hair.
Hermansky–Pudlak: Tyrosinase +, hemorrhagic diathesis, absent dense bodies in platelets, nystagmus, blue eyes, granulomatous colitis, pulmonary involvement, progressive pigment recovery, Puerto Ricans, Jews, Muslims. AR, HPS1–8 defects (includes DTNBP1 and BLOC1S3).
Piebaldism: White forelock, depigmented patch ("diamond-patches"). AD, C-KIT defects (inactivating mutations).
Waardenberg: Depigmented patches, sensorineural defects, white forelock, dystopia canthorum, iris heterochromia, broad nasal root, white eyelashes, cleft lip, scrotal tongue, megacolon (Type 4), limb defects (Type 3) AD>AR, Type 1: PAX3, Type 2A: MITF, Type 2D: SNAI2, Type 3: PAX3, Type 4: SOX10, endothelin-B receptor, or endothelin-3 defects.
IP/Bloch–Sulberger: Four stages: (1) Blistering, (2) Verrucous, (3) Hyperpigmented, (4) Hypopigmented/Atrophic; Eosinophilia/leukocytosis, pegged teeth, szs, MR, strabismus, scarring alopecia, onychodystrophy, ocular sxs. XLD, NEMO defects.
IP Acromians/hypomelanosis of Ito: Hypopigmented nevi (linear/whorled) + CNS anomalies, strabismus, szs, MR, mosaic chromosomal anomalies.
Linear and whorled/figurated nevoid hypo/hypermelanosis: No bullae, Blaschko distribution, often with MR, PDA, ASD.
Kindler–Weary: Acral, traumatic bullae during childhood, sclerotic poikiloderma, photosensitivity, periodontosis, pseudosyndactyly, scleroderma/XP-like facies, esophageal strictures, oral leukokeratoses, SCC. AR, KIND1 defects.
Dermatopathia pigmentosa reticularis: Generalized reticulate pigmentation, sweating disregulation, decreased dermatoglyphics, noncicatricial alopecia, onychodystrophy, PPK. AD, KRT14 defects.
Acromelanosis progressiva: Rare, black pigment of hands/feet, spread by age ~5 years.
Acropigmentation of Dohi/dyschromatosis symmetrica hereditaria: Hypo- and hyperpigmented macules on extremeties in a reticulated pattern, esp. dorsal hands/feets. AD, DSRAD defects.

Dowling–Degos: Postpubertal, progressive, brown, reticulate hyperpigmentation of the flexures, no hypopigmented macules, soft fibromas, pitted perioral scars, rarely hidradenitis suppurativa, path = elongated pigmented rete ridges, thinned suprapapillary plates, dermal melanosis. AD, KRT5 defects (**Galli–Galli** – acantholytic Dowling–Degos; Dowling–Degos shares features with **Haber** – early rosacea, trunkal keratoses (esp. axillae SK/VV-like), pitted scars, PPK).
Reticulate pigmentation of Kitamura: Linear palmar pits, reticulate, hyperpigmented macules, 1–4 mm on volar and dorsal hands, no hypopigmented macules. AD, KRT5 defects.
Familial progressive hyperpigmentation: Hyperpigmented patches at birth, spread, involve conjunctivae and buccal mucosa, AD.
Phakomatosis pigmentokeratotica: Speckled lentiginous nevus (usu checkerboard) + organoid nevus with sebaceous differentiation ± musculoskeletal, neuro, and ophtho abnormalities.
Hemochromatosis: Onset: 40–60 years old, Classic Tetrad: bronze skin (esp. face), hepatomegaly, DM2, cardiomyopathy; pigmentation due to (basilar) melanin and hemosiderin, cardiac dysrhythmia, arthropathy, black stasis dermatitis, Tx: phlebotomy and chelating agents. AR, HFE defects.

Non-hereditary syndromic disorders of pigmentation
Vogt–Koyanagi–Harada: Depigmented skin/eyelashes, chronic granulomatous iridocyclitis, retinal detachment, aseptic meningoencephalitis.
Alezzandrini: Unilateral degenerative pigmentary retinitis, ipsilateral vitiligo, poliosis.
Cronkhite–Canada: Melanotic macules on fingers, more diffuse hyperpigmentation than Peutz–Jeghers, alopecia, onychodystrophy, protein losing enteropathy, GI polyposis.
Riehl melanosis: Pigmented contact dermatitis on face, esp. brown-gray discolored forehead/temples, often due to cosmetics, interface reaction on path.
Gray baby syndrome: Chloramphenicol.
Bronze baby syndrome: Complication of phototherapy for bilirubinemia, elevated direct bili, hepatic dysfunction, induced by photoproducts of bilirubin and biliverdin.

Disorders of vascularization

Proteus syndrome: Partial gigantism of the hands/feet, lipomas, linear verrucous nevi, macrocephaly, hyperostosis, PWS, body hemihypertrophy, ocular anomalies, scoliosis.
Cutis marmorata telangiectatica congenita/Van Lohuizen: Persistant livedo, atrophy/ulceration, CNS defects, MR, craniofacial anomalies, glaucoma, syndromes with cutis marmorata: Adams–Oliver, Cornelia de Lange, Coffin–Siris (related condition: Macrocephaly-CMTC

syndrome – macrocephaly + cutis marmorata + several additional features among the following: hypotonia, toe syndactyly, segmental overgrowth, hydrocephalus, midline facial nevus flammeus, frontal bossing).

Maffucci: Enchondromas, increased osteosarcomas, vascular malformations. AD, PTHR1 defects not confirmed (Ollier – no vascular malformations).

Gorham–Stout/disappearing (aka vanishing or phantom) bone: Onset: childhood or young adulthood, progressive osteolysis of one or more bones, vascular malformations (bone and skin), pathologic fractures, limb tenderness and weakness, thoracic duct occlusion, chylothorax, Tx: radiation.

Beckwith–Wiedemann: Facial PWS, macroglossia, omphalocoele, hemihypertrophy, adrenocortical carcinomas, pancreatoblastomas, hepatoblastomas. Defects: p57/KIP2/CDKN1C or NSD1.

Cobb: Cutaneomeningospinal angiomatosis, hemangioma or vascular malformation of a spinal segment and its corresponding dermatome.

Blue rubber bleb nevus/Bean: Painful blue nodules with hyperhidrosis, GI bleeds.

Roberts/SC phocomelia/SC pseudothalidomide: Facial PWS, hypomelia, hypotrichosis, growth retardation, cleft lip/palate, limb defects. AR, ESCO2 defects.

Thrombocytopenia-absent radius/TAR: Absent radius, decreased platelets, PWS.

Alagille: Arteriohepatic dysplasia, nevus comedonicus, xanthomas, retinal pigment anomalies, peripheral arterial stenosis, pulmonic valvular stenosis, "butterfly" vertebrae, absent deep tendon reflexes, broad forehead, bulbous nasal tip, foreshortened fingers. AD, JAG1 or NOTCH2 defects.

PHACES: Posterior fossa abnormalities, Hemangiomas, Arterial anomalies (including intracranial aneurysms), Cardiac anomalies (often aortic coarctation), Eye anomalies, Sternal defects, usually females, most often left-sided hemangioma, Dandy–Walker malformation, cleft palate.

Sturge–Weber: V1 PWS, V2 and V3 may be involved but must be in conjunction with V1, full V1 involvement has greater risk than partial V1 involvement, glaucoma, szs, ipsilateral vascular malformation of meninges and train track calcifications, MR.

Klippel–Trenaunay: Capillary malformation with limb hypertrophy, venous/lymphatic malformations, angiokeratomas, lymphangiomas, AV fistula, phlebitis, thrombosis, ulcerations.

Von Hippel–Lindau: Capillary malformation of head/neck, retinal/cerebellar hemangioblastoma, renal cell CA, renal cysts, pheochromocytoma, adrenal CA, pancreatic cysts. AD, VHL defects.

Multiple cutaneous and mucosal venous malformations/VMCM: AD, TIE2 defects.

Capillary malformation–arteriovenous malformation/CM-AVM: Atypical capillary malformations + AVM, AV fistula, or Parkes Weber syndrome. AD, RASA1 defects.

Ataxia telangiectasia/Louis–Bar: Cerebellar ataxia starts first (at ~1 year old), wheelchair-bound by ~12 years old, oculocutaneous telangiectasias develop by 3–6 years old, sinopulm infxn, IgA & IgG are diminished, IgE and IgM may be diminished, premature aging, poikilodermatous and sclerodermatous skin, MR, insulin-resistant DM2, increased AFP (makes it difficult to screen for hepatic tumors) and CEA, radiosensitivity, lymphoid/solid (stomach, breast) malignancies, cutaneous granulomas. AR but cancer risk in heterozygotes, ATM defects.

Bloom: Short stature, telangiectatic facial erythema, malar hypoplasia, photosensitivity, hypogonadism/decreased fertility, high-pitched voice, leukemia, lymphoma, low IgM and IgA, recurrent pneumonia, CALM, crusted/blistered lips, narrow face, DM2 (and acanthosis nigricans), MR, loss of eyelashes. AR, RECQL3=RECQ2 defects.

Osler–Weber–Rendu/hereditary hemorrhagic telangiectasia: Telangiectasia of mucosa/ face/palms/soles, epistaxis, GI bleed, pulmonary AVMs. AD, Endoglin (HHT1), ALK-1 (HHT2), HHT3, or HHT4 defects.

Xeroderma pigmentosa: Types A–G, Type A most severe, A is most common in Japan, (30%) and D (20%) are most common overall, defective UV damage repair, ectropion, blepharitis, keratitis, low intelligence, dementia, ataxia, lentigines, premature aging, NMSC, melanoma, KA, AR.

De Sanctis–Cacchione: Type A XP, mental deficiency, dwarfism, hypogonadism. AR, ERCC6 defects.

Nonne–Milroy: Congenital lymphedema, unilateral or bilateral, pleural effusions, chylous ascites, scrotal swelling, protein-losing enteropathy, risk for lymphangiosarcoma and angiosarcoma, right > left leg. AD but F>M, FLT4/VEGFR3 defects.

Meige/lymphedema praecox: Most common form of primary lymphedema AD, FOXC2/MFH1 defects (also causes Yellow Nail, Lymphedema–Distichiasis, and Lymphedema and Ptosis syndromes).

Yellow nail: Lymphedema, pleural effusions, bronchiectasis, yellow nails. AD, FOXC2/MFH1 defects.

Non-hereditary syndromic vascular disorders

APACHE: Acral Pseudolymphomatous Angiokeratoma of CHildrEn.

Kasabach–Merritt: Consumptive coagulopathy associated with large vascular lesion esp. kaposiform hemangioendothelioma or tufted angioma.

Mondor: Thrombophlebitis of the veins in the thoracogastric area, often breast, sometimes strain/trauma.

POEMS/Crow–Fukase: Glomeruloid hemangiomas, Polyneuropathy, Organomegaly (liver, lymph nodes, spleen), Endocrinopathy, Monoclonal protein (IgA or G)/Myeloma (15% Castleman disease), Skin changes

(hyperpigmentation, skin thickening, hypertrichosis, sclerodermoid changes), sclerotic bone lesions, edema, papilledema.
Secretan: Acral factitial lymphedema.
Stewart–Treves: Mastectomy → angiosarcoma.
Stewart-Bluefarb: Pseudo-KS, leg AVM.
Wyburn-Mason: Facial PWS, ipsilateral AVM of retinal/optic pathway.
Hennekam: Congenital lymphedema, intestinal lymphangiectasia, MR.
Coats: Retinal telangiectasia, ipsilateral PWS.
Syndromes with photosensitivity: XP, Bloom, Rothmund–Thomson, Cockayne, Hartnup, porphyrias, TTD, Cockayne, Kindler, Prolidase deficiency, Hailey-Hailey, Darier.

Immunodeficiency syndromes

X-linked agammaglobulinemia/Bruton: Males, onset: infancy, recurrent infxns (Gram+ sinopulmonary, meningoencephalitis, arthritis), reduced or undetectable Ig levels, atopy, vasculitis, urticaria, no germinal centers or plasma cells, RA-like sxs, neutropenia, chronic lung disease, defect in PreB to B cell differentiation, tx: IVIG. XL, BTK defects.
Isolated IgA deficiency: 50% with recurrent infxns, 25% with autoimmune disease, Celiac, UC, AD, asthma, IVIG infusion may cause allergic rxn 2/2 IgA Ab, hard to confirm dx before 4 years old because IgA develops late in children.
CVID: Typical sx onset and diagnosis in late 20s, increased HLA-B8, DR3, recurrent sinopulmonary infxns, increased autoimmune disease, lymphoreticular and GI malignancies, arthritis, noncaseating granulomas (may be confused with sarcoidosis), some T-cell dysfxn, reduced Ig levels (esp. IgG and IgA, also IgM in ½ of patients), tx: IVIG.
Isolated IgM deficiency: 1/5 with eczematous dermatitis, VV, patients with MF and celiac disease may have secondary IgM deficiency, thyroiditis, splenomegaly, hemolytic anemia.
Hyper–IgM: Recurrent infxns, low IgG, E, A, respiratory infxn, diarrhea, otitis, oral ulcers, VV, recurrent neutropenia, tx: with IVIG, BMT. XL (CD40L), AR (CD40, AICD, HIGM3).
DiGeorge: Notched, low-set ears, micrognathia, shortened philtrum, hypertelorism, absent parathyroids → neonatal hypocalcemia, thymic hypoplasia, cardiac anomlies (truncus arteriosis, interrupted aortic arch), psychiatric sxs cleft lip/palate, CHARGE overlap, 1/3 with Complete DiGeorge have eczematous dermatitis. AD, deletion in proximal long arm of chromosome 22 (TBX1 is esp. important).
Thymic dysplasia with normal immunoglobulins/Nezelof: T-cell deficit, severe candidiasis, varicella, diarrhea, pulm infxns, nl Ig, AR.
Omenn/familial reticuloendotheliosis with eosinophilia: Exfoliative erythroderma, alopecia, eosinophilia, HSM, LAN, infections, diarrhea, hypogammaglobulinemia, hyper-IgE, decreased B cells, increased T cells. AR, RAG1, RAG2 defects.

SCID: Absent cellular and humoral immunity, monilithiasis, diarrhea, pneumonia. AR, Adenosine Deaminase, RAG1, RAG2 defects.
Wiskott–Aldrich: Young boys, triad (atopic, recurrent infxn – esp. encapsulated organisms, thrombocytopenia), small platelets, lymphoid malignancies, cellular and humoral immunodeficiency, autoimmune disorders, often present with bleeding (from circumcision or diarrhea), defects in cellular and humoral immunity: IgM deficiency with IgA and IgE often elevated and IgM often normal, HSM, Tx: BMT. XLR, WASP defects.
Chronic Granulomatous Disease/CGD: Recurrent purulent and granulomatous infxns of the long bones, lymphatic tissue, liver, skin, lungs, 2/3 in boys, eczema, defect in NADPH oxidase complex, autoimmunity, lupus-like sxs in XL carriers (rash, arthralgias, oral ulcers, fatigue, but usu ANA-), gene for XLR (60%): CYBB, AR forms: NCF1, NCF2, CYBA (p22–, p47–, p67–, and p91-phox).
Myeloperoxidase deficiency: Most asymptomatic. AR, MPO defects.
Hyper–IgE: AD-like lesions, recurrent pyogenic infxns/cold abscesses, eosinophilia, may have PPK, asthma, chronic candidiasis, urticaria, coarse facies with wide nose, deep-set eyes, hyperextensible joints, fractures, lymphomas, pneumatoceles, retained primary teeth, scoliosis, pathologic fractures. AD: STAT3 defects, AR: TYK2 defects (AR form has severe viral infections, HSV, extreme eosinophilia, neurologic complications, no skeletal/dental defects), subset with **Job:** Girls with red hair, freckles, blue eyes, hyperextensible joints.
APECED: Autoimmune Polyendocrinopathy, (chronic mucocutaneous) Candidiasis, Ectodermal Dystrophy, frequent Addison and/or hypoparathyroidism, selective T-cell anergy for candida, alopecia, vitiligo, oral SCC. AR, AIRE defects.
Leukocyte Adhesion Molecule deficiency: Delayed umbilical separation, periodontitis, gingivitis, poor wound healing, Tx: BMT. AR, CD18 β2 integrin (can't bind CD11, C3b).

	Chediak–Higashi	Elejalde	Griscelli
Neurologic	Normal (rarely defects in adult form)	Severe defects, mental and motor, regressive	Defects in Type 1, normal in Types 2 and 3
Immunologic	PMN, NK, and lymph cell defects, fatal accelerated phase (uncontrolled macrophage and lymphocyte activation)	Normal	Normal in Types 1 and 3, Defects in Type 2 (lymphs and NK cells), no fatal accelerated phase
Hair	Silvery, regular melanin clumps in small granules (6× smaller than granules of Elejalde or Griscelli)	Silvery, irregular melanin clumps in large and small granules	Silvery, irregular melanin clumps in large and small granules

Skin	Pigment dilution	Pigment dilution	Pigment dilution
Platelet	Dense granule defects	Dense granule defects	Dense granule defects
Ophtho	Defects	Defects	Defects
Inheritance	AR, LYST	AR, MYO5A	AR, MYO5A (Type 1), RAB27A (Type 2), MLPH or MYO5A (Type 3)

Hereditary periodic fever syndromes

Familial mediterranean fever/FMF: Recurrent fever (few hours to several days), recurrent polyserositis (peritoneum, synovium, pleura), AA amyloidosis, renal failure, erysipelas-like erythema esp. BLE, rare associations: HSP and PAN. AR or AD, MEFV/Pyrin defects.

TNF receptor-associated periodic/TRAPS/Hibernian fever: Recurrent fever (usu > 5 days, often 1–3 weeks), myalgia (w/ overlying migratory erythema), pleurisy, abdominal pain, conjunctivitis/periorbital edema, serpiginous, edematous, purpuric, or reticulated lesions esp. at extremities, AA amyloidosis, renal failure, leukocytosis, elevated ESR. AD, TNF-Receptor 1 defects.

Hyper-IgD with periodic fever/HIDS: Recurrent fever (3–7 days, 1–2 months apart), abdominal pain, diarrhea, headache, arthralgias, cervical lymphadenopathy, erythematous macules > papules and nodules, elevated IgD and IgA, rare associations: HSP and EED, mevalonic aciduria. AR, MVK defects.

Cryopyrin-associated periodic syndromes

Histo: Lots of PMNs, no mast cells.

Familial cold autoinflammatory/urticaria/FCAS: Urticaria-like eruption, limb pain, recurrent fever, flare with generalized cold exposure, normal hearing, AA amyloidosis. AD, CIAS1 defects.

Muckle–Wells: Urticaria-like eruption, limb pain, recurrent fever, AA amyloidosis (more common than FCAS), deafness. AD, CIAS1 defects.

Neonatal–onset multisystemic inflammatory disease/NOMID/CINCA: Triad of CNS disorder, arthropathy, and rash (edematous, urticarial-like papules and plaques, neutrophilic eccrine hidradenitis); also deafness and visual disturbance, recurrent fever, AA amyloidosis. AD, CIAS1 defects.

Pyogenic sterile arthritis, pyoderma gangrenosum and acne/PAPA: Periodic Fever with Aphthous Stomatitis, Pharyngitis, and Cervical Adenopathy (PFAPA), attacks last ~5 days. AD, PSTPIP1 defects (vs. SAPHO: synovitis, acne, pustulosis, hyperostosis, osteitis).

Blau: Arthritis, uveitis, granulomatous dermatitis – early onset sarcoidosis. AD, NOD2/CARD15 defects.

Majeed: Subacute or chronic multifocal osteomyelitis with neutrophilic dermatosis or Sweet syndrome. AR, LPIN2 defects.

Miscellaneous

Melkersson–Rosenthal: Scrotal tongue, orofacial swelling, facial nerve palsy.
Ascher: Blepharochalasis, double upper lip, endocrine abnormalities (goiter).
Epidermodysplasia verruciformis: HPV types 3, 5, 8, SCC. AR, EVER1 or EVER2 defects.
Prader–Willi: Obesity after 12 months of age, MR, skin picking, chromosome 15 deletion in 60% (paternal imprinting), downslanting corners of mouth, almond-shaped eyes, hypopigmentation.
Angelman: Happy puppet syndrome, MR, szs, pale blue eyes, tongue protrusion, unprovoked laughter, hypopigmentation, maternal chromosome 15 deletion or (1/4) Ubiquitin-protein Ligase E3A (UBE3A) defects.
Donahue: Leprechaunism, lipodystrophy, AN, hypertrichosis. AR, INSR defects.
CADASIL: Cerebral Arteriopathy, Autosomal Dominant, with Subcortical Infarcts and Leukoencephalopathy, recurrent ischemic strokes, early dementia, granular osmiophilic deposits around vascular smooth muscles cells and under the basement membrane on EM. AD, NOTCH3 defects.
Lafora: Onset: late adolescence with death within a decade, progressive myoclonic epilepsy, ataxia, cerebellar atrophy, PAS±cytoplasmic eccrine duct inclusions. AR, EPM2A/Laforin defects.
Heck/focal epithelial hyperplasia: Occurs in American Indians, Eskimos, Latin Americans, oral mucosa infections with HPV 13, 32.
Lhermitte–Duclos: Dysplastic gangliocytoma, isolated or associated with Cowden. AD, PTEN defects.
Branchio-oculofacial/BOF: Laterocervical psoriasiform lesions, similar to aplasia cutis congenital, abnormal nasolacrimal ducts → infections, sebaceous scalp cysts, low pinnae, accessory tragus, broad nose, hypertelorism, loss of punctae, premature aging, AD.
Barber–Say: Hypertrichosis, lax skin, abnormal fingerprints, ectropion, macrostomia, MR.
CHIME: Migratory ichthyosiform dermatosis, Coloboma, Heart defects, migratory Ichthyosiform dermatitis, Mental retardation, Ear defects (deafness); also szs, abnormal gait.
Van der Woude: Congenital lower lip pits, cleft palate, hypodontia. AD, IRF6 defects.
Fibrodysplasia Ossificans Progressiva: Malformed great toes, osteoma cutis (endochondral). AD, ACVR1 defects.
Riley-Day/Familial dysautonomia: Feeding difficulties, lack of emotional tears, absent fungiform papillae (vs. absent filiform papillae in geographic tongue), diminished reflexes/pain/taste, no flare with intraepidermal histamine, drooling, labile BP, blotchy erythema while eating, pulmonary infxn, Ashkenazi. AR, IKBKAP defects.

Miscellaneous non-genetic syndromes

Schnitzler: Urticarial vasculitis, bone pain, fever, hyperostosis, IgM monoclonal gammopathy, arthralgia, LAN, HSM, elev ESR.

Frey: Gustatory hyperhidrosis, usually following trauma/surgery to the parotid gland (auriculotemporal nerve).

Dermoscopy

Polarized (PD) vs. nonpolarized (NPD)
- NPD requires liquid interface, direct skin contact (using a gel rather than alcohol leads to less distortion from pressure)
- NPD better for milia-like cysts, comedo-like openings, peppering/regression, blue-white areas, lighter colors
- PD better for vessels, red areas, shiny-white streaks/fibrosis

Algorithms
- **Two-step algorithm** – (1) Melanocytic or non-melanocytic (2) If melanocytic, then use global pattern and local features to distinguish melanoma
- **CASH algorithm** – Color, architecture, symmetry, homogeneity

Pigment network
- Pigment network – either typical (brown, narrow, regular mesh) or atypical (thick black, brown, or gray lines, irregular meshes, suggestive of melanoma)
- Pseudopigmented network – on face
- Pigment network but not melanocytic – SK, DF, accessory nipple

Features suggestive of melanoma
Streaks – melanoma
Blue-white veil – melanoma, Spitz, angiokeratoma
Black blotches – if irregular, suggestive of melanoma (if uniform, consider Reed)
Regression structures – melanoma (esp. with melanin peppering)
Radial streaming/pseudopods/branched streaks/broken network – melanoma
Milky-red areas – early melanoma
Dots/globules – if irregular, suggestive of melanoma

Acral melanocytic lesions
- Parallel–furrow, fibrillar, lattice-like or homogeneous patterns – acral melanocytic nevi
- Parallel–ridge pattern – acral melanoma (acrosyringia open onto ridges, ridges are wider than furrows)

Features suggestive of SK
Milia-like cysts – SK, papillomatous IDN
Comedo-like openings – SK, papillomatous IDN

Exophytic papillary structures – SK
Fat fingers – SK
Cerebriform surface – SK, BCC

Features suggestive of BCC
(Maple) leaf-like areas – BCC
Blue-gray blotches/ovoid nests/globules – pigmented BCC
Pink-white shiny areas – BCC
Spoke wheels – BCC

Dermoscopic vessels
Comma-like vessels – benign melanocytic lesion
Arborizing vessels – BCC
Hairpin vessels – SK, melanoma (if irregular), KA, SCC
Dotted/Irregular vessels – melanoma
Polymorphous vessels – melanoma
Corkscrew vessels – amelanotic melanoma metastases
Corona/wreath/crown vessels – surround sebaceous hyperplasia (central yellow globular structure)
Glomerular vessels – SCC, SCCIS
Point vessels – melanocytic neoplasms, superficial epithelial neoplasms (AK, SCCIS)

Features suggestive of other lesions
Red-blue/black lacunae/saccules – hemangioma, angiokeratoma (dark lacuna), subcorneal/subungual hematoma
Central white patch – DF (star-like white area surrounded by delicate pigment network)
Reddish homogeneous region surrounded by white collarette – PG
Moth–eaten border and fingerprint pattern – solar lentigo
Steel blue areas – blue nevi
EB nevi – often demonstrate certain specific features associated with melanoma (atypical pigment network, irregular dots/globules, atypical vascular pattern), but not other features (blue-white veil, regression structures/blue-white areas, irregular streaks, black dots)
LPLK – depends on involution stage, localized (early) or diffuse (late) pigmented granular pattern, regressive features (blue-white scar-like depigmented or vascular structures)
Facial lentigo maligna – asymmetric pigmented follicular openings, dark rhomboidal structures, slate-gray dots and globules
Scabies – triangular shape (delta glider) resembling circumflex accent (corresponds to head and front legs) dihydroxyacetone may cause changes in nevi (increased globules and comedolike pseudofollicular openings)

Patterns of melanocytic nevi/Lesions – Reticular, globular, homogeneous (blue), starburst (complete starburst – reed, spitz; incomplete starburst – melanoma), parallel (acral), multicomponent (melanoma), cobblestone (papillomatous IDN and congenital nevi), non-specific

Histopathologic correlates of dermoscopic features:

- Color according to Melanin location:
  - Black – upper epidermis
  - Brown – DEJ
  - Slate Blue – papillary dermis
  - Steel Blue – reticular dermis
- Pigment network – lines = rete ridges; spaces = superpapillary plates
- Pseudopigmented network on face – adnexal structures = holes (face has minimal rete ridges)
- Dots and globules – nests of melanocytic cells at different depths
- Black blotches – pigment everywhere (radially, epidermal, dermal)
- Cerebriform surface – gyrus = fat fingers; sulcus = pigmented keratin
- Leaf-like areas – islands of pigmented BCC (large islands = blue-gray ovoid nests)
- Blue-white veil – white = orthokeratotic hyperkeratosis; blue = dermal melanin.

Pathology

Histochemical staining

Stain	Purpose
Hematoxylin–eosin	Routine
Masson trichrome	Collagen (green), Muscle (red), Nuclei (black). Helps to distinguishing leiomyoma (red) from dermatofibroma (green)
Verhoeff von Gieson	Elastic fibers
Pinkus acid orcein	Elastic fibers
Gomori's aldehyde fuchsin	Elastic fibers (blue); collagen (red)
Movat's pentachrome	Connective tissue
Silver nitrate	Melanin, reticulin fibers
Fontana Masson	Melanin
Schmorl's	Melanin
DOPA-oxidase	Melanin
Gram	Gram+: blue-purple; Gram−: red

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Stain	Purpose
Methenamine silver (Gomori, GMS)	Fungi, Donovan bodies, Frisch bacilli, BM, sodium urate
Grocott	Fungi
Periodic acid-Schiff (PAS)	Glycogen, fungi, neutral MPS (diastase removes glycogen)
Alcian blue pH 0.5	Sulfated MPS
Alcian blue pH 2.5	Acid MPS
Toluidine blue	Acid MPS
Colloidal iron	Acid MPS
Hyaluronidase	Hyaluronic acid
Mucicarmine	Epithelial mucin
Leder	Mast cells (chloroacetate esterase)
Giemsa	Mast cell granules, acid MPS, myeloid granules, leishmania
Fite	Acid-fast bacilli
Ziehl–Neelson	Acid-fast bacilli
Kinyoun's	Acid-fast bacilli
Auramine O	Acid-fast bacilli (fluorescence)
Perls potassium ferrocyanide	Hemosiderin/Iron
Prussian blue	Hemosiderin/Iron
Turnbull blue	Hemosiderin/Iron
Alkaline Congo red	Amyloid (the Congo red variant pagoda red No. 9/Dylon is more specific for amyloid)
Thioflavin T	Amyloid
Acid orcein Giemsa	Amyloid
Cresyl violet	Amyloid, ochronosis
Von Kossa	Calcium
Alizarin red	Calcium
Pentahydroxy flavanol	Calcium
Scarlet red	Lipids
Oil red O	Lipids
Sudan black	Lipids, lipofuscin
Osmium tetroxide	Lipids
Dopa	Tyrosinase
Warthin Starry	Spirochetes, Donovan bodies
Dieterle silver	Spirochetes

Stain	Purpose
Steiner	Spirochetes
Bodian	Nerve fibers
PGP 9.5	Nerve fibers
GFAP	Glial, astrocytes, schwann cells
Feulgen	DNA
Methyl-green pyronin	DNA
Foote's, Snook's	Reticulin fibers
PTAH	Fibrin, infantile digital fibromatosis Inclusions (also stained by trichrome), granules of granular cell tumor, amoeba
Methylene blue	Ochronosis
Brown–Hopps	Bacteria
Brown–Brenn	Bacteria
McCallum–Goodpasture	Bacteria
DeGalantha	Urate crystals (20% silver nitrate also stains Gout; Gout preserved with etoh)
Ulex europaeus lectin	Endothelial cells
Peanut agglutinin	Histiocytes
Neuron-specific enolase	Neural, neuroendocrine, Merkel, granular cell tumor
Gross cystic disease fluid protein	Apocrine, Paget's, met breast CA

Immunohistochemical staining

EPIDERMAL	
Cytokeratin 20	Merkel cell (perinuclear dot)
Cytokeratin 7	Paget's
EMA	Eccrine, apocrine, sebaceous (also plasma cells, LyP, anaplastic CTCL – primary systemic not primary cutaneous)
CEA	Met adenoca, Paget's, eccrine, apocrine
BerEP4	BCC+, Merkel cell+, SCC-
MESENCHYMAL	
Desmin	Muscle
Vimentin	Mesenchymal cells (AFX, melanoma, sarcomas)
Actin	Muscle, glomus cell tumors
Factor VIII-related Ag (VWF)	Endothelial cells, megakaryocytes, platelets

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Stain	Purpose
Ulex europasus agglutinin I	Endothelial cells, angiosarcoma, Kaposi, keratinocytes
CD31	Endothelial cells, vascular tumor, angiosarcoma, NSF, scleromyxedema
CD34	DFSP†: CD34+, Factor XIIIa-
	DF: CD34−, Factor XIIIa+
	Endothelial cells, NSF, scleromyxedema
	Morphea: CD34+ spindle cells selectively depleted
	Focal CD34+ spindle cells around trichoepithelioma but not BCC
Procollagen I	Scleromyxedema > NFD/NSF
GLUT1	Positive in infantile hemangiomas and placenta, negative in vascular malformations, RICH, NICH, PG, tufted angiomas, kaposiform hemangioendotheliomas (reduced or negative in subglottic infantile hemangiomas)
WT1 and LeY	Positive in infantile hemangiomas, negative in vascular malformations
D2-40* and LYVE-1	Lymphatics and kaposiform hemangioendothelioma
NEUROECTODERMAL	
S100	Melanocytes, nerve, Langerhans, eccrine, apocrine, chondrocytes, sebocytes
HMB-45	Melanocytes
MART-1	Melanocytes
Mel-5	Melanocytes
CD1A	Langerhans cells
Synatophysin	Merkel cells
Chromogranin	Merkel cells
HEMATOPOIETIC	
Factor XIIIa	PLTs, macrophages, megakaryocytes, dendritics (NSF**, scleromyxedema), DF but not DFSP
HAM-56	Macrophages
Alpha-1-antitrypsin	Macrophages
κ & λ	Mature B cells & plasma cells
BCL1	Mantle cell lymphoma
BCL2	Follicular center lymphoma (except primary cutaneous follicle center lymphoma), BCC, trichoepithelioma (bcl2- except outer layer)
BCL6	Follicular center lymphoma
CD2	T-cell

Stain	Purpose
CD3	Pan T-cell marker, NK cells
CD4	T helper cell, Langerhans
CD5	T cells, some B cells in mantle zone, depleted in MF†
CD7	T cells, depleted in MF
CD8	T cytotoxic cells
CD10	B cell in BL, follicular center lymphoma, lymphoblastic lymphoma, AFX
CD14	Monocytes
CD15	Granulocytes, Hodgkin's
CD16	NK cells
CD20	B cells
CD22	B cells
CD23	B cells, marginal zone lymphoma, CLL
CD25 (IL-2R)	Activated B/T/Macs, evaluate before denileukin diftitox
CD30 (Ki-1)	Anaplastic CTCL, LyP, anaplastic large cell lymphoma, activated T and B cells, RS cells, (Hodgkin's)
CD43 (Leu-22)	Pan T-cell marker, mast cells, myeloid cells
CD45 (LCA)	CD45RO: memory T cells CD45RA: B cells, naive T cells
CD56	NK cells, angiocentric T-cell lymphoma, Merkel cell
CD68	Histiocytes, AFX, NSF, scleromyxedema, mast cells, myeloid cells
CD75	Folicular center cells
CD79a	B cells, plasma cells (plasmacytoma)
CD99	Precursor B-lymphoblastic leukemia/lymphoma, Ewing's, PNET
CD117 (c-kit)	Mast cells
CD138	Plasma cells

‡ DFSP – CD34+ XIIIa- Stromelysin-3- CD68- CD163- HMGA1/2- vs. DF: CD34- XIIIa+ Stromelysin-3+ CD68+ CD163+ HMGA1/2+; Increased hyaluronate in the stroma of DFSP vs. DF; Tenascin positivity at DEJ overlying DF but not DFSP.

* D2-40 – Often negative, but may have focal positivity in congenital hemangioma and tufted angioma.

** "circulating fibrocyte" – procollagen I^+ $C11b^+$ $CD13^+$ $CD34^+$ $CD45RO^+$ $MHCII^+$ $CD68^+$.

† MF – usually CD3+ CD4+ CD5- CD7- CD8- Leu-8- CD45RO+ with $\alpha\beta$ TCR; MF is also usually CD30− but not all CD30+ cases undergo anaplastic large cell transformation (anaplastic large cell transformation from MF, Hodgkin's, or LyP is usually ALK- and EMA- similar to primary systemic anaplastic large T-cell lymphoma but unlike primary cutaneous anaplastic large T-cell lymphoma).

Pathologic bodies

Body/sign/clue	Features	Diagnosis
Antoni A tissue	Densely cellular areas with palisaded nuclei, fasicles and verocay bodies	Schwannoma
Antoni B tissue	Loose, gelatinous stroma, fewer cells, microcystic changes	Schwannoma
Arao-Perkins Bodies	Elastin bodies in conntective tissue streamers below vellus follicles	Androgenic alopecia
Asteroid bodies	Star-like cytoplasmic inclusions in giant cells	Sarcoidosis and other granulomatous diseases (TB, botryomycosis, sporotrichosis, actinomycosis, leprosy, foreign body granuloma, berylliosis)
Azzopardi effect	Basophilic vascular streaking (encrusted nuclear material/DNA around vessels)	Tumor necrosis, crush
Banana bodies	1. Curvilinear, membrane bround bodies in Schwann cells on EM	1. Farber disease
	2. Crescentic, ocher bodies in the dermis	2. Ochronosis
Beanbag cells	Large macrophages demonstrating cytophagocytosis	Subcutaneous panniculitis-like T-cell lymphoma/cytophagic histiocytic panniculitis
Birbeck granules	Tennis racket structures on EM	Langerhans cells
Busy dermis		GA, interstitial granulomatous dermatitis, resolving vasculitis, folliculitis, early KS, desmoplastic MM, chronic photodermatosis, breast CA mets

Caspary–Joseph spaces	Clefts at DEJ associated with basal layer injury, a.k.a. Max-Joseph cleft	LP, lichen nitidus
Caterpillar bodies	Eosinophilic, segmented, elongated (epidermal) bodies on roof of blisters (Col IV)	Porphyrias
Cholesterol clefts	Needle-like crystals	Sclerema neonatorum, subcutaneous fat necrosis of the newborn (may have more inflammation and calcification than sclerema), post-steroid panniculitis, NXG, cholesterol emboli, NLD, trichilemmal cyst
Chunks of coal	Large atypical lymphoid cells with hyperchromatic nuclei	Lymphomatoid papulosis
Cigar bodies	Oval, elongated yeast cells	Sporotrichosis
Colloid/Civatte bodies	Apoptotic bodies in epidermis (civatte) or extruded into papillary dermis (colloid)	Lichen planus and variants
Comma-shaped bodies	Cytoplasmic worm-like bodies on EM	Benign cephalic histiocytosis
Conchoidal bodies (Schaumann Bodies)	Shell-like, lamellated, basophilic, calcified protein complexes in giant cells	Sarcoidosis and other granulomatous diseases
Corps grains	Small, dyskeratotic, acantholytic keratinocytes with elongated grain-shaped nuclei seen in stratum corneum	Darier, Grover, warty dyskeratoma, Hailey–Hailey (rare)
Corps ronds	Enlarged, dyskeratotic, acantholytic keratinocytes with round nuclei and perinuclear halo seen in Malpighian layer and surrounding basophilic dyskeratotic material	Darier, Grover, warty dyskeratoma, Hailey–Hailey (rare)
Councilman bodies	Cytoplasmic inclusion	BCC

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Body/sign/clue	Features	Diagnosis
Cowdry Type A & B	Eosinophilic, intranuclear inclusions surrounded by clear halo	A – HSV, CMV (+ "owl's eye cells" – viral inclusions in endothelial cells), VZV; B – Polio
Cytoid bodies	Heterogeneous round, oval, or polygonal deposits, usually in dermis	Collective term for colloid bodies, Russell bodies, amyloid, elastic globes
Donovan bodies	Single or clustered rod safety pin-like bacteria in macrophages	Granuloma inguinale
Dutcher bodies	Intranuclear pseudoinclusions in malignant plasma cells, Ig	B-cell lymphoma, multiple myeloma
Farber bodies	Comma-shaped tubular structures in cytoplasm of fibroblasts and endothelial cells on EM	Farber disease
Flame figures	Poorly circumscribed, small areas of amorphous eosinophilic material adherent to dermal collagen	Eosinophilic cellulitis + flame figures = Well's syndrome > arthropod bites, parasites, BP, DH, eosinophilic panniculitis
Floret cells	Multinucleated giant cells with marginally placed nuclei	Pleomorphic (spindle cell) lipoma
Flower cells	Atypical CD4+ T cells, prominent nuclear lobation	HTLV-1, ATL
Ghost cells	Calcified necrotic anucleate adipocytes with thickened membrane	Pancreatic panniculitis (+saponification) (vs. shadow/ghost cells in pilomatricomas)
Giant granules in neutrophils	Large granules	Chédiak–Higashi
Globi	Globular clumps of AFB in macrophages (foam/lepra/virchow cells)	Lepromatous leprosy
Guarnieri bodies	Cytoplasmic, eosinophilic inclusions in epidermal cells	Smallpox, caccinia
Henderson–Patterson bodies	Large, cytoplasmic, eosinophilic inclusions in keratinocytes	Molluscum contagiosum

Homer–Wright Rosettes	Central nerve fibrils, peripheral small tumor cells	Cutaneous neuroblastoma
Jordans' anomaly	Vacuolated leukocytes on peripheral smear	Dorfman–Chanarin
Kamino bodies	Eosinophilic globules at DEJ made of BMZ components	Spitz nevus
Lafora bodies	Concentric amyloid deposits (=polyglucosan bodies)	Lafora disease
Lipofuscin-like granules	Yellow-brown granules in dermal macrophages	Amiodarone hyperpigmentation
Macromelanosomes	Large melanosomes	Café au lait macules, Chédiak-Higashi, XP macules, Hermansky–Pudlak
Marquee sign	Organisms at the periphery of macrophages	Leishmania
Medlar/sclerotic bodies	Muriform cells, "copper pennies," round thick-walled brown fungi	Chromoblastomycosis
Michaelis–Gutman bodies	Calcified, degraded bacteria in macrophages, lamellated	Malakoplakia
Mikulicz cells	Large macrophages containing Klebsiella rhinoscleromatis	Rhinoscleroma
Morulae	Leukocyte intracytoplasmic inclusions, Ehrlichia multiplying in cell vacuoles	Ehrlichiosis
Mulberry bodies	Dermal mulberry-like endosporulation/sporangia	Prototheca (vs. "mulberry-like figures" on EM in Fabry eccrine glands)
Mulberry cells	Moruloid, granular, eosinophilic adipocytes – "ping pong balls"	Hibernoma
Negri bodies	Eosinophilic, cytoplasmic inclusions in neurons	Rabies

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Body/sign/clue	Features	Diagnosis
Odland bodies	Small, lamellated granules rich in lipids in granular layer, membrane-coating granules on EM	Important for permeability barrier, absent in harlequin fetus
Onion skinning	Perivascular, hyaline material	Lipoid proteinosis (onion skin fibrosis in GF, angiofibroma)
Papillary mesenchymal bodies	Germinal hair bulb	Trichoblastoma, trichoepithelioma
Pautrier microabscesses	Three or more atypical lymphocytes within epidermis	Mycosis fungoides
Pericapillary fibrin caps		Venous leg ulcers, venous stasis, venous hypertension, non-venous leg ulcers
Pohl–Pinkus Marks	Isolated hair shaft narrowing (severe = bayonet hair)	Surgery, trauma
Psammoma bodies	Concentrically laminated, round, calcified bodies	Cutaneous meningioma, ovarian and thyroid neoplasms, papillary kidney carcinoma, mesothelioma
Pustulo-ovoid bodies of Milian	Large eosinophilic granules with clear halo	Granular cell tumor
Russell bodies	Immunoglobulin deposits in plasma cells	Rhinoscleroma, plasmacystosis
Spiderweb cells	Globular, striated, vacuolated cells	Adult rhabdomyoma
Splendore–Hoeppli deposits	Flame figure-like eosinophilic deposits around organisms	Parasites, fungus, bacteria
Verocay bodies	Palisading nuclei in rows around eosinophilic cytoplasm	Schwannoma
Weibel–Palade bodies	Dense rod or oval organelles on EM	Endothelial cells

Adapted from Solky BA, Jones JL, Pipkin CA. *Boards' Fodder – Histologic Bodies* (http://www.aad.org/members/residents/fodder.html)

Other derm path buzzwords, patterns, DDx

Findings	Association(s)
BUZZWORDS	
"Sawtoothing"	Lichen planus
"Ball and claw"	Lichen nitidus (also see histiocytes)
"Swarm of bees"	Alopecia areata
"Toy soldiers," "strings of pearls," "fettucine collagen"	Mycosis fungoides
"Coat-sleeve" perivascular lymphocytosis	Gyrate erythema (consider lymphocytic vasculitis)
"Tea cup" scale/Tea cup sign (oblique, upwardly angulated parakeratosis)	Pityriasis rosea
"Dirty feet"	Solar lentigo (vs. "dirty fingers" – lentigo simplex), Becker's nevus
"Bubblegum stroma"	Neurofibroma
"Glassy collagen"	Keloid
"Tadpoles/sperm in the dermis"	Syringoma (if clear cell variant, think diabetes)
"Corn flakes"	Keratin granuloma
"Red crayons" (blood vessels)	Atrophie blanche
Eyeliner sign ("the thin brown line" – basal layer preventing invasion), "windblown"	Bowen
"Caput medusa" (radially streaming follicles/sebaceous glands)	Trichofolliculoma
"Crazy pavement"	Colloid milium > nodular amyloidosis
Collagen trapping	DF, DFSP (+ fat entrapment)
Squamous eddies	Irritated seborrheic keratosis, inverted follicular keratosis, incontinentia pigmenti
Checkerboard alternating para/ortho-keratosis	Pityriasis rubra pilaris
Mounding parakeratosis	Pityriasis rosea (+spongiosis, RBC extravasation), guttate psoriasis (+PMNs), PL (interface, lymphocytic vasculitis), nummular eczema
Layered dermal infiltrate	Necrobiosis lipoidica diabeticorum (+ necrobiosis, plasma cells)
Sandwich sign (PMNs between ortho and parakeratosis)	Tinea

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Findings	Association(s)
Cysts with arabesques lining	Lipodermatosclerosis
Nuclear molding	Merkel cell carcinoma ("bunch of grapes"), metastatic neuroendocrine carcinoma
Comedonecrosis ("comedo" pattern with central necrosis)	Sebaceous carcinoma
Wiry collagen (fibroplasias of papillary dermis)	Mycosis fungoides
GROWTH PATTERNS	
Storiform/cartwheel pattern	Storiform/sclerotic/plywood collagenoma, DF, DFSP, fibromyxoid sarcoma, schwannoma, solitary fibrous tumor, perineurioma, primary cutaneous meningioma
Herringbone pattern	Fibrosarcoma
Jigsaw puzzle pattern (+ "pink cuticle")	Cylindroma
Tissue culture pattern (+ microcysts)	Nodular fasciitis ("myxoid scar")
Chicken-wire vascular pattern	Myxoid liposarcoma (collapsed linear blood vessels)
Swiss cheese pattern ("oil cysts")	Sclerosing lipogranuloma
Reticulated pattern	Fibroepithelioma of pinkus, reticulated seborrheic keratosis, tumor of the follicular infundibulum
Peripheral palisading	Tumors: BCC, trichoepithelioma, basaloid follicular hamartoma, trichilemmoma (thick BM), tumor of the follicular infundibulum, sebaceoma, pilar tumor, schwannoma, epitheliod sarcoma (necrobiosis); Rashes: GA (mucin), RA/RF nodule (fibrinoid necrosis), gout (urate crystals), NLD (necrobiosis), NXG (degenerated collagen), palisaded neutrophilic and granulomatous dermatitis, eruptive xanthoma
DIFFERENTIAL DIAGNOSES	
Eosinophilic spongiosis	Arthropod bite, incontinentia pigmenti (First stage) (look for necrotic keratinocytes), pemphigus (esp. vegetans), BP, CP, herpes gestationis, PUPPP, ACD, eosinophilic folliculitis, id, drug

Findings	Association(s)
Grenz zone	GF, EED, leprosy, lymphocytoma cutis, B-cell lymphoma/leukemia, acrodermatitis chronica atrophicans, DFSP/DF
Bland dermal spindle cell proliferations	DF, DFSP, neurofibroma, dermatomyofibroma, leiomyoma (perinuclear halo), solitary fibrous tumor
Atypical dermal spindle cell proliferations	AFX, melanoma, SCC, leiomyosarcoma, angiosarcoma ("falling apart" appearance), Kaposi (+ eosinophilic globules, promontory sign, plasma cells)
Small blue cell dermal proliferations	Glomus tumor, Merkel cell carcinoma, lymphoma, eccrine spiradenoma, metastatic carcinoma
Small red deep well-circumscribed tumor	Angioleiomyoma
Busy dermis	GA, interstitial granulomatous dermatitis, resolving vasculitis, folliculitis, early KS, desmoplastic MM, chronic photodermatosis, breast CA
Boxcar/square biopsy	Scleroderma, scleredema, scleromyxedema, NLD, nl back skin, radiation (prominent telangiectasia)
~Normal appearance	TMEP, amyloidosis (lichen/macular-look for pigment incontinence), connective tissue nevus, myxedema, ichthyosis, cutis laxa, anetoderma, tinea versicolor, GVHD, argyria
Single filing of cells	Leukemia, (pseudo)lymphoma, metastatic carcinoma (breast), glomus cell tumor, GA, congenital melanocytic nevus, microcystic adnexal carcinoma
Pseudobullae (massive superficial dermal edema)	PMLE, sweet, erysipelas, erysipeloid, arthropod bite reaction, chilblains/perniosis
Pale epidermis	Pellagra, acrodermatitis enteropathica, necrolytic migratory erythema, Hartnup, clear cell acanthoma/papulosis
Basement membrane thickening (with rash)	Lupus, lichen sclerosis, dermatomysosits
Accessory polypoid lesion	Accessory tragus (vellus hairs), accessory nipple (smooth muscle, traumatic/amputation neuroma), accessory digit (nerves – vs. prominent often vertical collagen in acquired digital fibrokeratoma)

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Findings	Association(s)
Pagetoid spread	Paget's (spares basal layer), melanoma, SCC, Bowen, sebaceous carcinoma, MF, neuroendocrine tumor, rectal carcinoma
Wedge-shaped	Lymphomatoid papulosis (infiltrate), tick bite reaction (infiltrate), Degos (infarct), PLEVA (infiltrate) (EM-like with parakeratosis), lichen planus (wedge-shape hypergranulosis), melanocytic nevi (esp. with halo)
Peripheral collarette	Lobulated capillary hemangioma, cherry angioma, myxoid cyst, angiokeratoma, AFX, sebaceous adenoma, clear cell acanthoma
Lymphoid follicles	ALHE, pseudolymphoma (top heavy, well-formed, tingible body macs), B-cell lymphoma (bottom heavy, poorly-formed)
ARTIFACTS	
Vacuolated keratinocytes	Freeze artifact
Ribbon-like blue material	Gel foam artifact
"Chafs of wheat" (spindled epidermal cells)	Electrodessication artifact
MINOCYCLINE PIGMENTATION	
Type I: Facial, blue-black, scars	Iron stains +, melanin stains − (unlike types II and III, type I is not related to prolonged exposure to MCN)
Type II: Extremities, blue-gray	Iron stains +, Fontana reaction + but not melanin
Type III: Photodistributed or generalized, muddy brown	Epidermal hypermelanosis, melanin stains +, iron stains −
GIANT CELLS	
Touton	Circumferential arrangement of nuclei ('wreath'), central glassy and foamy peripheral cytoplasm
Langhans	Horseshoe arrangement of nuclei
Foreign body	Haphazard nuclei

Cysts	Lining, contents	Clinical, hints
Keratinous, infundibular type (epidermoid)	Epidermis-like, includes granular layer, loose orthokeratin	Punctum, foreign body giant cell reaction
Milia	Like KCIT but thin wall and small	
Keratinous, trichilemmal type (pilar)	Stratified squamous, no granular layer, cholesterol clefts, compact keratin	Scalp, may calcify
Steatocystoma	Ruggated, thin stratified squamous, glassy pink surface, sebaceous glands	Pachyonychia congenital type II, KCIT-like keratin, trunk
Vellus hair cyst	Thin epidermal-like lining, laminated keratin, vellus hairs	Small, trunk, AD, numerous, ± pigment
Pigmented follicular	Stratified squamous, many pigmented hairs	M>F, pigmented, face
Apocrine hidrocystoma	Apocrine cells	Solitary, small, H/N, Schopf-Schulz-Passarge, focal dermal hypoplasia
Dermoid	Stratified squamous, adnexal structures	Lateral eyebrow, periocular, midline, newborn/infant
HPV-related	Epideral-like + inclusions, vacuolar changes, hypergranulosis, verrucous lining	HPV-60 related version on soles
Thyroglossal duct	Stratified squamous, may have cilia, columnar/ cuboidal elements	Thyroid follicles, midline neck
Branchial cleft	Stratified squamous, may have cilia, pseudostatified columnar elements	Lymph tissue, lateral neck, jaw, preauricular
Bronchogenic	Goblet cells, cilia, respiratory epithelial lining	Suprasternal, precordial, smooth muscle, cartilage, often neck
Cutaneous ciliated	Cilia, columnar/cuboidal	F>M, thighs/buttocks
Median raphe	Pseudostratified columnar, mucinous cells	Ventral penis/scrotum
Thymic	Stratified squamous or cuboidal, ± cilia	Thymic tissue, neck, mediastinum

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Pseudocyst of auricle	Within cartilage, no lining	Often asx, upper pinna
Digital mucous	No true lining, stellate fibroblasts, myxoid, thin overlying epidermis	Dorsal digit
Mucocele	No true lining, mucin, fibrous tissue, macs	Lower lip, buccal, salivary glands
Pilonidal	Sinus tract, inflammation, hair shafts	Sacrococcygeal

Part 2
Surgery

Handbook of Dermatology: A Practical Manual Margaret W. Mann
 ISBN: 978-1-405-18110-5

Surgical Margins Guidelines

Tumor type	Tumor characteristic	Excision margin
Melanoma	*In situ*	0.5 cm
	≤1 mm in depth	1 cm
	1.01–2 mm in depth	1–2 cm + SLN
	>2 mm	2 cm + SLN
	(see melanoma guide pg.)	
BCC	<2 cm in diameter	3–4 mm
	>2 cm in diameter	6 mm or Mohs
SCC	low risk*	4 mm
	high risk**	6 mm or Mohs

**Low-risk SCC*: well-defined margins, well differentiated, low-risk area, primary tumor. ***High-risk SCC*: poorly defined margins, large size (>2 cm), poorly differentiated histologically, high-risk tumor location, recurrent tumor, invasion to subcutaneous fat, perineural invasion, organ transplant, or immunosuppressed patient. Adapted from *Huang* C and *Boyce SM*. Surgical margins of excision for basal cell carcinoma and squamous cell carcinoma. *Semin Cutan Med Surg.* 2004; 23:167–73.

Indications for Mohs micrographic surgery

Location

- *Near functional/cosmetic structure*: eyes, nose, lips, fingers, hand, foot, genitals
- *High-risk locations*: H-zone of the face and skin overlying cartilage and bony structures: periorbital (inner canthus, eyelids); periauricular (ear, preauricular area, retroauricular sulcus); nose, temple; perioral (nasolabial folds, philtrum, upper lip, vermillion border).

Tumor features

- *Large size* (>2 cm any location; >1 cm on face, neck, scalp; >0.6 cm in H-zone)
- *Poorly defined* tumor
- *Recurrence/incomplete* prior excision
- *Aggressive histology*:
  - BCC with morpheaform, micronodular, basosquamous, or sclerosing type
  - SCC with poorly differentiated, acantholytic, adenosquamous, desmoplastic, infiltrative type
  - Perivascular/perineural invasion
  - Other tumors: microcystic adnexal carcinoma, DFSP, merkel cell carcinoma, malignant fibrous histiocytoma
- Location in scar, chronic ulcer (Marjolin's ulcer)
- Tumor arising in sites of *prior radiation Tx*.

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Patient features

- *Immunosuppression*, transplant recipient, chronic lymphocytic leukemia, HIV
- History of multiple skin cancers
- Basal cell nevus, XP, Bazex syndromes.

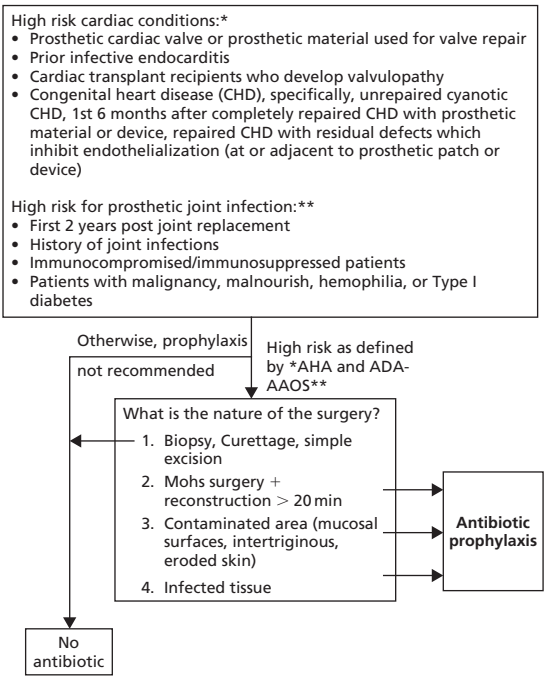
Guideline for Prophylactic Antibiotics

Use of antibiotic prophylaxis for endocarditis indicated for surgical procedure on infected tissue in patients with high-risk cardiac lesion or as detailed below

Antibiotic (trade size)	Adults	Children
Cephalexin (500 mg, 250 mg/5 ml)	2 g	50 mg/kg
Dicloxacillin (500 mg, 250 mg/5 ml)	2 g	50 mg/kg
If penicillin allergic		
Azithromycin (250, 500 mg)	500 mg	15 mg/kg
Clarithromycin (500 mg, 250 mg/5 ml)	500 mg	15 mg/kg
Clindamycin (300 mg)	600 mg	20 mg/kg
Oral site:		
Amoxicillin (500 mg, 250 mg/5 ml)	2 g	50 mg/kg
If penicillin allergic		
Azithromycin (250, 500 mg)	500 mg	15 mg/kg
Clarithromycin (500 mg, 250 mg/5 ml)	500 mg	15 mg/kg
Clindamycin (300 mg)	600 mg	20 mg/kg
Groin and lower extremity site		
Cephalexin (500 mg, 250 mg/5 ml)	2 g	50 mg/kg
If penicillin allergic		
Trimethoprim-Sulfamethoxazole, double strength 1 tab Levofloxacin	500 mg	

One hour prior to surgery: (all p.o. doses).

Algorithm for antibiotic prophylaxis



Adapted from *Wilson W. et al. Prevention of Infective Endocarditis. *Circulation* 2007; 116:1736–54; Messingham MJ and Arpey CJ. Update on the Use of Antibiotics in Cutaneous Surgery. *Derm Surg* 2005; 31:1068–78; **Wright TI, et al. Antibiotic prophylaxis in dermatologic surgery: advisory statement 2008. *J Am Acad Dermatol* 2008; 59:464–73.

Guideline for Prophylactic Antivirals

History of HSV infection of the orofacial area is an indication for prophylaxis for facial resurfacing or orofacial surgery. Treat for 7–14 days with acyclovir, valacyclovir, or famciclovir to suppress viral reactivation during reepithelialization

Acyclovir (Zovirax)	400 mg tid x 7–14 d
Valacyclovir (Valtrex)	500 mg bid x 7–14 d
Famciclovir (Famvir)	250 mg bid x 7–14 d

Anesthetics

Mechanism of action: Reversibly inhibit nerve conduction by blocking sodium ion influx into peripheral nerve cells = prevent depolarization of nerves.

Practical tips to decrease pain with injections

The patient
- Distract, pinch the skin
- Consider topical anesthesia (i.e. LMX) prior to infiltration.

The anesthetic agent
- Warming to 37–42°C
- Buffered lidocaine with bicarb (increase the pH 3.3 → 7.4)
  Add 1 cc 8.4% $NaHCO_3$ to 10 cc Lidocaine.

The injection technique
- Fine needle (27 or 30 gauge)
- Inject slowly
- If possible, through a dilated pore or wound edge
- Deeper injections into SQ area hurts less (go from deep subdermal to tight dermal)
- Minimize needle punctures by moving in a fan shape
- Consider nerve blocks or ring blocks.

Dose calculation

1% = 1 g/100 ml = 10 mg/cc
0.1% = 0.1 g/100 ml = 1 mg/cc

Tumescent anesthesia

Lidocaine 0.05–0.1% + epinephrine 1:1,000,000
Max tumescent is 35–50 mg/kg
Peak lidocaine level at 12–14 h

Ingredient	Quantity (ml)
Normal saline 0.9%	1000
Lidocaine 1%	50–100
Sodium bicarbonate 8.4%	10
Epinephrine 1:1000	1

Topical anesthetic (see drug section p. 253)

LMX4	Lidocaine 4%
EMLA cream*	2.5% Lidocaine + 2.5% prilocaine

*Risk of methemoglobinemia. Also, may create artefactual vacuolization/swelling of the upper epidermis and basal layer damage/clefting.
Cavef A et al. Histologic Cutaneous Modifications After the Use of EMLA Cream. *Arch Derm*. 2007; 143:1074–76.

Adverse reaction to local anesthetics

Condition	Pulse	BP	Signs and symptoms	Management
Vasovagal Rxn	▼	▼	Diaphoresis, hyperventilation, nausea	Trendelenburg, cool compress
Epinephrine Rxn	▲	▲	Sweating, tachypnea, HA, palpitation	Reassurance, beta-blocker
Anaphylaxis	▲	▼	Tachycardia, bronchospasm	Epinephrine 1:1000 × 0.3 ml SQ. Antihistamine, airway maintenance
Lidocaine Toxicity				
1–6 μg/ml	Nl	Nl	Circumoral paresthesia, metallic taste, tinnitus, lightheadedness	Observe
6–9 μg/ml	Nl	Nl	Tremors, nausea, vomiting, hallucination	Diazepam, airway maintenance
9–12 μg/ml	▼	▼	Seizures, cardiopulmonary depression	Respiratory support
>12 μg/ml	–	–	Coma, cardiopulmonary arrest	CPR/ACLS

Adapted from Snow SN, Mikhail GR. Mohs Micrographic Surgery. Madison: The University of Wisconsin Press, 2004, 2nd Edition. Chapter 14. Table 14-3.

Local anesthetic

Generic name	Trade name	Pregnancy category†	Potency	Onset (min)	Without epinephrine		With epinephrine	
					Duration (min)	Max dose (mg/kg) for adults	Duration (min)	Max dose (mg/kg) for adults
AMIDE ("I" before–caine = amide)								
Lidocaine	Xylocaine	B	Intermed	<2	30–120	4.5 (30 cc for 70 kg)	60–400	7 (50 cc for 70 kg)
Bupivacaine	Marcaine, Sensorcaine	C*	High	2–10	120–240	2.5	240–480	3
Mepivacaine	Carbocaine	C*	Intermed	3–20	30–120	6	60–400	8
Prilocaine	Citanest	B	Intermed	5–6	30–120	7	60–400	10
Etidocaine	Duranest	B	High	3–5	200	4.5	240–360	6.5
ESTER								
Procaine	Novocain	C	Low	5	15–30	10	30–90	14
Chloroprocaine	Nesacaine	C	Low	5–6	30–60	10	–	–
Tetracaine	Pontocaine	C	High	7	120–240	2	240–480	2

†Epinephrine is pregnancy category C.

*Bupivacaine and mepivacaine: pregnancy category C due to potential for fetal bradycardia.

	Metabolized by	Excretion	Allergic reaction
AMIDE	Liver dealkylation	Kidney	Rare, due to preservative methylparaben (if allergic: switch to preservative free lidocaine)
ESTER	Tissue (pseudocholinesterase)	Kidney	More common due to metabolite to PABA (*p*-aminobenzoic acid) (if allergic: switch to amides)

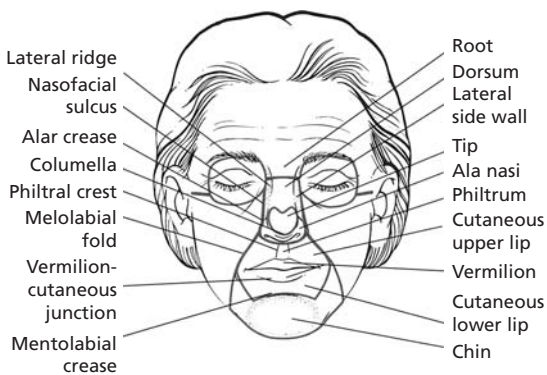
Nerve blocks*

See Plates 1–4.

Surgical Anatomy

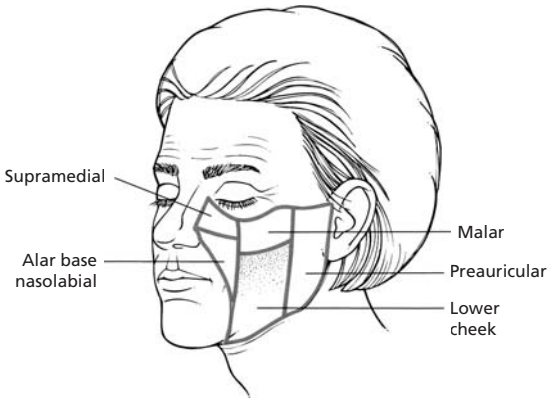
Anatomy of the face

Cosmetic unit of the central face



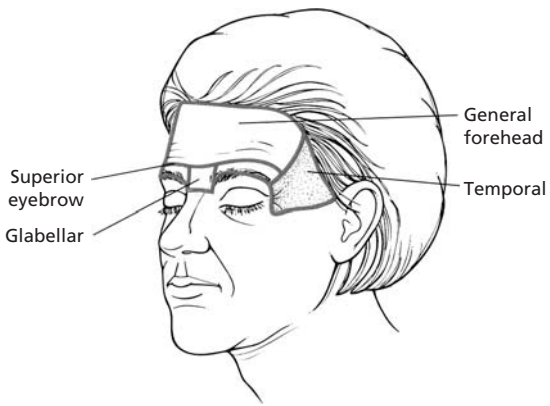
From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 2, with permission from Elsevier.

Cosmetic units of the cheek



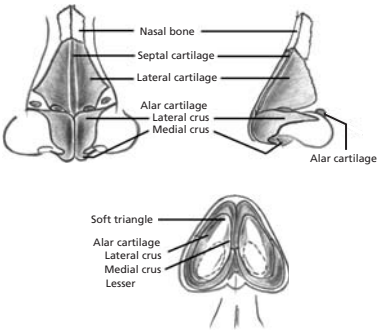
From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 2, with permission from Elsevier.

Cosmetic units of the forehead



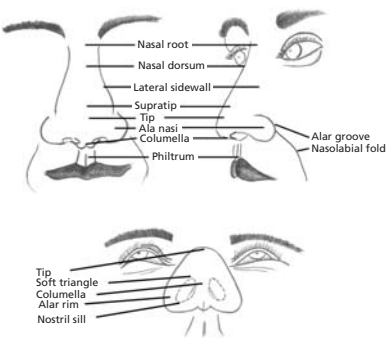
From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 2, with permission from Elsevier.

Cosmetic units of the nose



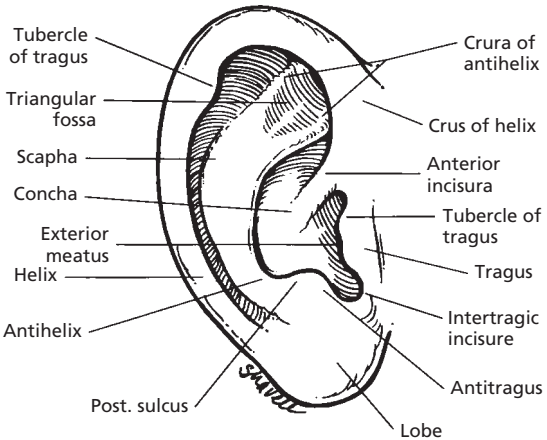
Courtesy of Dr. Quan Vu

Anatomy of the nasal cartilage



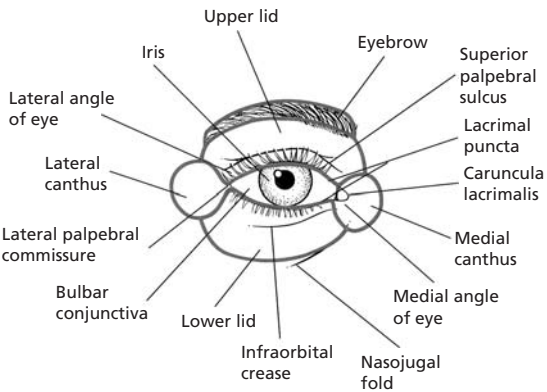
Courtesy of Dr. Quan Vu

Anatomy of the ear



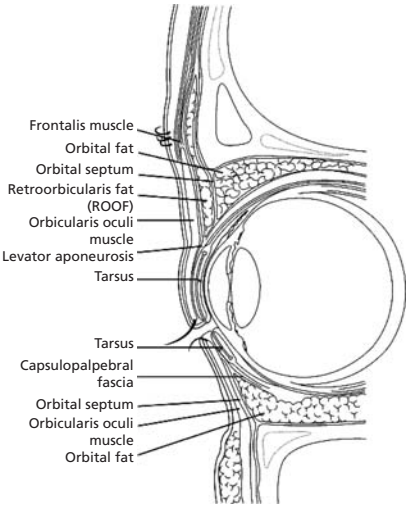
From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 186, with permission from Elsevier.

Cosmetic units of the eye



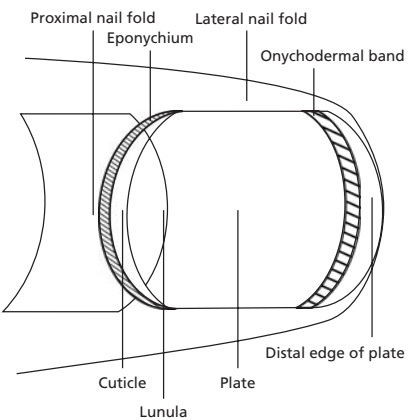
From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 3, with permission from Elsevier.

Anatomy of the eye

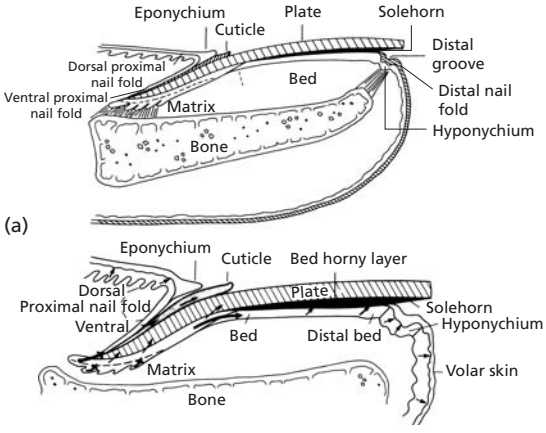


From Robinson JK (ed.). *Atlas of Cutaneous Surgery.* WB Saunders: 1996, p. 3, with permission from Elsevier.

Anatomy of the nail

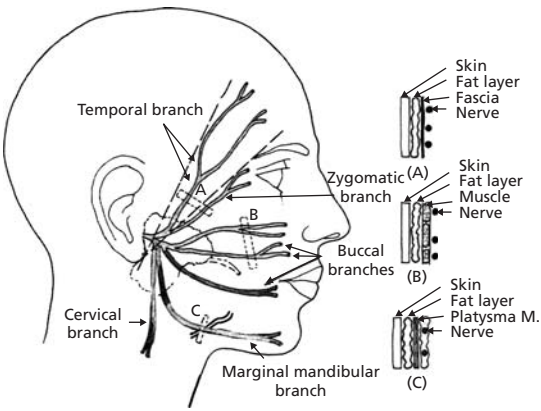


From Scher RK and Daniel CR. *Nails: Therapy, Diagnosis, Surgery.* WB Saunders: 1997, pp. 13–14, with permission from Elsevier.



Danger zones in surgery

Danger zones of the face



From Bernstein G. *J Dermatol Surg Oncol*. 12; 1986, p. 725, with permission from BC Decker Inc.

Danger zones: location and innervation

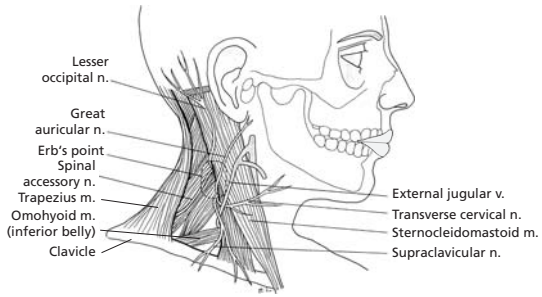
1. Temporal branch of CN VII
   Most vulnerable location: Mid-zygomatic arch.
   Nerve course: Nerve exits the superior–anterior portion of the parotid gland, then courses 0.5 cm below the tragus to 1.5 cm above the lateral eyebrow. Nerve lies just beneath the skin, subcutaneous fat, and SMAS.
   Motor innervation: Frontalis, upper portion of the orbicularis oculi and corrugator supercilii.
   Damage: Inability to raise eyebrow and wrinkle forehead. Results in a flat forehead and droopy eyebrow.

2. Marginal mandibular branch of CN VII
   Most vulnerable location: Mid-mandible 2 cm lateral to the oral commissure.
   Nerve course: Nerve exits the inferior–anterior portion of the parotid gland, then courses along the angle of the mandible across the facial artery and vein. May be 2 cm or more below the inferior edge of the mandible if the head is rotated or hyperextended. Lies beneath the skin, subcutaneous fat and SMAS.
   Motor innervation: Orbicularis oris, risorius, mentalis, and depressor muscles of the mouth.
   Damage: Drooping of the mouth, inability to pull the lip laterally and inferiorly with smiling.

3. Great auricular nerve (C_2 and C_3)
   Most vulnerable location: 6.5 cm below the external auditory canal along the posterior border of the sternocleidomastoid muscle.
   Nerve course: Nerve courses toward the lobule posterior to the external jugular vein.
   Damage: Sensory innervation, results in numbness of the inferior 2/3 of the ear and adjacent cheek and neck.

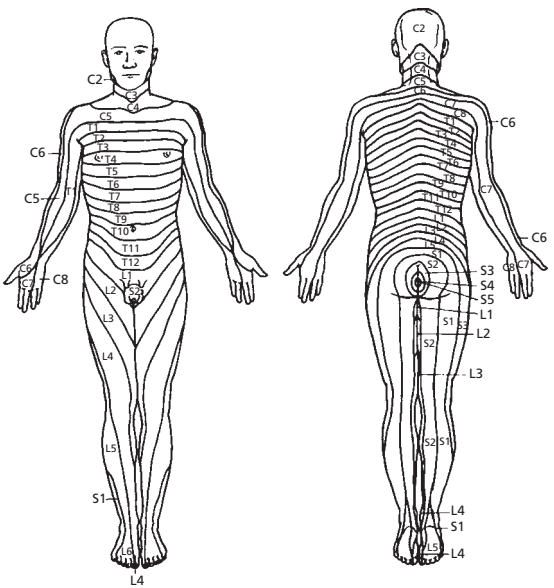
4. Spinal accessory nerve (CN XI)
   Most vulnerable location: Erb's point.
   Nerve course: Nerve exits from behind the SCM at Erb's point and courses diagonally and inferiorly across the posterior triangle. Draw a line from the angle of the jaw to the mastoid process – Erb's point is located 6 cm vertically below the midpoint of this line at the posterior border of the sternocleidomastoid (within a 2 cm area). Also may define area by drawing a line horizontally across the neck from the thyroid notch to the posterior border of the sternocleidomastoid (1 cm above and 1 cm below).
   Innervation: Location of the great auricular, less occipital, and spinal accessory nerve. The spinal accessory nerve innerves the trapezius muscle.
   Damage: Winged scapula – inability to shrug the shoulder and abduct the arm.

Danger zone of the neck: Erb's point



From Wheeland RG (ed.). *Cutaneous Surgery.* WB Saunders: 1994, p. 61, with permission from Elsevier.

Dermatomal distribution of sensory nerves

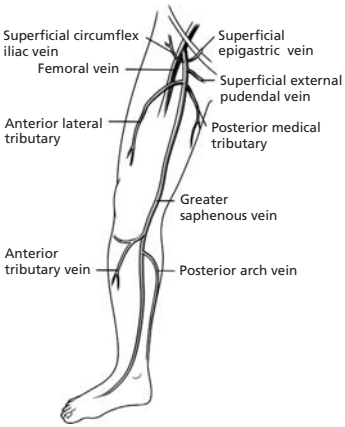


From Leventha. *Fractures, dislocations, and fracture–dislocations of the spine.* In: Canale ST et al. (eds). Campbell's operative orthopaedics, 10th edition. Mosby: 2003, with permission from Elsevier.

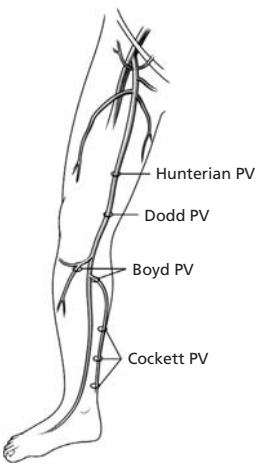
Anatomy of the lower extremity venous system

From Min RJ et al. Duplex ultrasound evaluation of lower extremity venous insufficiency. *J Vasc Interv Radiol* 2003; 14:1233–41, with permission from Elsevier.

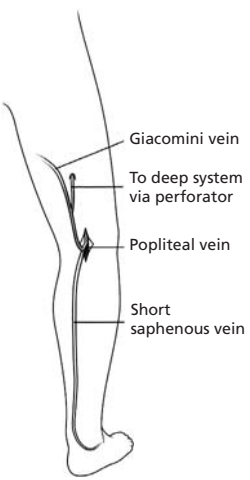
Anatomy of the greater saphenous vein



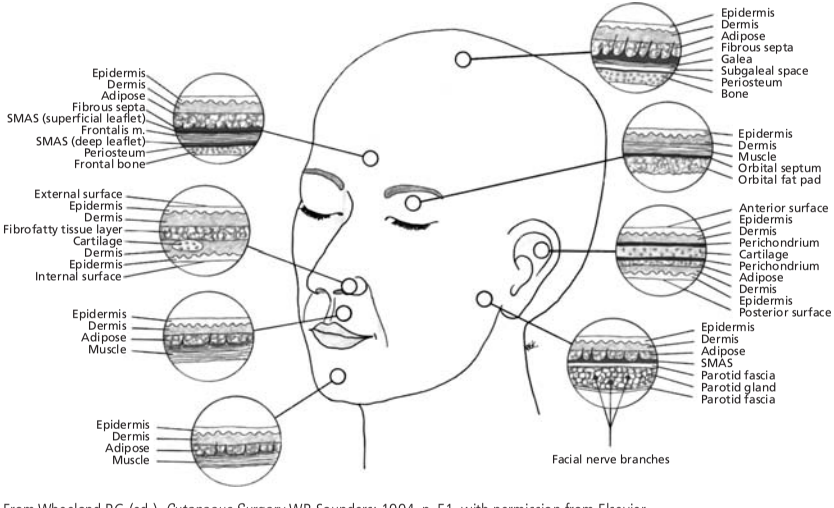
Anatomy of the perforator veins



Anatomy of the short saphenous vein



Cutaneous Reconstruction

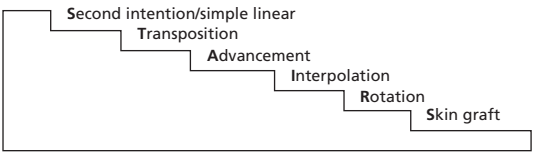


From Wheeland RG (ed.). *Cutaneous Surgery.* WB Saunders: 1994, p. 51, with permission from Elsevier.

Undermining depths in reconstruction

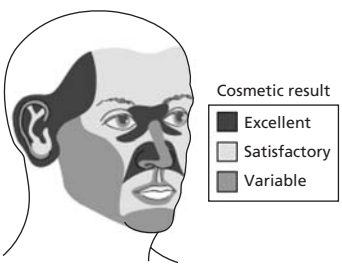
Scalp	Subgaleal
Forehead	Subgaleal or subcutaneous fat above frontalis fascia
Temple/zygomatic arch	Superficial subcutaneous fat above temporal branch of facial nerve
Mandible	Superficial subcutaneous fat above marginal mandibular branch of facial nerve
Ear	Above perichondrium
Lip	Above orbicularis oris
Nose	Above perichondrium/periosteum
Rest of face	Superficial subcutaneous fat, above the parotid duct
Terminal hair bearing area	Deep to hair papillae
Lateral neck	Superficial subcutaneous fat above spinal accessory nerve
Trunk/extremities	Above muscular fascia
Hands and feet	Subdermal

Repair Options: STAIRS



Second intention

Cosmetic result of wound healing by secondary intention according to anatomical site



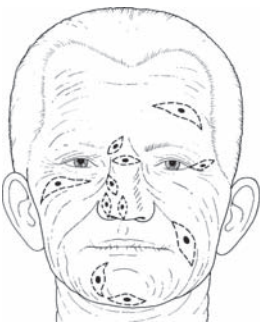
From Zitelli JA. Wound healing by secondary intention. *J Am Acad Dermatol.* 1983; 9:407–415, with permission from Elsevier.

- Ideal for
  - Concave areas: Periorbital (medial canthus), temple, conchal bowl, alar crease
  - Shallow defects (i.e. shins)
  - Fair skinned patient (wound tends to heal with whiten scar)
  - Poor operative candidates
- May take weeks/months to heal, so patient must be able to perform wound care
- May heal with atrophic, hypertrophic, white scar
- Can perform delayed repair/graft at 2–4 weeks.

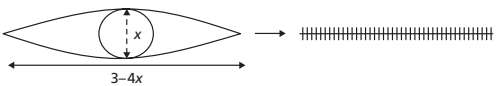
Simple linear closure

- 3–4:1 Length:width ratio
- Orient along relaxed skin tension lines at junction of cosmetic subunits.

Relaxed skin tension line (RSTL) on the face showing orientation of simple linear closure

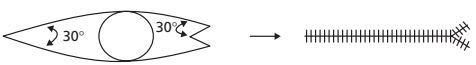


From Burge S and Rayment R. *Simple Skin Surgery.* Blackwell Scientific, 1986, with permission from Blackwell Publishing.



M-plasty

- Modification of the linear closure
- GOAL: Shortens the length of a scar

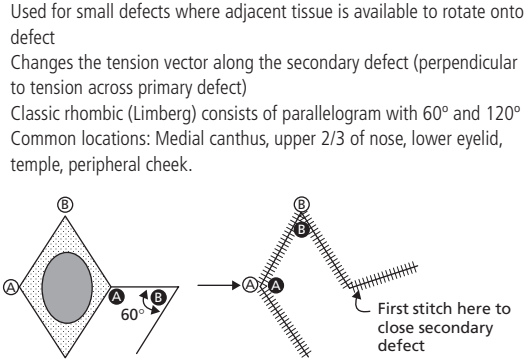


Transposition flap

- GOAL: Redistribute tension vectors
- Flap rotates about a pivotal point at the base of the pedicle and is transposed over an island of normal skin
- Pivotal restraints may limit its movement
- Wide undermining necessary to prevent pincushioning
- Common flaps: Rhombic, bilobe, z-plasty, banner, nasolabial (melolabial).

Rhombic

- Used for small defects where adjacent tissue is available to rotate onto defect
- Changes the tension vector along the secondary defect (perpendicular to tension across primary defect)
- Classic rhombic (Limberg) consists of parallelogram with 60° and 120°
- Common locations: Medial canthus, upper 2/3 of nose, lower eyelid, temple, peripheral cheek.



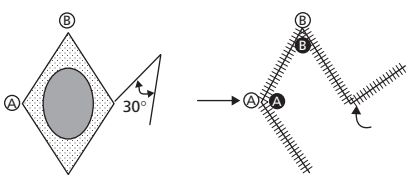
Tips

– Design flap off the short axis of the defect
– All sides of the triangle and parallelogram should be equal in length.

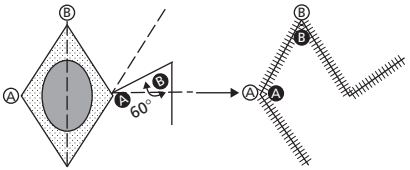
Modifications of rhombic flaps

Webster 30°

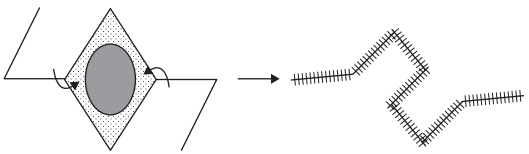
Narrower flap, easier to close secondary defect
Less reorientation of tension vectors



Dufourmental
Compromise between Limberg and Webster flap
Extend dotted lines then bisect them
Second incision parallel to defect midline

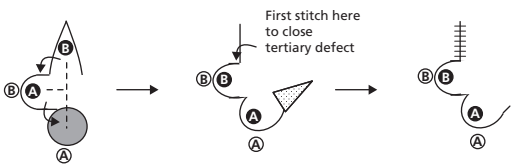


Bi-rhombic flap



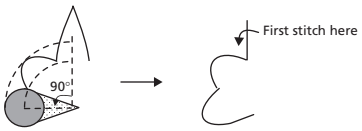
Bilobe

- Used for small defects 1–1.5 cm in size. Common location: lower 1/3 of nose
- Tension is shared between the secondary and tertiary defects.



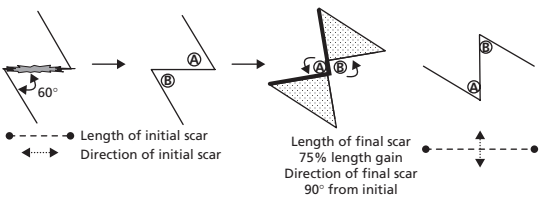
Zitelli-modified bilobe flap

- Determine location of standing cone, then draw ~90° (Zitelli modification) line
- First lobe is at 45° – equal or slightly smaller than defect
- Second lobe is at 90° to the standing cone
- Wide undermining in the submuscular plane to prevent trapdoor effect.

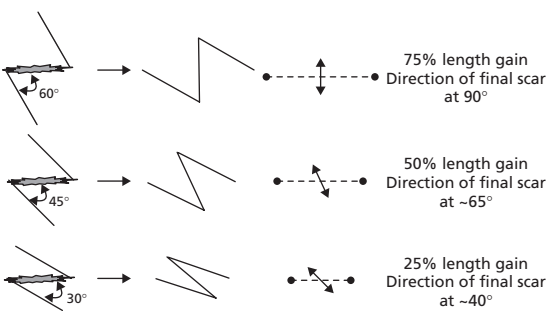


Z-plasty

- GOAL: Changing the direction of a scar or to elongate a scar
- Limbs of the Z should be of equal lengths



- The degree of the limbs determines both the direction and the length of final scar.

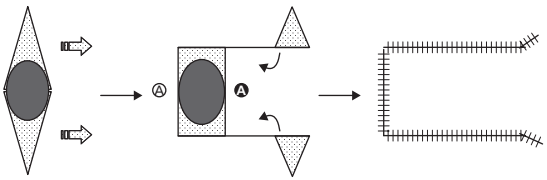


Advancement flap

- GOAL: Modification of the linear closure, with standing cones (Burow triangle) displaced to a more desirable position (i.e. away from free margin)
- Tension vector remains parallel to the motion of the flap
- Types of advancement flaps: U-plasty, H-plasty, Burow advancement, modified crescentic advancement, O → T, island pedicle.

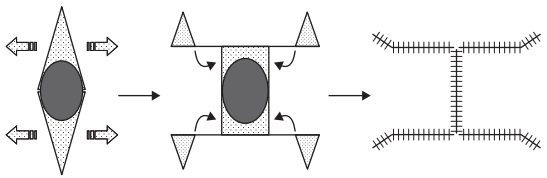
U-plasty/O → U: unilateral advancement

- Burow triangles created away from defect in one direction
- Useful along eyebrow and helical rim.



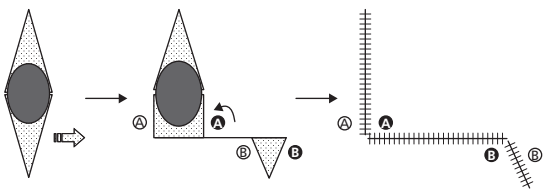
H-plasty/O → H: bilateral advancement

- Burow triangles created away from defect bilaterally
- Useful if tissue reservoir is available bilaterally.



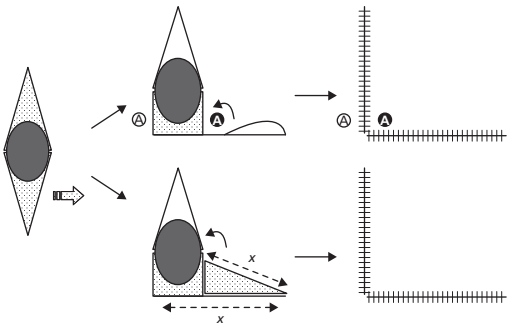
Burow's advancement flap: unilateral advancement

- Displaces one of the standing cone to a more desirable location
- Useful if defect is along lateral upper cutaneous lip → may displace one of the standing cone to the nasolabial folds.



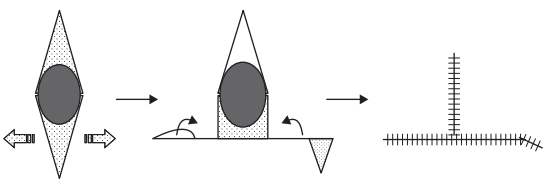
Modified crescentic advancement flap: unilateral advancement

- Modification of the Burow triangle
- Crescentic standing cone removed along the flap to lengthen it
- Eliminates the need for excision of a standing cone.



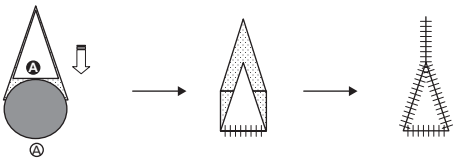
O → T/T-Plasty/A → T: bilateral advancement

- Displaces one of the standing cone bilaterally
- Useful adjacent to a free margin or along the junction between two cosmetic units (brow, eyelid, forehead, lip).



Island pedical flap/kite/V → Y advancement

- Island of tissue detached from periphery but with underlying subcutaneous and muscular pedicle
- Caution: no undermining to base of island – must keep flap attached to underlying pedicle to ensure good blood supply.



Interpolation flap

- GOAL: Coverage of large defects requiring flap with robust blood supply
- Commonly axial pattern flap-based on named direct cutaneous artery
- Robust blood supply allow greater ratio of length to width
- Two-staged procedure
- Base is usually located at some distance from defect. Pedicle must pass over or under an intervening bridge of intact skin
- Types of flaps: Paramedian, nasolabial, abbe.

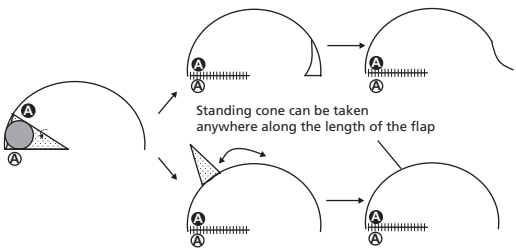
Flap	Arterial supply	Defect location	Pedicle division
Paramedian forehead	Supratrochlear artery	Large distal nasal defect	2–3 weeks
Retroauricular helical	Random flap: rich vascular supply from posterior auricular, superficial temporal, and occipital branches	Large helical rim defect	3 weeks
Nasolabial	Angular artery	Large ala defect	2–3 weeks
Abbe	Superior or inferior labial artery	Large lip defect	3 weeks

Rotation flap

- GOAL: Covering a defect when there is an abundant surrounding tissue reservoir
- Pivotal flap with a curvilinear incision–the flap and defect form a semicircle
- Rotates in an arc about a pivotal point near the defect
- Distributes the tension vector along the curvilinear line
- Common locations: Scalp, lateral cheek, infraorbital, temple
- Types of rotation flaps: Unilateral rotation, bilateral rotation (O → Z), pinwheel, dorsal nasal flap, Tenzel/Mustarde flaps.

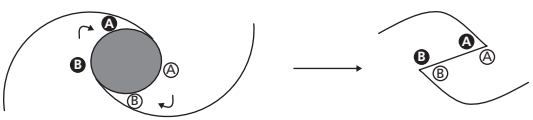
Unilateral rotation flap

- Usually flap is inferiorly/laterally based to improve lymphatic drainage and decrease flap edema
- Consider backcut to improve mobility.



O → Z Plasty/bilateral rotation flap

- Useful when there is insufficient tissue reservoir for unilateral flap
- Common location: scalp.



Dorsal nasal rotation/Reiger/hatchet flap

- Useful for nasal defect <2.5 cm on the lower 2/3 of the nose, best if midline
- Flap along the entire nasal dorsal
- Undermine at the level of the perichondrium/periosteum
- Backcut in the glabella.

Mustarde/Tenzel rotation flap

- Laterally based cheek rotation flap
- Useful for defect along supramedial cheek/lower eyelid
- Mustarde flap mobilizes entire cheek for defect >½ of eyelid
- Tenzel flaps mobilizes partial cheek for defect <½ eyelid.

Skin graft

- GOAL: Surgical defect which cannot be closed with adjacent local skin or allowed to heal by second intention; useful for larger wounds, especially in areas that require tumor surveillance
- Stages of skin graft

Stage	Events	Graft	Timeline
Imbibition	"Ischemic period" – nutrient through osmosis (bolster improves osmosis)	Dark color, edematous	24–48 h
Inosculation	Anastomosis of existing blood vessels	Pink	48–72 h (up to 10 days)
Neovascularization	New capillary ingrowth to graft from wound bed	Hypopigment, less edema	6–7 days

- Three major types:
  (1) Full thickness skin graft (FTSG) = epidermis + full dermis
  (2) Split thickness skin graft (STSG) = epidermis + partial dermis
  (3) Composite graft = skin (epidermis and dermis) + additional component (cartilage or fat).

FTSG

- Minimal contraction ~15%
- Better cosmesis than STSG – good color, texture, and thickness match
- Must have intact perichondrium/periosteum for survival – higher metabolic demand than STSG = higher rates of graft failure
- Most useful for defects less than 3 cm
- Common sites: Eyelids, medial canthus, helical rim, conchal bowl, nasal tip, digits
- Good donor sites: Preauricular/postauricular area, supraclavicular, standing cones (Burow graft), conchal bowl, upper eyelid, forehead.

STSG

- Higher risk for contraction, poor cosmesis
- Useful for very large defects: Can use fenestration/meshing to enlarge size

- Donor site heal by second intention can be painful
- Large grafts need to be harvested with special equipment
- Better survival than FTSG due to low nutritional requirements
  - Thin: 0.005–0.012 in.
  - Medium: 0.012–0.018 in.
  - Thick: 0.018–0.028 in.

Composite graft

- Less likely to contract, better cosmesis
- Highest risks for necrosis due to avascular tissue (cartilage) and thicker graft
- Useful when bulk and structural support is needed (i.e. nasal alar defects).

Types of graft	Nutritional needs	Risk of graft failure	Cosmesis and tissue match	Contraction risk	Durability/ Strength	Sensation
FTSG	High	Higher	Good	Low	Good	Good
STSG	Low	Lower	Poor	High	Poor	Fair
Composite	High	Highest	Good	Low	Excellent	Fair

Causes of graft failure

- Poor blood and nutritional supply: Nicotine use, nutritional deficiency, collagen vascular disease
- Poor graft bed contact: Graft movement (activity, trauma, poor immobilization), hematoma, seroma
- Infection: Immunosuppression, diabetes, systemic disease, poor wound care
- Physician technique: Incomplete defatting, high tension due to inadequate size, rough tissue handling, excessive cautery.

Sutures

Absorbable

Material	Origin	Filament	Tensile strength 50%	Absorption	Reactivity	Degradation
Plain gut	Animal collagen*	Twisted	1 week	14–80 days	High	Proteolysis
Fast absorbing gut	Animal collagen*	Twisted	3–7 days	21–42 days	High	Proteolysis
Vicryl rapide	Polyglactin	Braided	5 days	42 days	Moderate	Hydrolysis
Monocryl	Poliglecaprone	Monofil	1 week	90–120 days	Low	Hydrolysis
Chromic gut	Plain gut tanned with chromium salts	Twisted	2–3 weeks	30–80 days	High, less than plain gut	Proteolysis
Dexon	Polyglycolic acid	Braided	2–3 weeks	90 days	Low	Hydrolysis
Vicryl	Polyglactin	Braided	3 weeks	80–90 days	Moderate	Hydrolysis
PDS	Polydioxanone	Monofil	4 weeks	180 days	Low	Hydrolysis
Maxon	Polyglyconate	Monofil	4 weeks	180 days	Very low	Hydrolysis

*Gut made from mucosa/submucosa of sheep or beef intestine.

Non-absorbable

Material	Origin	Filament	Tensile strength	Reactivity	Elasticity	Handling
Silk	Silk	Braided or twisted	Low, 3–6 months	High	Inelastic Soft suture	Best
Prolene/ Surgilene	Polypropylene	Monofil	High, 2 years	Least	Very elastic Stiff suture	Fair–good
Ethilon/Monosol/ Dermalon	Nylon	Monofil	High, losing 10–20%/year	Low	Mild elasticity Stiff suture	Fair
Surgilon/Nurolon/ Mersilene	Nylon Polyester	Braided Monofil or braided	High, losing 10–20%/year High, permanent	Moderate Low	Mild elasticity Mild elasticity	Good Very good
Ethibond/Dacron Novafil	Polybutester	Monofil	High	Low	Very elastic	Very good

Suture removal time

Area	Removal time (days)
Face	4–5
Neck	5–7
Scalp	7
Trunk	7–12
Extremities	10–14

Electrosurgery*

Modality	Terminals	Gap output	Voltage	Amperage	Capability
Electrodessication	1	Markedly damped	High	Low	Superficial destruction
Electrofulguration	1	Markedly damped	High	Low	Superficial destruction (spark gap)
Electrocoagulation	2	Moderately damped	Mod	Mod	Deep penetration and destruction, Good hemostasis
Electrosection	2	Undamped	Low	High	Cutting

*Electrocautery: not electrosurgery, no electric current, uses heat conduction.

Wound Healing

Time	Tensile strength vs. baseline
1 week	5%
1 month	40%
1 year	80%

- Three phases of wound healing: Inflammatory (days) → Proliferation/Granulation (weeks) → Remodeling (months)
- Platelets are the first cells to appear
- Collagen: Early in wound healing, Collagen III predominates, then later replaced by Collagen I.

Wound dressing

	Brand name	Composition	Absorptive	Others	Indications
Adhesive dressing					
Hydrocolloids	Duoderm	Hydrophilic base and adhesive with polyurethane	Good, forms gel with exudates	May leave in place × 1 week	Pressure ulcers, second intention wounds
Film dressing	Tegederm Op-site Bioocclusive	Polyurethane file	None (may cause fluid collection) Gas permeable	Impermeable to bacteria	Best used in conjunction with alginate/hydrogen. Good for monitoring wounds. Lacerations/ abrasions/STSG donor site
Non-adhesive dressing					
Alginates	Sorbsan algiderm	Alginic acid	Highly	Hemostatic agent: releases Ca^{++}	Highly exudative wounds
Hydrogels	Vigilon tegagel	1% water, cross-linked polymers Semitransparent gel	Highly	Cooling/pain relief	Abrasion wounds (post laser, peels)
Foam dressing	Flexzan Allevyn Vigifoam	Hydrophilic foam, polyurethane, silicone	Moderate, gas and water permeable	Compresses chronic leg wounds, conforms to body contours	Pressure ulcer, exudative wound
Gauze dressing	Telfa pad Vaseline gauze, Xeroform		Excellent	Cheap, readily available	Use to cover nonocclusive, nonadherent dressing

Antiseptic Scrubs

Agent	Mechanism of action	Gram+	Gram−	Mycobacteria	Viruses	Fungi	Spores	Speed of action	Residual activity	Other
Alcohol 60–95%	Denature proteins (bacterial cell wall)	+++	+++	+++	+++	+++	−	Fast	None	Flammable with laser/cautery. Allow to dry on surface
Chlorhexidine 2–4% (Hibiclens)	Impairs cell membrane	+++	++	+	+++	+	−	Intermed	Excellent	Ototoxicity, keratitis, skin irritant
Iodine 3% (Lugol)	Oxidation	+++	+++	+++	+++	++	+	Intermed	Minimal	Skin irritant inactivated by blood/sputum
Iodophors-(Betadine) Povidone-iodine 7.5–10%	Oxidation/ substitution by free iodine: disrupts S–H and N–H bonds, C=C bonds in fatty acids	+++	+++	+	++	++	−	Intermed (needs to dry)	Minimal	Skin irritant (less than iodine). Inactivated by blood/sputum. May cross-react with radiopaque iodine. Surfactant + iodine = iodophor

TechniCare PCMX Chloroxylenol	Disrupt cell membrane	+++	+	+	+	+	Unknown	Slow	Good	Addition of EDTA increases its activity against Pseudomonas
Triclosan 0.2–2%	Disrupts cell wall, inhibits fatty acid synthesis, binds bacterial enoyl-acyl carrier protein reductase (ENR, *fabI*)	+++	++	+	+++	−	Unknown	Intermed	Good	Forms chloroform and dioxins when combined with chlorine in tap water
Benzalkonium (Quaternary ammonium)	Dissociation of cell membranes; disrupts intermolecular interactions	++	+	+/−	+ Lipophilic	+/−	Unknown	Slow	Good	Use only in combination with alcohols. Eyedrop preservative. Easily inactivated by cotton gauze/organic materials

Adapted from *CDC. MMWR Recomm Rep.* 2002; 25:51(RR-16):1–48

Lasers

Laser	Wavelength (nm)	Type	Depth (μm)	Target	Usage
CO_2	10,600	IR	20	Water	Resurface, destruction, coagulation, cut
Erbium:YAG	2940	IR	1	Water	Superficial resurface, destruction
Holmium:YAG	2100	IR	200	Water	Superficial resurface, destruction
Nd:YAG	1064	IR	1600	Mel, Hb	Deep dermal pigment, black/ blue tattoo, epilation, non-ablative resurface, leg veins, telangiectasia
Diode	800, 810, 930	R	1400	Mel	Dermal pigment, epilation, leg veins, vascular
Q-switched alexandrite	755	R	1300	Mel	Tattoo (black, blue, green), epilation, pigmentation
Q-switched ruby	694	R	1200	Mel	Epidermal/Dermal pigment, tattoo (black, blue, green), epilation
Argon-pumped dye	630, 514, 488	O, G, B	600	Hb, mel	Vascular, epidermal pigment
PDL	585–595	Y	600	Hb, mel	Vascular, hypertrophic scar
Copper (bromide) vapor	578, 511	Y, G	400, 300	Hb, mel	Vascular, epidermal pigment
Krypton	568, 531	Y G	400	Hb, mel	Vascular, epidermal pigment
Frequency doubled Q-switched Nd:YAG/ KTP	532	G	400	Mel, Hb	Vascular, epidermal pigment, red tattoo
Flash lamp pumped PDL	510	G	300	Mel, Hb	Vascular, hypertrophic scar
Argon	488, 514	B	200, 300	Mel, Hb	Vascular, epidermal pigment
Pulse excimer	351, 308, 193	UV	0.5	Protein	Psoriasis, vitiligo, LASIK

IR: infrared; R: red; O: orange; Y: yellow; G: green; B:blue; UV: ultraviolet; Mel: melanin; Hb: hemoglobin.

	Unit	Definition
Energy	J	
Power	W	Rate of energy delivery, laser output
Fluence	J/cm^2	Amount of energy delivered per area
Pulse width	sec	Duration of laser exposure
Spot size	mm	Diameter of laser beam
Thermal relaxation time	sec	Time needed for the heated target to cool by 50% of its peak temperature through diffusion
Chromophore		Target of laser

Laser principles (LASER = Light Amplification by Stimulated Emission of Radiation)

1. monochromatic (single wavelength)
2. coherent (in phase with time and space)
3. collimated (parallel waves)

Selective photothermolysis: Selective heating of a target chromophore occurs when

1. selected wavelength is preferentially absorbed by the target chromophore
2. energy is high enough to damage the chromophores
3. pulse duration of the laser is shorter than the thermal relaxation of the target

$$\text{Laser output} = \text{Power (W)} = \frac{\text{Fluence (J/cm}^2) \times \text{Spot size (mm)}}{\text{Pulse width (sec)}}$$

To increase laser output → Increase fluence
→ Increase spot size
→ Decrease pulse width

Thermal relaxation time

Chromophore target	Size (μm)	Thermal relaxation time
Melanosome	0.5–1.0	20–40 ns
Tattoo pigment particles	0.5–100	20 ns – 3 ms
Epidermis	50	1 ms
Telangiectasias	30–50	1 ms
Blood vessel	100–300	5–30 ms
Melanin in hair follicle	200	20–100 ms

Laser treatment of tattoo pigment

Tattoo	Pigment	Wavelength absorbed (nm)	Laser
Black	Carbon (India ink), iron oxide, logwood	1064 755 694	Nd:YAG Q-switched alexandrite Q-switched ruby
Blue	Cobalt aluminate	1064 755 694	Nd:YAG Q-switched alexandrite Q-switched ruby
Green	Chromic oxide, lead chromate, malachite, ferro- and ferricyanides, phthalocyanine dyes, Curcuma	755 694	Q-switched alexandrite Q-switched ruby
Yellow	Cadmium sulfide	No good laser	
Red	Mercury sulfide (cinnabar), cadmium selenide, iron oxide (may turn black with laser tx)	532 510	Q-switched Nd:YAG PDL

Photoinduced eye injury

	Wavelength (nm)	Exposure risk	Ocular target	Eye effect
UVB/UVC	200–320	Sunburn	Cornea	Photokeratitis (Snow blindness)
UVA	320–400	PUVA, Excimer	Lens	Photochemical UV cataract, delayed (years)
Visible	400–760	Ruby, PDL, Argon	Retina (melanin, photoreceptors)	Photochemical and thermal retinal injury (Flash blindness)
Infrared A	760–1400	Nd:YAG	Retina	Same as above
Infrared B	>1400	CO_2, Erb:YAG	Cornea (water)	Corneal burn

Depth of laser penetration
Stratum corneum
Epidermis
Dermis
Dermal vessels/subcutaneous fat
CO2 10,600 nm
Er:YAG 2940 nm
Nd:YAG 1064 nm
Diode 810 nm
Alexandrite 755 nm
Ruby 694 nm
PDL 585 nm
KTP 532 nm
UVA 320–400 nm
UVB 290–320 nm
UVC 200–290 nm
VISIBLE
V B G Y O R
Wavelength (nm)
100 200 300 400 500 600 700 800 900 1000 1500 2000 3000 5000 7500 10,000 20,000 nm
10^-4 10^-3 10^-2 10^-1 1 10 100 10^3 10^4 10^5 10^6 10^7 10^8 10^9 10^10
Wavelength (nm)
Gamma rays
X-ray
UV
Infrared
Microwave
Radio
Absorption coefficient
KTP PDL
Ruby
Alexandrite
Diode
Nd:YAG
Er:YAG
CO2
400 500 600 700 800 900 1000 1500 2000 3000 5000 10,000
Wavelength (nm)
Water
Melanin
OxyHb
Hb

Photodynamic Therapy

Basic principles

- Components: (1) Photosensitizer, (2) light source, and (3) tissue oxygenation
- Two steps: (1) Administration of photosensitizer (topical or systemic), and (2) irradiation with visible light
- Effects:
  - Through Type 2 photo-oxidative reactions, PDT produces cytotoxic reactive oxygen species (singlet oxygen, superoxide anion, hydroxyl radical, hydrogen peroxide) → oxidation of amino acids, proteins, lipids → necrosis, apoptosis
  - Modifies immune responses (i.e. cytokine expression)
  - For acne, targets sebaceous glands and decreases P. acnes (P. acnes accumulates porphyrins).

Applications

AKs, acne, BCC, Bowen, photoaging, verruca vulgaris, hidradenitis suppurativa, sebaceous hyperplasia.

Photosensitizer properties and options

Methyl aminolevulinic acid (MAL)	Aminolevulinic acid (ALA)
METVIX® cream 160 mg/g	Levulan® Kerastick® topical solution 20%
More lipophilic (some passive) transmembrane diffuse	More hydrophilic (needs active transport)
Deeper penetration	Poorer penetration*
Intracellularly, MAL is demethylated to ALA	Not a photosensitizer but converted to protoporphyrin IX (through heme biosynthesis pathway)
Red light (Aktilite)	Blue light (Blu-U)
FDA approved for treatment of AK. Approved in Europe for treatment of BCC	FDA approved for treatment of AK

* Can increase ALA penetration by increasing the application time, occluding, scrubbing with acetone, or using iontophoresis or electroporation.

- Selectivity: MAL and ALA (1) concentrate in tumor cells and newly formed endothelium and (2) require specific wavelengths to become activated
- Heme pathway:
  - In the cytoplasm, ALA → porphobilinogen → uroporphyrinogen III → coproporphyrinogen III
  - In the mitochondria, coproporphyrinogen III → protoporphyrinogen IX → protoporphyrin IX → iron incorporated by ferrochelatase

- Systemic photosensitizers have tetrapyrrolic structure and are given intravenously due to their low cutaneous penetration; examples: HpD and porfimer sodium (Photofrin®).

Light source

- ALA and MAL converts to protoporphyrin IX, which has an absorption peak at the Soret band (~405 nm, within blue light) as well as peaks at higher wavelengths (Q-bands – at 510, 545, 580, and 630 nm)
- Q-band peaks are ~15× smaller than the Soret band peak
- Red light (Aktilite 630 nm) penetrates deeper into skin than blue light (Blu-U – 405–420 nm).

Adverse effects

- Topical: Mild, transient burning pain, pruritus, erythema, edema, crusting, scaling
- Systemic: Longer-lasting generalized phototoxicity and sensitivity (sometimes months), photophobia, ocular pain, pigmentary changes, N/V, liver toxicity, metallic taste, SLE exacerbation.

Precautions/contraindications

- Contraindicated in patients with porphyria, cutaneous sensitivity to the light source's wavelength(s), allergies to porphyrins or any part of the ALA solution/MAL cream (MAL cream contains peanut/almond oils)
- Contraindicated in patients who are pregnant or breast-feeding
- Patients should review all medications (OTC, herbal, rx – TCNs, thiazides, griseofulvin, sulfonamides, sulfonylureas, phenothiazines) which may impact (1) photosensitivity and (2) ALA/MAL penetration (retinoids)
- Deep recurrence can occur with partial (superficial only) tx of malignancies.

Protocol

ALA PDT

- Wash treatment area with non-soap cleanser. Consider acetone scrub prior to applying ALA
- Per package instructions: Crush Levulan Kerastick at two points, then sequentially down the stick. Shake stick vertically for 2 min. Must be used within 2 h of resuspension
- Avoid applying ALA to ocular/mucosal surfaces
- For large areas, wait 30 min to 2 h after applying ALA (~15 h ok for small isolated lesion)
- For anesthetic effect, may apply topical lidocaine immediately following ALA application
- Avoid bright artificial light and sunlight during incubation period

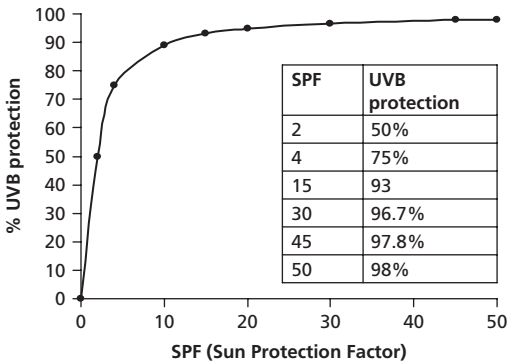
- Use protective glasses
- If situated 2–4 in. from Blu-U light, tx time ~ 16 min, 40 s (10 J/cm^2).
- After tx, avoid sunlight (or intense light) for 2 days (sunscreen will not block visible light)
- Re-tx in 2 months prn.

MAL PDT

- Curette treatment area to remove scale
- Apply MAL cream (nitrile gloves and spatula) under occlusion
- Avoid sunlight, bright artificial lights, or cold during 3-h incubation period
- Use protective glasses
- Tx time: 8–10 min. at 5–8 cm from red light (37 J/cm^2)
- Re-tx in 1 week prn.

UV Spectrum

Infrared	>760 nm	
Visible	400–760 nm	
UV	<400 nm	
UVAI	340–400 nm	Soret band (400–410 nm)
UVAII	320–340 nm	Wood lamp (320–400 nm, peak at 365 nm)
UVB	290–320 nm	NBUVB (311 nm)
UVC	200–290 nm	



SPF	UVB protection
2	50%
4	75%
15	93
30	96.7%
45	97.8%
50	98%

UV Protection Measurements

- SPF = Sun Protection Factor = sunscreen protected:unprotected ratio of duration of UVB exposure to produce 1 MED
- Water-resistant product maintains SPF level after 40 min of water immersion
- Waterproof (very water-resistant) maintains SPF level after 80 min of water immersion
- Measures of UVA protection: persistent pigment darkening, immediate pigment darkening, protection factor UVA
- Critical Wavelength (CW) = wavelength at which the integral of the spectral absorbance curves equals 90% of the integral from 290–400 nm (CW of at least 370 nm for broad-spectrum sunscreen).

Sunscreen	Max % Conc.*	UVB	UVA II	UVA I
Anthranilates – meradimate, menthyl anthranilate	5			
Avobenzone (Parsol, 1789)	3			
Benzophenones – oxybenzone	6			
dioxybenzone	3			
Cinnamates – octinoxate	7.5			
cinoxate	3			
Mexoryl SX (Ecamsule)	3			
PABA derivatives – padimate O	8			
benzoic acid	15			
Octocrylene	10			
Salicylates – homosalate	15			
trolamine salicylate	12			
Titanium dioxide	25			
Zinc oxide	25			

* % Maximum FDA-approved concentration.

Maxium protection

Partial protection

UV Associations/Specificities

UVA	UVB	UVA and UVB
Immediate tanning	Delayed tanning	AKs
Photoaging (UVA > UVB)	Photocarcinogenesis (UVB>UVA)	Fine wrinkles
Hydroa vacciniforme	Persistent light reaction	Solar urticaria (or visible light)
Phytophotodermatitis	Sunburn	
Photoallergic drug reaction	Xeroderma pigmentosa	
PMLE (UVA>UVB, UVC, or visible)	Cockayne syndrome	
	Lupus erythematosus photosensitivity (UVB>UVA)	

Glogau Wrinkle Scale

Glogau type	1	2	3	4
	No wrinkles	**Wrinkles in motion**	**Wrinkles at rest**	**Only wrinkles**
Age (years)	~20–30 s	~30–40 s	~50–60 s	~60–70 s and older
Photoaging	Early photoaging	Early-moderate photoaging	Advanced photoaging	Severe photoaging
Pigmentary changes	Mild/early pigmentary changes	Early lentigines	Dyschromia, telangiectasia	Yellow-gray discoloration
Keratoses/ skin cancers	No keratoses	Palpable keratoses	Visible keratoses	Skin cancers
Wrinkles	Minimal wrinkles	Dynamic wrinkles–parallel smile lines	Wrinkles without motion	Wrinkles throughout

Fitzpatrick Skin Type

Skin type	Color	Tanning response
Type I	White	Always burns, never tans
Type II	White	Usually burns, sometimes tans
Type III	White	Sometimes burns mildly, always tans
Type IV	Olive	Rarely burns, always tans
Type V	Dark brown	Never burns, tans very easily
Type VI	Black	Never burns, tans very easily

Peeling Agents

Depth of peel	Layer	Peel	Amount	Component
Very superficial	Strateum corneum/ ganulosum	Retinoids		Retinoic acid
		TCA 10–25%	1 coat	Trichloroacetic acid (TCA)
		Resorcin 20–30%	5–10 min	Resorcinol
		Gycolic 30–50%	1–2 min	Alpha hydroxy acid
		Salicylic acid		Beta hydroxy acid
		Jessner	1–3 coats	Resorcinol/ Salicylic acid/ Lactic acid/ETOH

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Depth of peel	Layer	Peel	Amount	Component
Superficial	Basal layer/ Papillary dermis	TCA 35%	1 coat	Trichloroacetic acid
		Gycolic 50–70% Resorcin 50%	5–20 min 30–60 min	Alpha hydroxy acid Resorcinol
Medium	Upper reticular dermis	Combination Peels		Jessner + 35% TCA CO_2 + 35% TCA Glycolic 70% + 35% TCA 50% TCA
Deep	Mid-reticular dermis	Baker-Gordon Phenol 88%		Phenol/ septisol/ croton oil Carbolic acid

TCA peel

- End point is frosting (self-neutralizing).
- Depth based on number/amount of application (wait 3–4 min after each application to assess amount of frost).
- May use cold compress after appearance of light frost to reduce discomfort.

TCA peel frost level

Level	Frosting	Depth of peel	Healing time
0	No frost, minimal erythema	Removes stratum corneum	
1	Partial light frost, some erythema	Superficial peel	2–4 days
2	White frost with erythema show through	Full thickness epidermal peel	5 days
3	Solid white frost, no pink	Papillary dermis	5–7 days

Jessner solution

Resorcinol (14 g); salicyclic acid (14 g); lactic acid (14 g); ethanol 95% (100 ml)

– Salicylate toxicity: Tinnitus, headache, nausea
– Recorcinol toxicity: Methemoglobinemia, syncope, thyroid suppression.

Baker-Gordon phenol

88% Phenol (3 cc); Distilled water (2 cc); Septisol (8 drops); Croton oil (3 drops)

– Rapidly absorbed through skin, metabolized by the liver, excreted by renal system
– Risk of renal failure, hepatotoxicity, and cardiac arrhythmias.

Cook total body peel

70% glycolic acid gel followed immediately by 35–40% TCA

– Neutralize with 10% sodium bicarbonate solution once scattered frosting is noted.

Pre-peel prep

- Cleanse with Septisol to remove oils. Rinse thoroughly.
- Wipe area with alcohol.
- Degrease area with 100% acetone to further debride oil and strateum corneum.
- Apply white petrolatum to corners of eyes, mouth and nose to protect areas.

Post-peel wound care

- Vinegar soak 3–4× per day with 0.25% acetic acid compress (1 tbs white vinegar in 1 pint warm water).
- White petrolatum or emollient to face and neck. May cover neck with saran wrap.

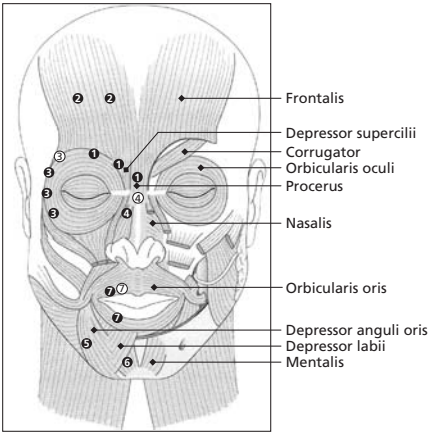
Botulinum Toxin

- Produced by *Clostridium botulinum* (Gram-negative anaerobic bacterium)
- FDA approved 4/2002 for glabella region. Off label use for other areas.
- Mechanism of action
  - Block Ach release from presynaptic nerve terminal by cleaving SNARE complex
    - BTX-A: cleaves SNAP-25
    - BTX-B: cleaves synaptobrevin/VAMP.
- Reconstitution
  - Potency can be maintained for up to 6 weeks
  - Reconstitution with sterile saline with preservative (0.9% benzyl alcohol) provides local anesthetic effect.
- Response
  - Clinical effect 1–3 days following injection with maximal effect by 2 weeks

Diluent added (0.9% NaCl)	1.0 ml	2.0 ml	2.5 ml	4.0 ml	8.0 ml
Resulting dose/units per 0.1 ml	10.0 U	5.0 U	4.0 U	2.5 U	1.25 U

- Benefits last 3–4 months
- Adverse effects/complications
  - *Common*: redness, ecchymosis, headache, bruising, edema, inflammation, erythema
  - *Ptosis*: minimize by careful selection of injection site (1–1.5 cm away from the orbital rim).
- If ptosis, use Iopidine (apraclonidine) drops. α2-adrenergic agonist which stimulates Muller's muscles to provide an elevation of 1–3 mm.
- Contraindications: infection at site of injection, known hypersensitivity to formulation.
- Caution:
  - Peripheral motor neuropathic disease, neuromuscular disorder (myasthenia gravis, Eaton-Lambert have increased risk of systemic side effects)
  - Aminoglycosides, penicillamine, and Ca^{+} channel blockers may potentiate BOTOX
  - Pregnancy category C
  - Lactation: not known whether toxin is excreted in human milk.

Botox injection sites



Recommended sites are denoted as dark numbered circles. Optional sites are denoted as white numbered circles.

Modified from Sommer B and Sattler G (eds). Botulinum toxin in aesthetic medicine. Boston: Blackwell Science, Ltd.: 2001, with permission from Blackwell Publishing.

Botox injection sites

Location	Muscles	Recommended units	Comments
❶ Glabella frown lines	Corrugator, procerus, orbicularis oculi, depressor supercilii	20–30 U women 30–40 U men	Keep >1 cm superior to orbital rim
❷ Horizontal forehead lines	Frontalis	10–20 U women 20–30 U men ~ 2–8 sites at 1 cm apart	Avoid treating lower 1/3 of lateral forehead to avoid brow ptosis
❸ Crow's feet	Lateral fibers of orbicularis oculi	6–15 U per side subdermal plane	keep >1–1.5 cm lateral to orbital rim
❹ Bunny lines	Upper nasalis Procerus	2–4 U per side	1 U midline if needed to procerus
❺ Marionette lines and mouth frown	Depressor anguli oris	5–10 U	Inject 1 cm lateral and 1–2 cm inferior to angle of mouth
❻ Mental crease	Mentalis	5–10 U	Deep injection
❼ Perioral rhytides	Orbicularis oris	1–2 U per quadrant	Superficially over vermillion
❽ Platysmal bands	Platysma	10–30 U women 10–40 U men	Grasp band and inject into belly of muscle

Fillers

Brand name (Company)	Composition	How supplied	Approx x. Cost (US$)	Duration of effect	FDA approval/CE mark	Location of injection	Side effects/ adverse effects
COLLAGEN							
Zyderm I (Inamed, division of Allergan)	Bovine collagen 35 mg/ml. Contains 0.3% lidocaine	0.5, 1.0, 1.5 ml	145 (1 ml)	3–4 months	FDA 1981 CE mark 1995	Superficial dermis – superficial rhytids, scars	Hypersensitivity to bovine collagen. Need two skin testing (2–4 weeks apart). Wait 4 weeks before treatment Lidocaine sensitivity
Zyderm II (Inamed)	Bovine collagen 65 mg/ml. Contains 0.3% lidocaine	0.5, 1.0 ml	150 (1 ml)	3–4 months	FDA 1983 CE mark 1995	Mid-dermis – moderate rhytids	
Zyplast (Inamed)	Bovine collagen 35 mg/ml cross-linked with glutaraldehyde. Contains 0.3% lidocaine	1.0, 1.5, 2.0, 2.5 ml	165 (1 ml)	3–5 months	FDA 1985 CE mark 1995	Deep dermis – deep rhytids, lip augmentation	
Cosmoderm I (Inamed)	Human collagen 35 mg/ml. Contains 0.3% lidocaine	1.0 ml	175–205 (1 ml)	3–4 months	FDA 2003	Superficial dermis – superficial rhytids, scars	Lidocaine sensitivity
Cosmoderm II (Inamed)	Human collagen 65 mg/ml. Contains 0.3% lidocaine	1.0 ml	200 (1 ml)	3–4 months	FDA 2003	Mid-dermis – moderate rhytids	

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Brand name (Company)	Composition	How supplied	Approx x. Cost (US$)	Duration of effect	FDA approval/CE mark	Location of injection	Side effects/ adverse effects
Cosmoplast (Inamed)	Human collagen 35 mg/ml crosslinked with glutaraldehyde. Contains 0.3% lidocaine	1.0, 1.5 ml	235 (1 ml)	3–4 months	FDA 2003	Deep dermis – deep rhytids, lip augmentation	
Evolence (ColBar LifeScience/ OrthoNeutrogena)	Porcine collagen 35 mg/ml. Glymatrix technology crosslink type I collagen to ribose – mimic human collagen. Dispersed in phosphate buffered saline	1.0 ml	250+(1 ml)	Up to 12 months	FDA 2008. CE 2004.	Upper to mid-dermis	Non-human collagen with potential for allergic reaction, though pre-testing is not required
HYALURONIC ACID							
Restylane fine line (Medicis)	Hyaluronic acid 20 mg/ml. Gel bead size 100μ. By bacterial fermentation from streptococci bacteria	0.4 ml	250–500 (0.4 ml)	3–6 months	Not FDA approved. CE mark	Superficial dermis – superficial rhytids, scars	
Restylane (Medicis)	Hyaluronic acid 20 mg/ml. Gel bead size 250μ. By bacterial fermentation from streptococci bacteria	0.4, 1.0 ml	200 (1 ml)	4–6 months	FDA 2003. CE mark	Mid-dermis – moderate/ severe rhytids, folds, lip	Rare allergic/ hypersensitivity reactions, granulomas

Perlane (Medicis)	Hyaluronic acid 20 mg/ml Gel bead size 1000 μ. By bacterial fermentation from streptococci bacteria	1.0 ml	250 (1 ml)	3–9 months	FDA 2007	Deep dermis – severe rhytids, folds	Rare allergic/ hypersensitivity reactions, granulomas
Hylaform (Inamed)	Hyaluronic acid 5.5 mg/ml 20% cross-linking. Derived from rooster comb	0.4, 0.75 ml	175 (0.7 ml)	3–6 months	FDA 2004 CE 1995	Mid/deep dermis – moderate/severe rhytids, lips	Contraindicated if allergic to avian product. Rare allergic/hypersensitivity reactions, granulomas
Hylaform plus (Inamed)	Hyaluronic acid 5.5 mg/ml 20% cross-linking. Larger particle size. Derived from rooster comb	0.4, 0.75 ml	200 (0.7 ml)	3–6 months	FDA 2004 CE 1995	Deep dermis – severe rhytids	
Juvederm ultra (Allergan)	Hyaluronic acid 24 mg/m produced by Streptococcus equi	0.8 ml	200 (0.8 ml)	6–12 months	FDA 2006	Mid/deep dermis – mod/ severe rhytids, folds, lip	
Juvederm ultra plus (Allergan)	Hyaluronic acid 30 mg/ml produced by Streptococcus equi	0.8 ml	250 (0.8 ml)	6–12 months	FDA 2006	Deep dermis – severe rhytids, folds	
Captique (Allergan)	Hyaluronic acid 5.5 mg/ml	0.75 ml	200 (0.75ml)	3–5 months	FDA 2004	Mid/deep dermis – mod/ severe rhytids, folds, lip	

Adapted from Injectables at Glance. The American Society for Aesthetic Plastic Surgery. http://www.surgery.org/download/injectablechart.pdf, 11/25/07. Sengelmann RD et al. Soft-tissue augmentation. In Robinson JK et al. (eds). Surgery of the Skin. Philadelphia: Mosby, 2005.

Brand name (Company)	Composition	How supplied	Approx x. Cost (US$)	Duration of effect	FDA approval/CE mark	Location of injection	Side effects/ adverse effects
SYNTHETIC FILLERS							
Radiesse formerly Radiance (Bioform Medical)	55.7% calcium hydroxylapatite (25–45 μ) microspheres	0.3, 1.3 ml	500 (1.3 ml)	12 months +	FDA 2006	Subdermis – deep rhytids and folds, lipoatrophy	Rare allergic reactions. Reports of granulomas, lumps
Artefill (Artes Medical)	20% polymethylmethacrylate microspheres (32–40 μ) suspended in 3.5% bovine collagen with 0.3% lidocaine	0.4, 0.8 ml	700–800	Permanent filler up to 5 years +	FDA 2006 CE 1994	Deep dermis – deep rhytids, folds	Lidocaine sensitivity. Potential for sensitivity to bovine collagen, need skin test 4 weeks prior. Reports of allergic reactions, foreign body granulomas 0.01%
Sculptra Or New-Fill (Dermik Laboratories)	Poly-l-lactic acid Mix 5 cc sterile water + 1 cc 1%. Lidocaine for total 6 cc product	1 vial (150 μg) reconstituted to 6 ml	480	Up to 2 years after 1st tx. Need 3–6 tx spaced 2–4 weeks apart	FDA 2004	Deep dermis/subcutaneous plane – restoration and correction of facial fat loss (HIV lipoatrophy)	Potential for lumpiness – need to massage area post treatment
Silikon (Alcon) AdatoSil (Bausch & Lomb)	Silicone, pure polymers from siloxane	1 vial 8.5 ml (2 ml max per tx)		Permanent	Off-label use. FDA approved for retinal tamponade	Subcutaneous plane – deep rhytids, folds	Granuloma formation, migration, inflammatory reactions

HOMOLOGOUS MATERIAL

Autologen (Collagenesis)	Autologous human collagen, elastin, glycosaminoglycans, and fibronectic. Prepared from patient tissue	No longer available	–	4 months–2 years	No longer available	Mid-dermis – mod/severe rhytids, lip, folds	
Dermalogen (Collagenesis)	Pooled human cadaveric proteins, primarily type I and III collagens	No longer available	–	3–6 months	No longer available	Mid and deep dermal filler for rhytids and folds	
Fascian (Fascia Biosystems)	Freeze-dried irradiated cadaveric fascia lata reconstituted with saline and 0.5% lidocaine	3 ml various particle size	125	3–8 months	FDA approved not required. Tissue bank regulations	Superficial, mid, deep dermis based on particle size	Potential for hypersensitivity to polymyxin B sulfate, bacitracin, gentamicin
Isolagen (Isolagen Technologies)	Autologous fibroblasts culture from 3 mm punch biopsy from patient	3 ml	1000–1500	Unclear	Phase III trials	Mid-/deep dermis	Need test dose 2+ weeks before tx

Sclerotherapy

Mechanism of action	Brand name	Sclerosing agent	FDA approval	Maximum dosage	Pain	Necrosis	Pigmentation	Other
Detergent/ emulsifier	Sotradecol Fibro-vein	Sodium tetradecyl sulfate	Yes, 1946	10 cc of 3% solution	Mild/Minimal	Occasional, at conc. >1%	+++	0.1–0.3% anaphylaxis
	Sclero-vein Aethoxysklerol	Polidocanol	Approved in Europe only	20 cc of 3% solution	Minimal	Rare	++ at high concentrations	0.2% anaphylaxis
	Scleromate	Sodium morrhuate	Yes, 1930	10 cc	Moderate	Frequent	+++	3–10% cases of anaphylaxis (highest risk)
	Etholamin	Ethanolamine oleate	Off-label use; for esophageal varices only	10 cc	Mild	Occasional	+++	Risk of RBC hemolysis and renal failure allergic rxn

Hyperosmotic agent	Hypertonic saline	Hypertonic saline 23.4% (NaCl)	Off-label use	10–20 cc	Painful, muscle cramps	Significant if extravasated	++	No allergic rxn
	Sclerodex	10% Saline + No 5% dextrose	No	10–20cc	Painful	Significant if extravasated	+	Low risk of allergic rxn
Chemical irritant	Chromex Scleremo	Glycerin 72%	No	5–10 cc	Moderate	Rare	Least likely	Viscous solution, rare allergic rxn
	Varigloban, Variglobin, Sclerodine	Polyiodine iodine	No	3 cc of 6%	Painful	Occasional	++	Viscous solution, rare allergic rxn- to iodine Renal insufficiency

Adapted from Sadick N, Li C. Small Vessel Sclerotherapy. *Dermatol Clin.* 2001; 19:475–81; Duffy DM. Cutaneous necrosis following sclerotherapy. *J Aesthetic Dermatol Cosmetic Surgery*. 1999; 1:157–68.

Determine vessel size using needle gauge

Use needle gauge to determine vessel size

Needle Gauge	Vessel Size
30 gauge	0.32 mm
25 gauge	0.50 mm
18 gauge	1.25 mm

Recommended maximum effective concentration of sclerosant to minimize side effects

Vessel size (mm)	Recommended maximum effective concentration (%)			
	Sotradecol	Polidocanol	Hypertonic saline	Glycerin
0.1–0.5	0.1–0.2	0.25–0.5	11.7	50–72
0.6–0.9	0.2–0.3	0.25–0.75	11.7–23.4	–
1.0–3.0	0.2–0.5	0.5–2.0	23.4	–
> 4 mm	0.5–1.0	2.0–5.0	–	–

Part 3
Drugs and Therapies

Handbook of Dermatology: A Practical Manual Margaret W. Mann
 ISBN: 978-1-405-18110-5

Medication Quick Reference

Topical steroids

CLASS 1 – SUPERPOTENT				
Betamethasone dipropionate	Diprolene	O/G	0.05%	15, 50 g
Clobetasol propionate	Temovate	O/Cr	0.05%	15, 30, 45 g
	Temovate	S	0.05%	25, 50 ml
	Cormax	S	0.05%	25, 50 ml
	Olux	F	0.05%	100 g
Diflorasone diacetate	Psorcon	O	0.05%	15, 30, 60 g
Halobetasol propionate	Ultravate	O/Cr	0.05%	15, 50 g
CLASS 2 – POTENT				
Amcinonide	Cyclocort	O	0.1%	15, 30, 60 g
Betamethasone dipropionate	Diprosone	O	0.05%	15, 50 g
Desoximetasone	Topicort	O/Cr	0.25%	15, 60 g
	Topicort	G	0.05%	15, 60 g
Diflorasone diacetate	Florone	G	0.05%	15, 60 g
	Maxiflor	O	0.05%	15 g
Fluocinonide	Lidex	O/Cr G	0.05%	15, 30, 60, 120 g
Halcinonide	Halog	O/Cr	0.1%	15, 30, 60, 240 g
CLASS 3 – UPPER MID-STRENGTH				
Betamethasone dipropionate	Diprosone	Cr	0.05%	15, 50 g
Betamethasone valerate	Valisone	O	0.1%	15, 45 g
Diflorasone diacetate	Florone, Maxiflor	Cr	0.05%	15 g
Fluticasone propionate	Cutivate	O	0.005%	15, 30, 60 g
Mometasone furoate	Elocon	O	0.1%	15, 45 g
Triamcinolone acetonide	Aristocort	Cr	0.5%	15 g
CLASS 4 – MID-STRENGTH				
Betamethasone valerate	Luxiq	F	0.12%	100 g
Desoximetasone	Topicort LP	Cr	0.05%	15, 60 g
Fluocinolone acetonide	Synalar-HP	Cr	0.2%	15, 60 g
	Synalar	O	0.025%	60 g
Flurandrenolide	Cordran	O	0.05%	15, 30, 60 g
Triamcinolone acetonide	Aristocort, Kenalog	O	0.1%	15, 60, 240 g, 1 lb
CLASS 5 – LOWER MID-STRENGTH				
Betamethasone dipropionate	Diprosone	L	0.05%	20, 60 g
Betamethasone valerate	Valisone	Cr/L	0.1%	15, 45 g
Clocortolone	Cloderm	Cr	0.1%	15, 45, 90 g

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 ISBN: 978-1-405-18110-5

Fluocinolone acetonide	Synalar	Cr	0.025%	15, 60 g
Fluocinolone acetonide	Dermasmooth/ FS	Oil	0.01%	4 oz
Flurandrenolide	Cordran	Cr	0.05%	15, 30, 60 g
Fluticasone propionate	Cutivate	Cr	0.05%	15, 30, 60 g
Hydrocortisone butyrate	Locoid	Cr	0.1%	15, 45 g
Hydrocortisone valerate	Westcort	Cr	0.2%	15, 45, 60 g
Prednicarbate	Dermatop	Cr	0.1%	15, 60 g
Triamcinolone acetonide	Kenalog	Cr/L	0.25%	15, 60, 80 g

CLASS 6 – LOW

Alclometasone dipropionate	Aclovate	O/Cr	0.05%	15, 45, 60 g
Betamethasone valerate	Valisone	L	0.1%	60 g
Desonide	DesOwen	Cr	0.05%	15, 60, 90 g
	Tridesilon	Cr	0.05%	5, 15, 60 g
	Desonate	G	0.05%	60 g
	Verdeso	F	0.05%	50, 100 g
Fluocinolone acetonide	Synalar	Cr/S	0.01%	15, 60 g
Triamcinolone acetonide	Aristocort	Cr/L	0.1%	15, 60, 240 g

CLASS 7 – LEAST POTENT

Topicals with hydrocortisone 0.5%, 1.0%, 2.5% (Cortisporin, Hytone, U-cort, Vytone), dexamethasone, flumethasone, methylprednisolone and prednisolone

Cr: Cream; F: Foam; G: Gel; L: Lotion; O: Ointment; S: Solution.

Non-steroidals

Tacrolimus	Protopic	O	0.03, 0.1%	30, 60 g
Pimecrolimus	Elidel	Cr	0.1%	15, 30, 100 g

Commonly used drugs in dermatology

Acne Vulgaris/Rosacea

Accutane 0.5 – 1 mg/kg/day divided qd-bid (Goal = 120–150 mg/kg). 10,20,30,40 mg
Azelex 20% Cr – 30, 50 g
BP LQ 2.5,5,10%; bar 5, 10%; L &Cr 5, 10%; G 2.4,4,5,6,10,20%
Cleocin T 1% S, L – 60 ml, 1% G – 30, 60 g, 1% pledgets – 60/box
Differin 0.1% Cr, G – 15, 45 g
Erythromycin 2% O – 25 g; 2% G – 27, 50 g
Evoclin 1% F – 50, 100 g
Finacea 15% G – 30 g
Klaron L – 59 ml
Metronidazole 1% Cr – 30 g; 0.75% Cr – 30,45 g; 0.75% G – 29 g; 0.75% L – 59 ml
Retin-A Micro 0.04%, 0.1% G – 20, 45 g; Generic 0.025%, 0.05%, 0.1% Cr –20, 45 g; Generic 0.025%, 0.1% G – 15, 45 g
Sulfacet R L – 25 ml

Tazorac 0.05%, 0.1% Cr – 15, 30, 60 g

Antibiotics – topical
Mupirocin/Bactroban bid/tid 2% Cr, O – 15, 30 g
Polysporin – (bacitracin + polymyxin) – OTC
Silvadene 1% Cr – 20, 50, 400, 1000 g

Antibiotics – systemic
Bactrim DS bid
Keflex 500 mg bid-qid; 250, 500 mg tab
Tetracycline 500 mg bid; 250, 500 mg tab
Doxycycline 100 mg bid; 50, 100 mg tab
Minocycline 100 mg bid; 50, 100 mg tab

Antibiotic preoperative prophylaxis
1 h prior to surgery
Amoxicillin: 2 g; 500 mg tab
Cephalexin: 2 g; 500 mg tab
If allergic to penicillin
Clindamycin: 600 mg; 300 mg tab
Azithromycin/Clarithromycin: 500 mg; 500 mg tab

Antifungal
Ciclopirox (Penlac) 8% nail S – 6.6 ml
Diflucan/Fluconazole 150–300 mg Qwk; 150 mg
Griseofulvin 20 mg/kg/d; 250, 500 mg, 125 mg/5 ml
Lamisil/Terbinafine 250 mg po qd, 250 tab; OTC 1% C, S, spray
Loprox/Ciclopirox 1% Cr, L – 15, 30, 90 g
Mentax/Butenafine 1% Cr – 15, 30 g
Micatin/Miconazole 2% Cr – 15, 30, 90 g
Nizoral/Ketoconazole 400 mg then sweat, 200 mg tab; 2% Cr – 15, 30, 60 g; 2% wash – 120 ml
Specatazole/Econazole 1% Cr – 15, 30, 85 g
Sporanox/Itraconazole 200 mg qd or pulse dose 200 mg bid × 7 days q month
Thymol 4% in alcohol: 30 cc disp. c dropper.
Naftin 1% G, Cr – 15, 30, 60 g
Zeasorb – AF powder/miconazole 2%

Antiparasitics
Elimite/Permethrin – Cr 5% – 60 g
Ivermectin 0.2 mg/kg × 1; 6 mg tab

Antivirals
Aldara/Imiquimod 3×/week qhs; Cr 5% – 1 box = 12 pks
Abreva/Docosanol 5×/day OTC Cr 10% – 2 g
Denavir/Penciclovir Q2 h × 4 days; Cr 1% – 2 g
Valtrex 2 g bid × 1 day; 500, 1000 mg tab
Zovirax/Acyclovir Q3 h × 5 – 7 days; O 5% – 2, 10 g

Antihistamines

Allegra/Fexofenadine 60 mg bid or 180 mg qd; 60, 180 mg tab
Atarax/Hydroxyzine 10–50 mg q4–6 h; 10, 25 mg, 10 mg/5 ml
Clarinex/Desloratadine 5 mg qd; 5 mg tab
Claritin/Loratadine 10 mg qd; OTC 10, 5/5 ml
Doxepin 10–75 qhs; 10, 25, 50 mg tab
Zyrtec/Cetirizine 5–10 mg; 5, 10, 5/5 ml

Bleaching agents

Azelex 20% Cr – 30, 50 g
Hydroquinone (Epiqquin Micro, Lustra, Triluma, others) bid. 4% Cr – 30, 60 g

Chemotherapy

Aldara/Imiquimod. For AK, BCC qhs × 8–12 weeks. Cr 5% – 1 box = 12 single use 250 mg packets
Efudex/Fluorouracil. For AK qd-bid × 2–6 weeks. 5% Cr – 25 g; 2%, 5% S – 10 ml
Solaraze/diclofenac bid × 3 months; Cr 5% – 30, 45 g

CTCL

Bexarotene tabs 200–300 mg/m^2 qd; 75 tab
Nitrogen mustard bid.10 mg% in Aquaphor 2 lb
Targretin/Bexarotene Gel qd-bid. 1% G – 60 g

Psoriasis

Dovonex/Calcipotriene bid. 0.005% O, Cr – 30, 60, 100 g; scalp S – 60 ml
Dermazinc with clobetasol spray. Write Dermazinc 4 oz. compound with 50 mcg micronized clobetasol, disp. 4 oz.
Liquor Carbonis Detergens (LCD): Must be compounded: TMC 0.1% oint compounded with 10% LCD, disp.1 lb.
Oxsoralen ultra 0.4–0.6 mg/kg 1–2 h prior to PUVA. 10 mg tab
Tazorac/Tazorotene qd. Cr 0.05%, 0.1% – 15, 30, 60 g, G 0.05%, 0.1% – 30, 100 g

Miscellaneous

Biotin 2.5 mg qd
Colchicine 0.3 mg, titrate to diarrhea; 0.6 mg tab
Drysol 20% solution; QHS until effective then spaced out; S – 35, 37.5, 60 ml
Elidel/Pimecrolimus bid; Cr 1% – 15, 30, 100 g
Folic acid 1 mg qd; 1 mg tab
Lac-hydrin (lactic acid) bid; Cr 12% – 140, 385 g; L 12% – 150, 360 ml
Niacinamide 500 mg Tid; 500 mg tab
Propecia/Finesteride 1 mg qd; 1 mg tab
Protopic/Tacrolimus bid; Cr 0.03, 0.1% – 30 g
Robinul 1 mg qd, titrate to effect; 1 mg tab
Trental 400 mg Tid; 400 mg tab
Vaniqa/Eflornithine bid. Cr 13.9% – 30 g

Systemic Medications

Anti-malarials

Drug (Brand name) Trade size	Dose	Labs to follow	Mechanism	Side effects	Interactions	♀
Diaminodiphenyl sulfone (Dapsone) 25/100 mg	50 mg/day then increase to 100–200 mg/day (take with food)	Baseline: CBC, **G6PD**, CMP, UA, neuro exam (check reflex). F/U: CBC qwk × 4, qmos × 6, then q6mos; CMP, neuro exam q3–4 mos	*Antimicrobial* (antagonist of dihydropteroate synthetase → prevents formation of folic acid) and *anti-inflamm* (inhibits PMN chemotaxis, Ig binding; inhibits myeloperoxidase)	**Hemolysis** (dose-related), **methemoglobinemia** (dose-related; decreased incidence with cimetidine), **agranulocytosis** (idiosyncratic), hypersensitivity syndrome – mono-like, **neuropathy** (motor), hepatitis	Rifampin, antimalarials, sulfonamides, probenecid, folate antagonists, TMP	C
Hydroxychloroquine (Plaquenil) 200 mg	200–400 mg/day (6.5 mg/kg/day)	Baseline: eye exam, **G6PD**, CBC; F/U: **eye exam**: q1–5 years; **Amsler grid** qmos, CBC qmo (→ q6mos)	ALL anti-malarials: Intercalate into DNA preventing transcription; disrupt UV O_2 radical formation; inhibit IL-2 synthesis; inhibit chemotaxis; reduce platelet aggregation; Inhibit endosome acidification	**Blue pigment**, GI upset (brand name medication with decreased GI upset), corneal deposition, hemolysis, **retinopathy (peripheral fields)**, **psoriasis/ PCT flares**, cardiac toxicity with overdose (2–6 g), CNS stimulant	Cimetidine, digoxin, kaolin, magnesium trisilicate; Avoid combination of chloroquine/ hydroxychloroquine	C
Chloroquine (Aralen) 250/500 mg	250 mg/day (4.0 mg/kg/day)	Same as Plaquenil		SAME as Plaquenil PLUS bleaches hair, increased ocular risk	*Smoking decreases effectiveness and worsens underlying lupus	C
Quinacrine (Atabrine) 100 mg	100 mg/day	Same as Plaquenil EXCEPT no eye exam, no G6PD		SIMILAR to Plaquenil BUT **no ocular toxicity, yellow hyperpigment**, no hemolysis	SAME as above BUT safe to use with chloroquine or hydroxychloroquine	C

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Immunosuppressive agents

Drug	Dose	Labs to follow	Mechanism	Side effects	Interactions	♀
Prednisone (1,2.5,5, 10,20,50 mg)	Variable	If long-term therapy (>3 months of >20 mg/day): BP, PPD, DEXA-scan; supplement Ca^{++} (1000 mg)/Vit D (800IU) and bisphosphonate	Decreases AP-1, cyclooxygenase, NF-kB. Decreases proinflammatory cytokines (esp. IL-2)	Hyperglycemia, insomnia, HTN, infection, osteoporosis, avascular necrosis, poor wound healing, peptic ulcer, water retention, adrenal insufficiency, cushingoid, glaucoma, myopathy, electrolyte imbalance (hypoK, hyperNa)	Metabolized by CYP3A4	C
Methotrexate (Rheumatrex) 2.5 mg	Begin at 5 mg up to 25 mg qwk PO/IM ****dose with folate** 1 mg qd	Baseline CBC, CMP, Hep panel F/U: CBC/LFTs qwk x 4 → q3mo; **LIVER BX**: q1–1.5 gm; Grade I/II = continue; IIIA (mild fibrosis) = continue, rebx in 6 months; IIIB (severe)/IV (cirrhosis) = stop	Inhibits **dihydrofolate reductase;** Cell-cycle specific (**S phase**); inhibits thymidylate synthetase, methionine synthetase, and AICAR; increases local adenosine (anti-inflammatory effects related to adenosine)	**Hepatotoxic,** cancer, **BM depression,** HA, pulm fibrosis/pneumonitis, alopecia, photosensitivity, UV burn recall, GI; increases homocysteine (↑ CV risk), anaphylactoid rxn reported (test dose at 5 mg); Leucovorin rescue	EtOH, NSAIDs, TCNs, retinoids, TMP/SMX, dapsone cyclosporin, probenecid, phenytoin, dipyridamole, chloramphenicol, phenothiazines	X
Azathioprine (Imuran) 50 mg	1–3 mg/kg/day, increase by 0.5 mg/kg/day q4wks	Baseline: CBC, LFT, **TPMT**; F/U: CBC. LFT qmo × 3 → q2mo Consider PPD	6-Thioguanine (active metabolite via HGPRT) incorporates into DNA; inhibits de novo purine synthesis (lymphocytes)	N/V, **BM suppression**, oral ulcers, **hepatotoxicity, cancer** (lymphoma, SCC), infxn, curly hair, hypersensitivity syndrome at 14 days (fever/shock)	Allopurinol (↓ dose by 75%), warfarin, ACE-I, TMP/SMX, sulfasalazine, IUDs	D

Mycophenolate mofetil (Cellcept 500 mg; Myfortic 180/360 mg)	0.5–2 g bid (cellcept 1000 = myfortic 720)	Baseline: CBC, LFTs; F/U: CBC: qwk × 4 → qmo, LFTs qmo	Inhibits **inosine monophosphate dehydrogenase → de novo** purine biosynthesis (lymphs)	GI symptoms (Myfortic = enteric coated, less GI effects), BM depression, hepatotoxicity	Cholestyramine, iron, magnesium/aluminum hydroxide, acyclovir	D
Thalidomide (Thalidomid) 50 mg	50–300 mg qh	Baseline: hCG, neuro exam, **SNAP;** F/U: hCG qwk × 4 then q2–4 wks; neuro q3mos; SNAP prn	Decreases TNF-α; inhibits angiogenesis; inhibits PMN phagocytosis; inhibits monocyte chemotaxis	Birth defects, sedation, constipation, peripheral **neuropathy** (sensory), leukopenia	Sedatives, histamine, serotonin, prostaglandin	X
Cyclosporine (Neoral) 25/100 mg	Start at 2.5 mg/kg/day max 5 mg/kg/day (without food)	Baseline, q2wks (→ qmo): CBC, BMP, LFTs, FLP, Mg, Uric Acid, BP; F/U: **Creatinine Cl** q6mo; Trough levels if > 5 mg/kg/day	Binds cyclophilin → inhibits calcineurin activation of NF-AT; inhibits IL-2, IFN-γ synthesis	**Nephrotoxic**, **HTN** (use CCB, no ACE/diuretic), hyperlipidemia, infxn, cancer, HA, acne, hyperK/uricemia, hirsutism, hypoMg, paresthesias, gingival hyperplasia	Metabolized by CYP3A4 (liver), P-gp (intestine) – Azoles, Macrole, CCB, **grapefruit juice**, MTX, SSRI, ticlopidine; additive toxicity with nephrotoxic drugs	C
Cyclophosphamide (Cytoxan) 25/50 mg	1–3 mg/kg/day or IV pulse 1 g/m^2 qmo; increase fluid intake (>3 l/day)	Baseline: CBC, CMP, UA; F/U: CBC qwk x 8 then qmo; CMP qmo; **UA** qwk × 12 then q2–4 wks **forever**; cystoscopy: yearly or if microscopic hematuria; **urine cytology** @ >50 gm	**Cell cycle-independent**; Covalent DNA binding; B-cell suppression	**BM depression**, **hemorrhagic cystitis** (acrolein metabolite), **carcinogenesis** (esp. TCC of bladder), hepatotoxicity, reproductive toxicity, anagen effluvium, mucositis, SIADH, pneumonitis/fibrosis, infections, nail ridging, pigmented bands on teeth, diffuse hyperpigmentation	Allopurinol, chloramphenicol, succinylcholine, digoxin, doxorubicin, barbiturates, cimetidine, halothane, nitrous oxide	D

♀: Pregnancy Category

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Systemic retinoids

Drug	Dose	Labs to follow	Mechanism	Side effects	Interactions	♀
Isotretinoin (Accutane) 10/20/30/40 mg	0.5–1 mg/kg/day with food. Total dose based on body weight = 120–150 mg/kg	Baseline: hCG, LFT, FLP; F/U: hCG, LFT, FLP qmo. Half Life: 10–20 h Pregnancy Avoidance = 30 days	*All Retinoids:* Affect cell growth/differentiation, morphogenesis, inhibit malignant cell growth, alter cellular cohesiveness, inhibit AP-1, NF-kB, ornithine decarboxylase, TLR-2; Increase dermal collagen I, hyaluronic acid, elastic fibers, fibronectin, transglutaminase and Th1 skewing	**Dryness,** myalgia/arthralgia, tendinitis, hyperostosis (long term), pseudotumor cerebri, HA, depression, transaminase elevation, alopecia (telogen effluvium), decreased night vision, PGs, photosensitivity, staph infxns, IBD association	Tetracyclines (risk of pseudotumor cerebri), MTX (hepatotoxicity) Vitamin A, macrolides, azoles, rifampicin, alcohol, phenytoin, mini-pill contraceptive, photosensitizers, carbamazepine	X
Acitretin (Soriatane) 10/25 mg	25–50 mg/day with food	Baseline: CBC, LFT, FLP, hCG, BUN/Cr; F/U: hCG, CBC qmo; LFT, FLP q2wks → qmo → q3mo *Half life:* 50 h Pregnancy Avoidance = 3 years	*Isotretinoin:* no specific receptor; *Acitretin:* all RAR receptor subtypes; *Bexarotene:* all RXR receptor subtypes	SAME as Accutane but difference is duration of tx; **longer pregnancy avoidance** (3 years), more alopecia, more hyperostosis. Alcohol can convert acitretin to etretinate (accumulates in fat)		X
Bexarotene (Targretin) 10/75 mg	300 mg/m^2/day with food (fatty foods improve bioavailability for retinoids)	Baseline: FLP, CBC, LFT, **TSH/T4**, hCG; F/U: FLP qwk until stable then q1–2 mo; CBC, LFT, hCG qmo × 3–6 months; TSH/T4 q8wks *Half life:* 7 h Pregnancy Avoidance = 30 days		SAME as other retinoids PLUS more marked **hypertriglyceridemia, central hypothyroidism, leukopenia,** cataracts, hypoglycemia	Same as above; gemfibrozil	X

Biologics

Drug	Dose	Labs to follow	Mechanism	Side effects	Interactions	♀
Alefacept (Amevive) 15 mg	15 mg IM qw × 12 wks (in office)	Baseline: WBC, CD4, PPD; F/U: CD4 qwk (hold dose if <250 cells/μl)	Recombinant fusion protein Fc IgG1 to **LFA-3**; binds to **CD2** on T cells (CD45RO+); causes activated T-cell apoptosis	**Leukopenia**, infection, cancer, chills, hepatic injury (transaminitis)	None	B
Efalizumab (Raptiva)	1 mg/kg SQ weekly	Baseline: PPD, CBC (platelets); F/U: CBC qmo x 3, then q3mos	Humanized murine antibody (anti-CD11a); inhibits **LFA1 – ICAM 1** interaction by binding CD11a subunit of LFA1 on T cells; prevents T cell activation & diapedesis	Rebound with discontinuation, flare on therapy, infection, cancer, injection site reaction, **thrombocytopenia**	None	C
Etanercept (Enbrel) 25/50 mg	25–50 mg SQ 2× per wk × 3 mos then 50 mg qwk	Baseline: PPD and/or CXR Consider CMP, HepB, HepC, CBC, HIV	Recombinant fusion protein Fc IgG1 to TNF receptor; binds **soluble TNF-α**	Injection site rxn, infection (**TB** reactivation), cancer, CHF, **demyelinating disease**, lupus-like syndrome, paradoxical pustular psoriasis	None	B
Infliximab (Remicade)	3–10 mg/kg IV; Week 0, 2, 6 then q8wks	Baseline: PPD and/or CXR. Consider CMP, HepB, HepC, CBC, HIV	Murine chimeric monoclonal antibody to TNF-α; binds **soluble and transmembrane TNF- α**	SAME as Enbrel but slightly increased risk; infusion reactions	None	B

♀: Pregnancy Category

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Drug	Dose	Labs to follow	Mechanism	Side effects	Interactions	♀
Adalimumab (Humira)	40 mg SQ q other week	Baseline: PPD and/or CXR. Consider CMP, HepB, HepC, CBC, HIV	Humanized monoclonal antibody to TNF-α; binds **soluble and transmembrane TNF-** α	SAME as Enbrel	None	B
Rituximab (Rituxan)	Chemo: 375 mg/m2 × 4, q week RA: 1g × 2, qo week	Baseline: CBC Follow CD19 q6–12 mos	Anti-CD20 monoclonal antibody	Infusion rxn (worst with first infusion), JC virus infx resulting in PML, severe mucocutaneous reactions	None	C
Kineret (Anakinra)	RA dosing: 100 mg SQ daily Indicated for Periodic Fever Syndromes	Baseline: PPD and/or CXR. Consider CMP, HepB, HepC, CBC, HIV	IL-1 receptor antagonist	SAME as Enbrel	None	C
IVIg	2 g/kg over 2–5 days. Also see TEN protocol p. 285	Baseline: IgA levels (use Gammagard in IgA deficiency), BMP, evaluate for heart failure	Immunomodulatory	Fluid overload, anaphylactic shock (in IgA deficiency), rare reports of hemolytic anemia, ARF, and aseptic meningitis	None	C

Nomenclature of biologics: mab (monoclonal antibody); ximab (chimeric); zumab (humanized); umab (human); cept (receptor-antibody fusion protein).
♀: Pregnancy Category

General Reference

Metric measurements

15 ml = 15 cc = 1 tablespoon
5 ml = 5 cc = 1 teaspoon
250 ml = 8 oz
454 g = 16 oz
30 g = 1 oz

Dose calculations

1% = 1 g/100 ml = 10 mg/cc
0.1% = 0.1 g/100 ml = 1 mg/cc

Drug dispensing and absorption

1 g Cream (or ~0.95 g Ointment) → covers 100 cm^2
1 Fingertip Unit (FTU) = 2 cm of cream on fingertip = 0.5 g

	1 Application(G)	bid × 1 week(G)
Adult full body	10–30	170
Head and neck	2	10
Hands and feet	2	10
Single arm	3	15
Single leg	4	30
Trunk	8	60

Percutaneous absorption by anatomic site: scrotum > cheeks > abdomen and chest > scalp and axillae > back > forearms > palms > ankles > soles.

Corticosteroid

	Equivalent dose (mg)	Glucocorticoid potency	Mineralo-corticoid potency	Duration (h) (half life)
Hydrocortisone	4	1	1	8–12
Cortisone acetate	5	0.8	0.8	8–12
Prednisone	1	3.5–5	0.8	18–36
Prednisolone	1	4	0.8	18–36
Triamcinolone	0.8	5	0	18–36
Methylprednisolone	0.8	5–7.5	0.5	18–36
Dexamethasone	0.15	25–80	0	36–54
Betamethasone	0.12–0.15	25–30	0	36–54

Drug name (Trade Name)* –Formulation, dosage	Trade size	♀

*Available in Generic ♀: Pregnancy Category

Acne – Topical

Antibiotics

Benzoyl peroxide 5%/clindamycin 1%

Duac gel	45 g	C
Benzaclin gel	25, 50 g	C

Benzoyl peroxide 5%/erythromycin 3%*

Generic gel	23, 46 g	C
Benzamycin	46 g, 60/box	C

Clindamycin*

Cleocin T 1% solution, lotion	60 ml	B
1% gel	30, 60 g	B
1% pledgets	60/box	B
Evoclin 1% foam	50, 100 g	B

Erythromycin*

Akne-Mycin 2% ointment	25 g	B
Emgel 2% gel	27, 50 g	B

Metronidazole

Noritate 1% cream	30 g	B
MetroCream 0.75%	30, 45 g	B
MetroGel 0.75% gel	29 g	B
MetroLotion 0.75% lotion	59 ml	B

Sodium sulfacetamide 10%

Klaron lotion	59 ml	C

Sulfa 5%/sodium sulfacetamide* 10%

Generic lotion	25 ml	C
Novacet lotion	30, 60 ml	C
Plexion TS cream	30, 90 g	C
Avar Gel; Avar Green gel	45 g	C
Clenia emollient cream	28 g	C
Sulfacet R lotion	25 ml	C
Rosula gel	45 ml	C

Keratolytics

Azelaic acid

Azelex 20% cream	30, 50 g	B
Finacea 15% gel	30 g	B

*Available in Generic

Benzoyl peroxide* (BP) – Antibacterial/keratolytic for comedonal acne; may bleach clothing

Rx	Benzac AC 2.5%, 5%, 10% emollient gel	60, 90 g	C
	Benzagel 5%, 10% gel	45 g	C
	Brevoxyl 4%, 8% gel, lotion/cleanser	42.5, 90 g	C
	Generic BP 2.5%, 5%, 10% gel, wash		C
	Triaz 3%, 6%, 10% gel	42.5 g	C
OTC	Clearasil 10% cream, lotion		C
	Oxy balance 10% gel		C

Retinoids:

Adapalene *(specific for RAR-beta and gamma)*

Differin 0.1% cream, gel	15, 45 g	C
Differin 0.3% gel	45 g	C

Tretinoin* *(binds all RAR, no RXR)*

Avita 0.025% cream, gel	20, 45 g	C
Retin-A Micro 0.04%, 0.1% gel	20, 45 g	C
Generic 0.025%, 0.05%, 0.1% cream	20, 45 g	C
Generic 0.025%, 0.1% gel	15, 45 g	C
Renova 0.02%, 0.05% cream	40, 60 g	C
Ziana 0.025% (+ clindamycin 1.2%) gel	30, 60 g	C

Tazarotene *(specific for RAR-beta and gamma)*

Avage 0.1% cream	15, 30 g	X
Tazorac 0.05%, 0.1% cream	15, 30, 60 g	X
Tazorac 0.05%, 0.1% gel	30, 100 g	X

Acne – Systemic

Antibiotics

Tetracycline* (Sumycin) 250–500 mg bid-qid Do not use in age < 8 years	250, 500 mg Susp 125/5 ml	D
Doxycycline* (Adoxa, Doryx, Vibramycin) po qd-bid (Periostat) po bid (Oracea) po qd SE: photosensitivity, dizziness, esophagitis: take w/8 oz water. Do not take w. calcium. Not for age <8 years	50, 100 mg 20 mg 40 mg	D
Minocycline* (Dynacin, Minocin) 50–100 mg po qd-bid SE: gray discoloration of skin/teeth, lupus-like syndrome, pseudotumor cerebri. Not for age <8 years	50, 75, 100 50 mg/5 ml	D
Erythromycin* (E-mycin, Erytab) 250–500 mg po qid or 333 mg po tid, or 500 mg po bid PEDs: 50 mg/kg/day divided qid SE: nausea, diarrhea	250,333,500 mg Susp 200/5, 400/5 ml	B

*Available in Generic

Retinoids

Isotretinoin* (Accutane, Amnesteem, Sotret, Claravis) 13-cis RA – unclear receptor affinity) 0.5–1 mg/kg/day divided qd-bid ☑LABS: Baseline – 2 neg βhcg, lipids, LFTs (for Medicaid + CBC, glucose). Monthly – βhcg, lipids, LFTs. SE: dryness, teratogen, HA, arthralgias/myalgias, ↓ night vision, depression, lipid abnormalities.	10, 20, 40 mg	X

Others

Spironolactone* (Aldactone) 25–200 mg qd, start 25–50 mg Weakly antiandrogenic effects for PCOS patients SE: hyperkalemia, gynecomastia, hypotension	25, 50, 100 mg	X

Alopecia

Finasteride (Propecia) Androgenetic alopecia in men: 1 mg po qd	1 mg	X
Minoxidil* (Rogaine) For men or women: usually use 5% solution. 1 ml bid to dry scalp	2% women; 5% men 60 ml	C

Analgesics

Dose: 1–2 tabs po q4–6 h PRN pain (in increasing strength)

Darvocet	Propoxyphene + Acetaminophen N-50 (50/325); N-100 (100/325)	50/325 mg 100/325 mg	C
Tylenol #3	Codeine + Acetaminophen *Can cause constipation-Rx w Colace 100bid	15/300 mg (#2) 30/300 mg (#3) 60/300 mg (#4)	C
Vicodin	Hydrocodone + Acetaminophen	5/500 mg 7.5/500 mg	C
Percocet	Oxycodone + Acetaminophen * Very strong, almost never prescribed in Derm. Use for 5/325 mg major abd surgeries, etc.	2.5/325 mg 5/325 mg 7.5/325 mg	C

*Available in Generic

Anesthetics – Topical

EMLA Lidocaine 2.5% + prilocaine 2.5% — 5, 30 g — B

Age area	Weight (kg)	Max dose (g)	Max area (cm^2)
1–3 months	<5	1	10
4–12 months	5–10	2	20
1–6 years	10–20	10	100
7–12 years	>20	20	200

May cause methemoglobinemia in children.

LMX 4 Lidocaine 4% cream — 30 g — B

LMX 5 Lidocaine 5% cream — 15, 30 g — B

Lida-Mantle Lidocaine 3% cream — 28, 85 g — B

Lida-Mantle HC Lidocaine 3% + 0.5% HC — 28, 85 g — C

Pramosone Pramoxine + 1% or 2.5% hydrocortisone – topical for itching — 60, 120 ml solution; 30, 60 g cream; 30 g ointment — C

Antibiotics

Topical/Antiseptic

Mupirocin* (Bactroban/Centany) 2% cream, ointment
apply bid-tid for impetigo, wound infections; for nasal MRSA eradication, use 0.5 g in each nostril bid × 5 days — 15, 30 g — B

Bacitracin + **Polymyxin*** (Polysporin) — OTC — C

Silver sulfadiazine* (Silvadene) 1% cream — 20, 50, 400 1000 g — B

Retapamulin (Altabax) 1% ointment bid × 5 days for methicillin sensitive s. aureus or s. pyogenes — 5, 10, 15 g — B

Chlorhexidine* (Hibiclens 4% cleanser) Good antimicrobial agent for bacteria, fungus, and yeast. For MRSA eradication — 120, 240, 480, 960, 3840 ml — B

Gentamicin* (Garamycin cream/ointment 0.1%) For pseudomonas coverage (i.e. nails, wound) — 15 g — D

*Available in Generic

Systemic

Amoxicillin* (Amoxil) 250–500 mg po tid Child: 20–40 mg/kg/day po divided tid	250, 500 mg Susp 125/5 250 mg/5 ml	B
Augmentin* (Amoxicillin + Clavulanic acid) 500–875 mg po bid/250–500 mg po tid Peds: 20–40 mg/kg/day divided bid/tid	250, 500, 875 mg Susp 200/5 400 mg/5 ml	B
Azithromycin* (Zithromax) macrolide. 500 mg po × 1; then 250 mg qd 5 days 500 mg po qd for 3 days	 Zpak: 250 mg TriPak: 500 mg	B
Cefaclor (Ceclor) second gen. cephalosporin. 250–500 mg po tid. 250 mg/5 ml Peds: 20–40 mg/kg/day po divided tid	250, 500 mg Susp 125/5, 250 mg/5ml	B
Cephalexin* (Keflex) first gen cephalosporin 250–500 mg po qid Peds: 40 mg/kg/day po divided bid	250, 500 mg Susp 250 mg/5 ml	B
Ciprofloxacin* (Cipro) second gen. quinolone. 250–750 mg po bid Interactions: antacids, sucralfate, Fe, Zn, theophylline, warfarin, cyclosporine	250, 500, 750 mg	C
Clarithromycin* (Biaxin) 250–500 mg po bid Peds: 7.5–mg/kg po bid	250, 500 mg Susp 125/5, 250 mg/5 ml	C
Clindamycin* (Cleocin) 150–450 mg po qid Peds: 8–25 mg/kg/day divided tid-qid May cause C. difficile colitis	75, 150, 300 mg Susp 75 mg/5 ml	B
Doxycycline* (Adoxa, Doryx, Vibramycin) 50–100 mg po qd-bid SE: photosensitivity, dizziness, esophagitis: take w/8 oz water. Do not take with calcium. Not for age <8 years	50, 100 mg	D
Erythromycin* SE: nausea, diarrhea E-mycin, Erytab 250–500 mg po qid or 333 mg po tid, or 500 mg po bid Erythromycin ethyl succinate – EES,Eryped 400 mg po qid Peds: 50 mg/kg/day divided qid	 250, 333, 500 mg 400 mg 200 mg/5 ml 400 mg/5 ml	B B B B
Minocycline* (Dynacin, Minocin) 50–100 mg po qd-bid. SE: blue-gray discoloration of skin/teeth, lupus-like syndrome, pseudotumor cerebri. Not for age <8 years	50 mg/5 ml 50, 75 100 mg	D

*Available in Generic

Rifampin* 10–20 mg/kg/day, max 600 mg qd P450 drug interactions: antacids, calcium channel blockers, steroids, cyclosporine, digoxin, dapsone, quinolones, warfarin, L-thyroxine.	150, 300 mg	C
Tetracycline* (Sumycin) 250–500 mg bid-qid Not for age < 8 years	250, 500 mg	D
Trimethoprim-sulfamethoxazole* (Septra, Bactrim) 1 tab (double-strength) po bid Peds: 0.5 mg/kg po bid; 10 kg – 1 tsp bid 20 kg – 2 tsp bid 30 kg – 3 tsp bid >40 kg –4 tsp bid or 1 DS tab bid	Sulfa (mg)/TMP (mg) 400/80 800/160 (DS) Sus 200/40 per 5 ml	C

Antibiotic preoperative prophylaxis

See p. 184 for use of antibiotic prophylaxis for endocarditis indicated for surgical procedure on infected tissue in patients with high-risk cardiac lesion.

Antibiotic regimens

	First line	Second line
Acne, perioral dermatitis	MCN 50–100 mg qd-bid DCN 50–100 mg qd-bid TCN 500 mg bid	Erythromycin TMP-SMZ
Anthrax	Cipro 500 mg bid × 60 days Peds: 20–30 mg/kg/d divided q12 × 60 days	DCN 100 mg bid × 60 day Peds > 8 years 2.2 mg/kg bid × 60 days
Bacillary angiomatosis	Clarithro 500 mg bid Azithromycin 250 mg qd Cipro 500–750 mg bid	Erythromycin 500 mg Qid DCN 100 mg bid
Bite: Cat *Pasteurella multocida*	Augmentin 875/125 mg bid Or 500/125 mg tid	Cefuroxime 0.5 g q12 h DCN 100 mg bid
Bite: Dog *Pasteurella multocida*	Augmentin 875/125 mg bid Or 500/125 mg tid	Clinda 300 Qid + TMP-SMX Cinda + Floroquinone
Bite: Human	Augmentin 875/125 mg bid × 5 days	If infxn: Clinda + Cipro

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*Available in Generic

	First line	Second line
Bite: Spider – (Brown Recluse)	Dapsone 50 mg qd may help	
Borrelia recurrentis	Doxycycline	Erythromycin
Campylobacter jejuni	Floroquinone	Erythromycin
Cellulitis (extremity)	Nafcillin 2 g Q4 h IV Dicloxacillin 500 Q6 h Cefazolin 1 g Q8 h IV	Erythromycin, Z-Pak Augmentin 875/125 mg bid
Cellulitis (Face)	Vanco 1 g IV Q12h	Amoxicillin/Penicillin
Clostridium perfringens	Clindamycin + PCN G	Doxycyline
Erythrasma (*Corynebact. minutissimum*)	Erythro 250 mg Qid × 14 days	Topical agents
Kawasaki syndrome	IVIG 2 g/kg over 12 h + ASA 80–100 mg/kg/day divided in 4 doses then 3–5 mg/kg/day qd × 6–8 weeks	
Impetigo	Dicloxicillin 125–500 mg Qid Bactroban topically	Azithromycin, Clarithromycin Erythromycin
Lyme disease (*Borrelia burgdorferi*)	Exposure: DCN 200 mg ×1 Tx: for 14–21 days DCN 100 bid Amoxicillin 500 Tid Cefuroxime 500 bid	Erythro 250 Qid
Meningococcus (*N. meningitides*)	PCN G	Cefuroxime
Mycoplasma	Azithromycin Clarithromycin Erythromycin Fluoroquinone	Doxycyline
Pseudomonas aeruginosa	Cipro 500–750 mg bid	Third generation Cephalo Imipenem, Aztreonam
Rickettsia: RMSF	DCN 100 mg bid × 7 days	Chloramphenicol 500 mg Qid × 7 days
Staphylococcus	Clindamycin TMP-SMX	Erythromycin
Staph scalded skin	Nafcillin or Oxacillin 2 g IV Q4 h × 5–7 days Ped: 150 mg/kg divided Q6 h	
Streptococcus	PCN G	Erythromycin Azithromycin Clarithromycin

Bites: need tetanus prophylaxis.

Modified from the Sanford Guide 2006

STDs

Disease	Symptoms	First line therapy	Second line therapy
Gonorrhea (and treat for Chlamydia)	Male: urethritis with discharge	Cefixime 400 mg	Gatifloxacin 400 mg
	Female: endocervicits with discharge	Cipro 500 mg Ofloxacin 400 mg and Azithromycin 1 g DCN100 mg bid × 7 days	Enoxacin 400 mg Lomefloxacin 400 mg and Azithromycin 1 g DCN 100 mg bid × 7 days
Chancroid (*Haemophilus ducreyi*)	Deep ulcer, Pain, 50% adenopathy	Azithromycin 1 g × 1 Ceftriazone 250 mg IM ×1	Erythromycin 500 mg Qid×7 days Cipro 500 mg bid × 3 days
Lymphogranuloma Venereum (*Chlamydia trachomatis*)	Herpetiform vesicle, NO PAIN, +LAD/ Groove sign	DCN 100 mg bid × 21 days	Erythromycin 500 mg Qid × 21 days
Granuloma Inguinale (*Klebsiella granulomatis, formerly Calymmato-bacterium granulomatis)*	Ulcer with beefy granulation tissue, NO PAIN, NO LAD + Donovan bodies	DCN 100 bid × 21 days TMP-SMX DS bid × 21 days	Erythromycin Cipro
Syphilis (*Treponema pallidum*)	Indurated chancre, NO PAIN, +LAD	Benzathine PCN G 2.4 million units IM x 1, repeat in 1 week	DCN 100 mg bid × 14 days TCN 500 mg Qid × 14 days

*Pregnant mothers who are PCN allergic should get desensitization then treat with PCN.

Antifungals

Topical

Classes: polyenes bind ergosterol; azoles inhibit 14-alpha demethylase; allylamines inhibit squalene epoxidase.

Rx	**Butenafine*** (Mentax) 1% cream	15, 30 g	B
	Ciclopirox (Loprox) 1% cream, lotion	15, 30, 90 g	B
	Ciclopirox (Penlac) 8% nail solution	6.6 ml	B
	Econazole* (Spectazole) 1% cream	15, 30, 85 g	C
	Ketoconazole* (Nizoral) 2% cream	15, 30, 60 g	C
	Ketoconazole (Nizoral) 2% shampoo	120 ml	C

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*Available in Generic

	Ketoconazole (Xolegel) 2% gel	15 g	C
	Miconazole* (Micatin) 2% cream, powder, spray	15, 30, 90 g	C
	Naftifine* (Naftin) 1% gel, cream	15, 30, 60 g	B
	Oxiconazole (Oxistat) 1% cream	15, 30, 60 g	B
	Sertazconazole (Ertazco) 2% cream	30 g	C
	Thymol 4% in alcohol	30 ml with dropper	
OTC	**Clotrimazole** (Lotrimin, Mycelex)1% cream, solution, lotion		B
	Ketoconazole (Nizoral) 1% cream, shampoo		C
	Miconazole (Zeasorb-AF Powder) 2% powder		C
	Miconazole (Monistat) 2% cream		C
	Terbinafine (Lamisil) 1% cream, solution, spray		B
	Selenium sulfide (Selsun, Head and Shoulder) 1%, 2.5% shampoo		C

Systemic

Griseofulvin* (Grifulvin, Grisactin, Fulvicin)		C
Microsize: 500–1000 mg po qd.	250, 500 mg	
Peds: 20 mg/kg/day divided bid, max 1 g/days × 6–8 weeks	125 mg/5 ml	
Take with food (fatty meals increase absorption)		
Do not take if pregnant, h/o hepatic failure, porphyria, lupus		
May cause agranulocytosis, OCP failure, lupus, photosensitivity, disulfiram-like reaction		
CYP3A4 inducer: decreases levels of warfarin, CSA, OCPs		
Mechanism: inhibits microtubules		
Fluconazole* (Diflucan)	50, 100, 150,	
Onychomycosis: 150–300 mg 1 dose q wk, for 3–12 months	200 mg 10 or 40 mg/ml	C
Peds: 3–6 mg/kg/day		
Do not take: cisapride – fatal arrhythmia		
Increases effects of: warfarin, CSA, phenytoin, zidovudine, theophylline, terfenadine (CYP2C9 and 3A4 inhibitor)		
Rifampin decreases Fluconazole levels & cimetidine/HCTZ increase Fluconazole levels		
Mechanism: inhibits lanosterol 14-α demethylase		
Itraconazole* (Sporanox)	100 mg	C
Onychomycosis: 200 mg qd or pulse dose 200 mg bid × 1 week/month	10 mg/ml	
Peds: pulse dose 1 week/month (10–20 kg = 50 mg qd; 20–30 mg = 100 mg qd; 30–40 mg =		

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*Available in Generic

100/200 alternate; 40–50 kg = 200 mg qd;
>50 kg = 200 mg bid)
☑ Check LFTs after 4 weeks.
Treat 6 weeks-fingernails, 12 weeks-toenails
Tinea versicolor: 200 mg ×1, repeat in 1 week
Tinea capitis: 3–5 mg/kg/day divided qd-bid for 1 month
Take with orange juice/ carbonated beverage
Do not take: cisapride (arrhythmia)
Contraindication: ventricular dysfunction
CYP3A4 inhibitor: increases effects of: felodipine, CSA, digoxin, warfarin, statins, oral hypoglycemics
Mechanism: inhibits lanosterol 14-α demethylase

Ketoconazole* (Nizoral) 200 mg po qd. — 200 mg — C
Tinea versicolor: 400 mg ×1, repeat in 1 week
Peds >2 years: 3.3–6.6 mg/kg/day po given qd.
☑ Check LFTs if long-term use, Q2wks × 2 mos
Take with orange juice/ carbonated beverage
CYP3A4 inhibitor
Do not take: cisapride, pimozide, quinidine (arrhythmia)
Increases effects of: warfarin, CSA, phenytoin, theophylline
Rifampin, PPI decrease Ketoconazole levels
Mechanism: inhibits lanosterol 14-α demethylase

Nystatin* Swish and swallow 4–6 ml Qid — 100,000 units/ml — C
For oral candidiasis
Mechanism: associates with ergosterol to produce pores

Terbinafine* (Lamisil) — 250 mg — B
Onychomycosis: 250 mg po qd × 12 weeks, or pulse dose 250 mg bid for 1 wk/mo × 3 months
Tinea capitis: Peds 3–6 mg/kg/day for 1 month.
<20 kg – ¼ tab po qd; 20–40 kg – ½ tab po qd;
>40 kg – 1 tab po qd.
☑ Check LFTs baseline and q6wks.
May cause SCLE, taste or visual disturbance, headache, diarrhea
Lowers CSA level. CYP2D6 inhibitor: increases theophylline, TCA, narc levels. Rifampin decreases and cimetidine/terfinadine increases terbinafine levels. Caution with hepatic or renal insufficiency.
Mechanism: inhibits squalene epoxidase

Amphotericin B (Amphocin) — B
For Systemic Fungal Infection dose varies
0.3–1 mg/kg/day IV, start 0.25 mg/kg/day and increase by 5–10 mg/day. Max 1.5 mg/kg/day
☑ Check renal function, Mg, K+, LFT, CBC.
Mechanism: associates with ergosterol to produce pores

*Available in Generic

Antifungal regimens

Candidal infection

Perleche: Ketoconazole cream, Miconazole cream bid until resolve
Intertrigo: Clotrimazole cream, Miconazole cream bid until resolve
then use Miconazole or Zeasorb AF powder to keep area dry
Oral Candidiasis/ Thrush: Nystatin swish and swallow qid
Clotriamazole troche 5×per/day
Chronic Paronychia: Thymol solution bid

Pityrosporum folliculitis: (P. ovale or P. orbiculare)

Topical: Loprox cream, lotion; Nizoral cream, shampoo; Selenium sulfide
Oral: Nizoral 200–400 mg qd

Onychomycosis

Also need to use topical antifungal cream bid indefinitely

Topical	**Ciclopirox (Penlac)**: Apply lacquer to affected nails qd; apply new coats on top of previous coats.	6.6 ml	B
	Thymol 4% in alcohol Drip onto & around affected nails bid	30 ml with dropper	
Oral	Treat fingernails for 6 weeks, toenails for 12 weeks.		
	Itraconazole (Sporanox) 200 mg po qd; pulse dose 200 mg po bid for 7 days, off for 21 days. ☑Labs: +/ − LFTs after 4 weeks	100 mg	C
	Terbinafine (Lamisil) 250 mg po qd ☑Labs: LFTs baseline, Q6wks	250 mg	B
	Fluconazole (Diflucan) 150–300 qwk No need to check labs	50,100,150, 200 mg	C

Tinea versicolor

Mild: Topical treatment with Nizoral shampoo, Nizoral cream
Severe: Oral agents

Ketoconazole (Nizoral) [200 mg]
200 mg po qd × 5 days
Or 400 mg po × 1, 1–2 h before exercise. Let sweat dry, leave on as long as possible. Repeat in 1 week

Itraconazole (Sporanox) [100 mg]
200 mg po × 1, repeat in 1 week

Maintenance treatment with Nizoral shampoo, Nizoral cream

Tinea capitis (almost exclusively in children)
Griseofulvin: 20 mg/kg/d divided bid × 6–8 weeks [250, 500 mg or 125/5 ml]
Itraconazole (Sporanox): 3–5 mg/kg/d × 4–6 weeks [100 mg or 10 mg/ml]

Tinea corporis
Rx: Spectazole, Naftin bid to area until resolve
OTC: Lamisil, Lotrimin bid to area until resolve

Antiparasitics

Permethrin* (Elimite) For scabies: Apply from neck to soles of feet, leave on overnight for 8–12 h, wash off in am; repeat in 1 week	5% cream 60 g	B
Permethrin* (Nix) For lice: Apply cream rinse to hair/scalp, leave on 10 min, shampoo hair. Repeat in 1 week. Use nit comb	1% soln. 60 ml	B
Ivermectin (Stromectol) For scabies	6 mg	C

Single dose of 0.2 mg/kg

Weight:(kg)	Dose
15–24	½ tab (3 mg)
25–35	1 tab (6 mg)
36–50	1 ½ tab (9 mg)
51–65	2 tab (12 mg)
66–79	2 ½ tab (15 mg)
⩾ 80	0.2 mg/kg

Mechanism: blocks invertebrate glutamate-gated Cl channels, leading to paralysis and death

Precipitated sulfur For scabies Apply to entire body below head on three successive nights; bather 24 h after each application	6% in petrolatum	C
Lindane (Kwell) For scabies	1% lotion or cream	C
Adults: apply thin layer from chin to toes; use on dry skin and shower off 10 h later; repeat in 1 week *Second-line secondary to neurotoxicity (not for use in neonates or infants)*		
Malathion (Ovide) For lice Apply to dry hair/scalp. Wash out after 8–12 h. Repeat in 1 week. Use nit comb. *(Best efficacy among chemical pediculicides)*	0.5% lotion	B

*Available in Generic

Antivirals

For HSV labialis – topical agents

Penciclovir (Denavir)	Apply cream to lesions q2 while awake x 4 days	1% cream 2 g	B
Acyclovir (Zovirax)	Apply ointment 5×per/day for 5 days	5% ointment 2, 10 g	B
Docosanol (Abreva)	Apply cream 5×per/day for 5–10 days (efficacy same as placebo)	OTC 2 g	B

For HSV 1 or 2 – oral agents

	Primary	Recurrent	Suppression	Dosage	
Valacyclovir (Valtrex)	Labialis: 2 g q12 h × 1 day, OR 500 mg bid × 5 days Genital: 1 g bid × 10 days	500 mg bid × 5 days	<10×/year: 500 mg qd >10×/year: 1 g qd	500 mg, 1 g	B B
Famciclovir (Famvir)	Labialis: 500 mg tid×5 days Genital: 250 mg tid × 7–10 days	125 mg bid × 5 days	250 mg bid	120, 250, 500 mg	B B
Acyclovir* (Zovirax)	400 mg tid ×10 days 200 mg 5×per/day × 10 days 5 mg/kg/d IV q8 h	400 mg tid × 5 days, OR 800 mg bid× 5 days	400 mg bid	200, 400, 800 mg 200 mg/5 ml 250, 500 mg IV	B

For HSV disseminated disease

Acyclovir* (Zovirax)	5–10 mg/kg IV q8 h for 7 days if > 12 years	200, 400, 800 mg	B
	Neonatal: 400 mg tid during third trimester	250, 500 mg IV	

For herpes zoster/VZV

Valacyclovir (Valtrex)	1 g po tid × 7 days	500 mg, 1 g	B
Famciclovir (Famvir)	500 mg po qid × 7 days	125, 250, 500 mg	B
Acyclovir* (Zovirax)	800 mg 5×/day × 7–10 days	200, 400, 800 mg	B

Mechanism: These nucleoside analogs are phosphorylated by viral thymidine kinase to form a nucleoside triphosphate which then inhibits HSV DNA polymerase action.

*Available in Generic

For genital warts

Imiquimod (Aldara)	Apply to genital warts 3× weekly at night	5% cream 1 box = 12 or 24 pks of 250 mg each	C
Podofilox (Condylox)	Apply to genital warts bid 3 days/week consecutive	0.5% gel, soln 3.5 g	C
Podophyllin/Benzoin (Podocon-25)	MD applies. Pt leave on for 1–6 h then wash off	15 ml	X

For verruca vulgaris

Compound W pad	40% Salicylic Acid	OTC	/
Compound W gel	17% SA with colloidion		
Canthacur-PS	30% SA, 5% podophyllin, 1% cantharidin	MD applies	
Cidofovir	3% topical solution bid until resolve	Compound by pharm	C
Bleomycin	Place 0.5–1 mg/ml solution onto wart then prick it into wart with needle		
Candida Antigen	Inject intradermally into wart by MD. Dilute 1:1 with 1% Lidocaine. Inject 0.1–0.2 cc per wart. Limit total to 0.3–0.5 cc. Repeat q 3 weeks x 3 visit to see if respond.		

For molluscum

Canthacur	0.7% cantharidin. Apply by MD with toothpick

Antihistamines

Sedating (usually use at night)

Diphenhydramine* (Benadryl)	25–50 mg q6–8 h. Peds: 5 mg/kg/d divided q4–6 h	OTC 25, 50 mg 12.5 mg/5 ml	B
Hydroxyzine* (Atarax, Vistaril)	10–50 mg po q4–6 h. Peds (<6 years): 2 mg/kg/d divided q6 h	10, 25, 50 mg Susp 10 mg/5 ml	C
Cyproheptadine* (Periactin)	4 mg tid; max 32 mg/d Peds (2–5 years): 2 mg bid-tid Peds (6–12 years): 4 mg bid-tid	4 mg Susp 2 mg/5 ml	B

*Available in Generic

Non-sedating

Loratadine* (Claritin)	10 mg po qd Peds (2–5 years): 5 mg qd	OTC 10 mg Susp 5 mg/5 ml	B
Desloratadine (Clarinex)	5 mg po qd	5 mg	C
Fexofenadine (Allegra)	60 mg po bid or 180 mg po qd Peds (6–12 years): 30 mg bid	30, 60, 180 mg	C
Cetirizine (Zyrtec)	5–10 mg qh Peds (2–6 years): 2.5 mg qh max 5 mg qd. *(may be sedating)*	5, 10 mg Susp 5 mg/5 ml	B

H2-blockers for angioedema, systemic mastocystosis

Famotidine (Pepcid)	20 mg qd-bid	20, 40 mg 40 mg/5 ml	B
Cimetidine (Tagamet)	400 mg qd-qid	300, 400, 800 mg	B
Ranitidine (Zantac)	150 mg qd-bid	150, 300 mg 15 mg/ml	B

Antipruritic

Topical

Pramoxine (Pramosone) – topical anesthetic +1% or 2.5% hydrocortisone	30 g O 30, 60 g C 60, 120 ml L	C
Doxepin (Zonalon) 5% Cream – Apply q 3–4 h × 1 week max; may cause systemic effect if applied to >10% BSA	30, 45 g C	B
Sarna lotion (Menthol 0.5%, Camphor 0.5%)	OTC	/
Aveeno anti-itch cream (calamine 3%, Camphor 0.47%, Pramoxine 1%)	OTC	/
Calamine lotion	OTC	/
Gold bond cream (Menthol 1%, Pramoxine 1%)	OTC	/

Oral

Doxepin (Sinequan)	10–75 mg qh Tricyclic antidepressant with high affinity for H1 receptor. Do NOT use with MAOI	10, 25, 50 mg	B

*Available in Generic

Promethazine hydrochloride (Phenergan)	12.5 mg Qid, 25 mg qh CNS depressant, antiemetic, anticholinergic, sedative antihistamine (H1)	12.5, 25, 50 mg	C
Amitriptyline (Elavil)	10–25 mg to 150 mg qd For anxiety, neuropathic pain. TCA	10, 25, 50 mg	D
Naltrexone (RevVia, Depade)	25–50 mg qd Opioid antagonist	25, 50 mg	C
Ondansetron (Zofran)	8 mg bid Blocks serotonin 5HT3 & opioid receptors	4, 8, 24 mg	B
Cholestyramine (Questran)	4–16 mg qd For cholestastic pruritus. Bile acid resin. Do not take other meds for 4 h	4, 378 g	B
Rifampin	300–600 mg qd (10 mg/kg/d) For pruritus from primary bilary cirrhosis. Increases metabolism/ excretion of bile acid	150, 300 mg	C
Pimozide (Orap)	Start 1 mg qd to 0.2 mg/kg/d For delusions of parasitosis Increases toxicity of MAOI, CNS depressant May cause extrapyramidal effects ☑ Check ECG-may cause long QT	1, 2 mg	C

Bleaching Agents/Depigmenting Agents

All contain hydroquinone which inhibits enzymatic oxidation of tyrosine to 3-(3,4-dihydroxyphenyl-alanine [dopa]). Some agents also contain topical steroids, retinoids, sunscreen (SS); glycolic acid (G).

Hydroquinone* 4% cream		$30, 60	30, 60 g	C
EpiQuin Micro		$80–100	30 g	C
Lustra 4% cream	G	$80, 140	28.4, 56.8 g	C
Lustra AF 4% cream	G, SS	$80,140	28.4, 56.8 g	C
Claripel 4% cream	SS	$100–150	28, 45 g	C
Glyquin 4% cream	10% G, SS	$80–100	30 g	C
Triluma 4% cream	0.01% Fluocinolone 0.05% Tretinoin	$120	30 g	C

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*Available in Generic

Benoquin 20% cream – final depigmentation	Monobenzone 20% Apply bid until effect (2–4 months)	$ 50–70	35.4 g	C

Others

Azelex cream 20%	bid to affected area	30, 50 g	B

Topical Chemotherapy

Actinic keratoses (AK)

Fluorouracil (Efudex)	Apply qd-bid × 2–6 weeks or until irritated	5% Cream 25 g	X
Fluorouracil (Carac)	Apply qd-bid × 2–6 weeks or until irritated	0.5% Solution 10 ml	X
Diclofenac (Solaraze)	Apply bid × 8–12 weeks NSAID	3% Gel 50, 100 g	B
Imiquimod (Aldara)	Apply qh × 8–12 weeks	5% Cream 1 box = 12 pks of 250 mg each	C

Basal cell carcinoma (BCC) – superficial BCC

Imiquimod (Aldara)	Apply qh × 8–12 weeks	5% Cream 1 Box = 12 pks of 250 mg each	C

CTCL

Topical agents (see also Class I topical steroids and CTCL in General Dermatology section for systemic treatments)

Bexarotene (Targretin Gel)	Apply to area qd-bid as tolerated	1% gel 60 g tube	X
Nitrogen mustard Mechiorethamine (Mustargen)	Apply to plaques of CTCL bid	10 mg% in Aquaphor. 2 lb	D

Oral agent

Bexarotene (Targretin)	200–300 mg/m^2 qd with meal	75 mg	X

Other agent

Interferon α 2a (Roferon A)	6–9 million IU SC 3×per/wk Use in combination with PUVA	3, 6, 9 million IU prefilled syringes	C

Psoriasis

Topical agents (see also topical steroids)

Dermazinc with Clobetasol Spray	DermaZinc 4 oz compound with 50 mcg micronized clobetasol	4 oz	C
Calcipotriene (Dovonex)	0.005% Ointment 0.005% Cream Scalp solution	30, 60, 100 g 30, 60, 100 g 60 ml	C
Tazorotene (Tazorac)	0.05%, 0.1% Cream 0.05%, 0.1% Gel	15, 30, 60 g 30, 100 g	X
Betamethasone/ calcipotriene (Taclonex)	0.064%/0.005% ointment	60, 100g	C

Tar (apply in direction of hair growth)

Crude coal tar (CCT)	1–10% Compound in petrolatum base		C
Tar Gel (Estar 5%, Psorigel 7.5%)	Cover with vaseline to prevent drying	90, 120 ml	C
Liquor Carbonis Detergens (LCD)	Triamcinolone 0.1% ointment compound with 10% LCD	1 lb	C
Tar Shampoo Neutrogena T-Gel	Apply to scalp, leave for 5–10 min then rinse	OTC	C

Systemic agents

Methoxypsoralen (Oxsoralen Ultra)	0.4–0.6 mg/kg po 1–2h prior to PUVA	10 mg	C

Weight (kg)	Dose (mg)
<30	10
30–65	20
65–90	30
>90	40

See toxic drug chart

Retinoids: **acitretin** (Soriatane); Biologics: **alefacept** (Amevive), **efalizumab** (Raptiva), **etanercept** (Enbrel), **infliximab** (Remicade).

Seborrheic Dermatitis

(see Topical Steroids, Keratolytics)

Carmol scalp treatment	Sodium sulfacetamide 10% lotion	90 ml Lotion	B
Derma-Smoothe/FS	Fluocinolone acetonide 0.1%, peanut oil, mineral oil	120 ml Oil	C
Ovace	Sodium sulfacetamide 10% wash	180, 360 ml wash	B
Nizoral	Ketoconazole 2% cream	15,30,60 g	C
	Ketoconazole 2% shampoo	120 ml	C
	Ketoconazole 1% shampoo	OTC	C
Selsun, Head and Shoulders	Selenium sulfide 1%, 2.5% shampoo	OTC	C

Hypertrichosis

Eflornithine 13.9% (Vaniqa)	Apply to affected area bid	30 g	C

Hyperhidrosis

Aluminum Cl (Drysol 20% CertainDry 12.5% Xerac-AC 6.25%)	Apply to underarms qh until desired effects, then space out. Combines with intraductal keratin to produce a functional closure.	35, 37.5, 60 ml	/
Glycopyrrolate (Robinul)	Start 1 mg, titrate to effect Antimuscarinic anticholinergic – inhibits ACh at autonomic cholinergic nerves. SE: anhidrosis/hyperthermia, blurred vision, urinary retention, constipation, tachycardia	1 mg	B
Botulinum Toxin A (Botox)	50 units per axilla q4–6 mos Blocks release of ACh via inhibiting SNAP-25		C

Other treatment modalities include iontophoresis and liposuction.

Wound Care

Acetic acid		35, 37.5, 60 ml	C
Burow's solution/ Domeboro Aluminum acetate	Dissolve one pack into 1 pint of water	12, 100, 1000 tabs/box	/
Dakin's solution Sodium hypochlorite	0.25% Solution 0.5% Solution	480, 3840 ml 480 ml	C

Vitamins/Nutritional Supplements

Biotin (Appearex 2.5 mg)	1 tab qd – for nails/ biotin deficiency	30 tabs	/
Folic Acid (Vitamin B9)	1 mg qd For MTX toxicity prophylaxis	100 tabs	A
Niacinamide (Niacin, Vitamin B3)	500 mg tid Suppression of antigen/ mitogen-induced lymphoblast transformation. For BP	500 mg	C
Nicomide (NOT niacin)	Contains nicotinamide 750 mg + copper 1.5 mg, folic acid 0.5 mg, zinc 25 mg for acne rosacea	60 tabs	A

Miscellaneous Meds

Colchicine	Start 0.3 mg qd- titrate to diarrhea 0.6 mg po bid-tid Prevents assembly of microtubules ☑ Check CBC, U/A, BMP q3mos	0.6 mg	C
Pentoxyfyline (Trental)	400 mg Tid For treatment of peripheral vascular disease, painful diabetic neuropathy ☑ Check serum creatinine/BUN baseline	400 mg	C
SSKI/Potassium Iodide 1 drop = 47 mg KI	5–15 drops Tid Alters host immune/non-immune response, for use in EM, E. nodosum, Sporothrichosis ☑ Check TSH, T4. Monitor for Wolff-Chaikoff effect – excess iodide can inhibit binding of iodine in the thyroid gland resulting in cessation of thyroid hormone synthesis	30, 240 ml	D

Cytochrome P-450 Interactions

CYP2D6	Substrates	Amiodarone, Antipsychotics, Beta Blockers, Antidepressants (TCA's, SSRIs, Venlafaxine) Narcotics (Codeine, Tramadol)
	Inducers	**Rifampin, Dexamethasone**
	Inhibitors	Potent: Amiodarone, SSRIs, Ritonavir Antipsychotics, Celecoxib, H1-Antagonists: Cimetidine, Hydroxyzine
CYP3A4	Substrates	Antiarrhythmic (Amidarone, Digoxin, Quinidine) Anticonvulsant (Carbamazepine, Verapamil) Antidepressant (Amitriptyline, SSRI) Immunosuppressive (Steroids, Dapsone, Tacrolimus, Cyclophosphamide, Cyclosporine) Others: Antihistamines, Benzodiazepine, CCBs, Estrogens, Erythromycin, Omeprazole, Statins, Protease Inhibitors, Theophylline,
	Inducers	**Anticonvulsants (Phenobarbital, Phenytoin, Carbamazepine)** **Anti-TB (INH, Rifampin), Glucocorticoids, St. John's Wort, Efavirenz, Nevirapine, Glitazones, Griseofulvin**
	Inhibitors	Antibiotics (Erythromycin, Clarithromycin Fluoroquinolone) Azoles, CCBs, Cimetidine, Protease Inhibitors, SSRI,Grapefruit Juice
CYP1A2	Substrates	TCA's, Theophylline, Haloperidol, Propranolol, Verapamil, R-Warfarin Estradiol, Tacrine, Clozapine, Naproxen, Zileuton, Zolmitriptan
	Inducers	**Omeprazole, Rifampin, Ritonavir**

		Nafcillin, Phenobarbital, Phenytoin **Smoking, Charbroiled meats** **Broccoli, Brussel Sprouts, Cabbage**
	Inhibitors	Fluoroquinolones, Fluvoxamine, Paroxetine, Amiodarone, Cimetidine, Ticlopidine Grapefruit Juice
CYP2C9	Substrates	Phenytoin, S-Warfarin, NSAIDs, Sartans (Losartan), Sulfonylureas Tricyclic antidepressants, Valproic acid
	Inducers	**Rifampin, Secobarbital, Ethanol**
	Inhibitors	Azoles, Ritonavir, INH, TMP-SMX Statins, Fluvoxamine Zafirlukast, Amiodarone

Pregnancy Categories of Commonly Used Dermatologic Agents

Class B	Class C
Acyclovir	Adapalene (Differin)
Alefacept (Amevive)	Bacitracin preps (Polysporin)
Amoxicillin	Benzaclin & Benzamycin
Amphotericin topical	Benzoyl peroxide
Augmentin	Calcipotriene (Dovonex)
Azithromycin (Zithromax)	Carmol
Azelaic acid (Azelex, Finevin)	Ciprofloxacin
Butenafine (Mentax)	Clarithromycin
Cephalexin (Keflex)	Cyclosporine
Cetirizine (Zyrtec)	Desloratadine (Clarinex)
Chlorhexidine (Hibiclens)	Econazole (Spectazole)
Ciclopirox (Loprox, Penlac)	Eflornithine (Vaniqa)
Clindamycin	Fexofenadine (Allegra)
Clotrimazole topical	Fluconazole (Diflucan)
Cimetidine	Griseofulvin – po
Cyproheptadine	Hydroquinones – topical
Diclofenac (Solaraze)	Hydroxychloroquine (Plaquenil)
Diphenhydramine	Hydroxyzine
Docosanol (Abreva)	Imiquimod
Doxepin	Itraconazole (Sporanox)
Erythromycin po/ topical	Ivermectin
Etanercept (Enbrel)	Ketoconazole (Nizoral)
Famciclovir	Levofloxin
Famotidine (Pepcid)	Methoxypsoralen
Glycopyrrolate (Robinul)	Miconazole (Micatin, Zeasorb)
Imiquimod	Minoxidil
Infliximab (Remicade)	Neomycin preps (Neosporin)
Lidocaine cream (LMX)	Nystatin
Loratadine (Claritin)	Pimecrolimus
Metronidazole topical	Rifampin
Mupirocin (Bactroban)	Sertazconazole (Ertaczo)
Naftifine (Naftin)	Sirolimus (Rapamune)
Oxiconazole (Oxistat)	Sodium sulfacet/sulfur (Avar, Plexion, Rosula)
Penciclovir topical	Sodium sulfacetamide (Klaron)
Penicillin	Steroids – systemic & topical
Permethrin (Elimite, Nix)	Sulfonamides
Silvadene	Tacrolimus – systemic & topical
Solaraze	Tretinoin (Renova)
Terbinafine – po & topical	Trimethoprim-sulfamethoxazole
Valacyclovir	
Zithromax	

Class D	Class X
Azathioprine (Imuran)	Acitretin
Doxycycline	Finasteride (Propecia)
Gentamicin topical	Fluorouracil (Efudex, Carac)
Minocycline	Isotretinoin (Accutane, Amnesteem)
Mycophenolate mofetil (Cellcept)	Methotrexate
Nitrogen mustard	Tazarotene (Tazorac)
Tetracycline	Thalidomide

B: Generally considered safe to use.
C: No evidence of harm to fetus.
D: Some significant risks. Use only if benefits outweigh risks.
X: Evidence of fetal abnormalities. Should not be used in pregnancy.

Common Dermatologic Drugs and Teratogenic Effects

	Medication	Teratogenic effects
Analgesics	Acetaminophen	Analgesic of choice, low dose not linked with identifiable risk throughout pregnancy
	NSAIDs	Caution in final trimester: fetal/neonatal hemorrhage and premature closure of ductus arteriosus
	Opioids	Respiratory depression and withdrawal symptoms
Antimicrobial	Tetracyclines	Dental staining and enamel hypoplasia (limited data for minocycline and doxycycline)
	Voriconazole	Known teratogen
	Lindane, malathion, permethrin	Although FDA category B, low risk and historically well tolerated, precipitated sulfur is often preferred given theoretical toxicity
Miscellaneous	Prednisone	Small risk of orofacial clefts
	Lidocaine with epinephrine	No appreciable risk for small excisional biopsies

From Leachman and Reed. The use of dermatologic drugs in pregnancy and lactation. *Dermatol Clin.* 2006 24: 167–97.

Dermatologic Drugs Reportedly Associated with Contraceptive Failure

Medication	Contraceptive agent	Proposed mechanism
Azathioprine	Intrauterine devices	Unknown
NSAIDs	Intrauterine devices	Unknown
Griseofulvin	Oral contraceptives	Increased estrogen metabolism by hepatic microsomal enzyme induction

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Medication	Contraceptive agent	Proposed mechanism
Rifampin	Oral contraceptives	Increased estrogen metabolism by hepatic microsomal enzyme induction or reduced enterohepatic circulation of estrogens
Tetracycline	Oral contraceptives (unlikely to play causal role in contraceptive failure)	Reduced enterohepatic circulation of estrogens
Sulfonamides	Oral contraceptives (unlikely to play causal role in contraceptive failure)	Reduced enterohepatic circulation of estrogens

Drug Eruptions

Common medications that can cause cutaneous eruptions. When these diseases start abruptly, flare, or are not controlled by conventional therapies, re-evaluate diagnosis and consider complicating factors such as medication list.

Disease	Medications
Acne	Corticosteroids, oral contraceptives, androgens, ACTH, lithium, phenytoin, halogens, isoniazid, haloperidol, radiation, sirolimus
AGEP	Beta-lactam antibiotics (most common), macrolides, mercury (association with loxocelism), diltiazem, hydroxychloroquine, terbinafine, imatinib
Alopecia	ACE inhibitors, allopurinol, anticoagulants, antidepressants, antiepileptics, azathioprine, bromocriptine, beta-blockers, cyclophosphamide, didanosine, ECMO, hormones, indinavir, interferons, NSAIDs, oral contraceptives, methotrexate, retinoids, tacrolimus
Beau lines/ onychomadesis	Carbamazepine, cefaloridine, chemotherapy (taxanes), cloxacillin, dapsone, fluorine, itraconazole, lithium, metoprolol, phenophtaleine, psoralens, retinoids, radiation, sulfonamides, tetracyclines
Bullous pemphigoid	Ampicillin, captopril, chloroquine, ciprofloxacin, enalapril, furosemide, neuroleptics, penicillamine, penicillins, phenacetin, PUVA, salicylazosulfapyridine, sulfasalazine, terbinafine
Dermatomyositis-like	Hydroxyurea (most common), lovastatin, simvastatin, omeprazole, BCG vaccine, penicillamine, tegafur, tamoxifen
Hypersensitivity/ DRESS	Phenobarbital, phenytoin, carbamazepine, minocycline, sulfonamides, dapsone, allopurinol, gold, nevirapine, abacavir, lamotrigine
Erythema nodosum	Oral contraceptives (most common), echinacea, halogens, penicillin, sulfonamides, tetracycline

Fixed drug eruptions	Trimethoprim-sulfamethoxazole, phenolphthalein, NSAIDs, anticonvulsants, tetracyclines
GA-like	Gold therapy, diclofenac, allopurinol, quinidine, intranasal calcitonin, amlodipine
Hair curling/kinking	Retinoids, indinavir, antineoplastics, valproate, azathioprine
Hair straightening	Interferon, lithium
Hypertrichosis	Acetazolamide, cyclosporin, minoxidil, phenytoin, psoralens, steroids, streptomycin, zidovudine
Interstitial granulomatous drug reaction	Anti-hypertensives (ACE inhibitors, calcium channel blockers, beta-blockers), antidepressants, anticonvulsants, antihistamines, lipid lowering agents
Leukocytoclastic vasculitis	Allopurinol, penicillins, sulfonamides, anti-TNF agents, quinolones, hydantoins, insulin, tamoxifen, OCP, phenothiazines, thiazides, retinoids, anti-influenza vaccines, interferons, sympatomimetic illicit drugs (ANCA+ vasculitis: hydralazine, propylthiouracil, MCN, leukotriene inhibitors; Necrotizing – bortezomib)
Lichenoid eruptions (usually sun-exposed areas, may be confluent)	Antimalarials, thiazides, demethylchlortetracycline, fenofibrate, enalapril, quinine, quinidine
Linear IgA dermatosis	Vancomycin, atorvastatin, captopril, carbamazepine, diclofenac, glibenclamide, lithium, phenytoin, amoidarone, piroxicam
Lupus erythematosus, definite association	Minocycline, methyldopa, chlorpromazine, procainamide, hydralazine, quinidine, isoniazide
Lupus erythematosus, possible association	Beta-blockers, methimazole, captopril, nitrofurantoin, carbamazepine, penicillamine, cimetidine, phenytoin, ethosuximide, propylthiouracil, sulfasalazine, levodopa, sulfonamides, lithium, trimethadione
Lupus erythematosus, unlikely association	Allopurinol, penicillin, chlorthalidone, phenylbutazone, gold, salts, reserpine, griseofulvin, streptomycin, methysergide, oral contraceptives
Lupus erythematosus, subacute cutaneous	Thiazides>terbinafine, verapamil, diltiazem, buproprion, enalapril, nifedipine, infliximab, etanercept, statins, interferon-alfa, leflunomide, acebutolol
Melanonychia	Chemotherapy, hydroxyurea, psoralens, zidovudine
Nail brittleness	Antiretrovirals, chemotherapy, retinoids
Nail, decreased growth	Cyclosporin, heparin, lithium, methotrexate, zidovudine
Nail, increased growth	Azoles, levodopa, oral contraceptives
Nail pigmentation	Antimalarials (blue-brown), anthraline (brown-black), clofazamine (dark brown), gold (yellow), minocycline (blue-gray), tar (brown-black), tetracyclines (yellow)
Paronychia	Antiretrovirals, cyclophosphamide, EGF receptor antagonists, fluorouracil, methotrexate, retinoids
Pemphigus	*Thiols*: ACE inhibitors, penicillamine, gold sodium thiomalate, mercaptopropionylglycine, pyritinol, thiamazole, thiopronine

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Disease	Medications
	Nonthiols: aminophenazone, aminopyrine, azapropazone, cephalosporins, heroin, hydantoin, imiquimod, indapamide, levodopa, lysine acetylsalicylate, montelukast, oxyphenbutazone, penicillins, phenobarbital, phenylbutazone, piroxicam, progesterone, propranolol, rifampicin
Photoonycholysis	Quinolones, tetracyclines, psoralens, quinine, captopril, chlorpromazine, thiazides, taxanes
Photosensitivity	ACE inhibitors, amiodarone, amlodipine, celecoxib, chlorpromazine, diltiazem, furosemide, griseofulvin, lovastatin, nifedipine, phenothiazine, piroxicam, quinolones, sulfonamides, tetracycline, thiazides
Pseudolymphoma	Phenytoin, ACE inhibitors, penicillamine
Pseudoporphyria	Amiodarone, bumetanide, chlorthalidone, cyclosporine, dapsone, etretinate, fluorouracil, flutamide, furosemide, hydrochlorothiazide/triamterene, isotretinoin, NSAIDs, oral contraceptives, tetracycline
Pseudotumor cerebri	Minocycline, tetracycline, doxycycline (most frequently reported tetracyclines in descending order), vitamin A analogs, corticosteroids (especially in withdrawal), nalidixic acid, sulfonamides, lithium, thyroxine, growth hormone, amiodarone, tamoxifen
Psoriasis	Antimalarials, beta-blockers, NSAIDs, penicillin, tetracycline, ACE inhibitors, G-CSF, interferons, lithium, corticosteroid withdrawal, anti-TNF agents
Pyogenic granulomas	Cyclosporin, EGF receptor antagonists, indinavir, retinoids,
Raynaud phenomenon	Ergot compounds (methysergide), OCPs containing estrogen and progesterone, non-selective beta-blockers (propranolol), chemotherapy, polyvinyl chloride
Serum sickness	Antithymocyte globulin, penicillin, vaccines (pneumococcal, rabies, horse serum derivatives)
Serum sickness–like	Cefaclor (most common), other beta-lactams, minocycline, propranolol, streptokinase, sulfonamides, NSAIDs, rituximab, buproprion, infliximab
SJS/TEN	Sulfonamides, antiepileptics, allopurinol, NSAIDs, antiretrovirals
Sweet syndrome	All-*trans*-retinoic acid, celecoxib, GCSF, nitrofurantoin, oral contraceptives, tetracyclines, trimethoprim-sulfamethoxazole
Thrombotic microangiopathy	CSA, mitomycin C, tacrolimus
Urticaria	Opiates, ibuprofen, aspirin, polymyxin B, tartrazine, beta-lactams (immunologic), dextran

Adapted from Knowles and Shear. Recognition and management of severe cutaneous drug reactions. *Dermatol Clin.* 2007; 25:245–53; Callen JP. Newly recognized cutaneous drug eruptions. *Dermatol Clin.* 2007; 25:255–61; Piraccini and Iorizzo, Drug reactions affecting the nail unit: diagnosis and management. *Dermatol Clin.* 2007; 25:215–21; Bolognia, Jorizzo and Rapini. *Dermatology.* St. Louis: Mosby, 2003.

Chemotherapeutic Agents and Skin Changes

Cutaneous manifestation	Chemotherapeutics
Alopecia (most common reaction to chemotherapy, usually anagen effluvium)	
Irreversible alopecia	Cyclophosphamide, busulfan
Hair texture change upon regrowth *(dry and dull)*	Doxorubicin
Hyperpigmentation	
Serpentine supravenous hyperpigmentation	Fluorouracil, fotemustine, vinorelbine, docetaxel, sometimes with combination chemotherapy
Hair color change from light to black	Cyclophosphamide
Flag sign	Methotrexate
Flagellate streaks with pruritus	Bleomycin
Dusky pigmentation, similar to Addison's except no mucous membrane involvement	Busulfan – "busulfan tan"
Areas of pressure	Cisplatin
Acral	Tegafur
Occluded areas	Thiotepa, BCNU
Banded hyperpigmentation of nails	Bleomycin, cyclophosphamide, daunorubicin, doxorubicin, fluorouracil, melphalan, vincristine
Oral hyperpigmentation: mucous membrane	Doxorubicin, fluorouracil
Oral hyperpigmentation: gingival	Cisplatin (transient lead line)
Oral hyperpigmentation: teeth	Cyclophosphamide
Yellowish discoloration	Sunitinib
Interaction with ultraviolet light	
Most phototoxic	Fluorouracil, dacarbazine, methotrexate
Photoallergy	Flutamide, tegafur
Photo-onycholysis	Mercaptopurine, taxanes
Ultraviolet recall	Methotrexate, suranim
Reverse UV recall (reactivation of healed extravasation ulcer)	Mitomycin
Squamous cell carcinoma	Fludarabine
Inflammation of keratoses	
Actinic keratosis	Fluorouracil, doxorubicin, sorafenib, capecitabine
Seborrheic keratosis	Cytarabine
Hypersensitivity reactions	
Type I hypersensitivity (i.e. urticaria, anaphylaxis) most common	L-asparaginase, paclitaxel, docetaxel, mitomycin-C
Type I hypersensitivity (i.e. urticaria, anaphylaxis) severe	Methotrexate

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Cutaneous manifestation	Chemotherapeutics
Type IV hypersensitivity (i.e. contact dermatitis)	Mitomycin-C (groin), mechlorethamine, carmustine
Fixed drug in patients with SLE on cyclophosphamide	Mesna
Flushing (results in skin thickening and hyperpigmentation, stop treatment)	Mithramycin, mitomycin, plicamycin
Nail dystrophies	
Subungal abscess	Docetaxel (subungual hemorrhage – docetaxel, sunitinib)
Nail bed changes	EGFR inhibitors (splinter hemorrhages – sunitinib, sorafenib)
Onycholysis	Bleomycin, cyclophosphamide, fluorouracil, methotrexate, mitoxantrone, doxorubicin, paclitaxel
Leukonychia	Anthracyclines, cisplatinum, cyclophosphamide, vincristine
Miscellaneous	
Raynaud's phenomenon (vasoconstriction)	Bleomycin, vinblastine, cisplatin, gemcitabine, rituximab
Flushing (vasodilation)	Anthracyclines, asparaginase, bleomycin, cisplatin, dacarbazine, taxanes
Capillary leak syndrome – edema (skin and lungs), erythema, pruritus, vascular collapse	Taxanes, gemcitabine, IL-2, sirolimus, docetaxel, G-CSF
Scleroderma-like reaction	Bleomycin, docetaxel, paclitaxel, melphalan, gemcitabine
Ulcers	Hydroxyurea (leg), methotrexate, interferon, bleomycin
Acanthosis nigricans	Diethylstilbestrol
Furunculosis	Fluoxymesterone, methotrexate
Pustular psoriasis	Aminoglutethimide
Sticky skin (acquired cutaneous adherence)	Doxorubicin, ketoconazole
Acute intermittent porphyria	Chlorambucil, cyclophosphamide
Dermatomyositis-like reaction	Hydroxyurea, tamoxifen, tegafur
Discoid lupus	Fluorouracil, tegafur (SCLE-taxanes)
Bullous pemphigoid	Dactinomycin, methotrexate
Exacerbation of psoriasis and autoimmune disorders (also injection site reactions)	Interferons, IL-2
Sweet's syndrome	GCSF
Erythema nodosum	Azathioprine
Increased skin neoplasms	Hydroxyurea, suranim
Folliculitis	Dactinomycin
Lichen planus	Hydroxyurea, tegafur
Leukoderma	Topical thiotepa
Acneiform eruption	EGF receptor inhibitors (i.e. cetuximab), actinomycin D, docetaxel

Cutaneous manifestation	Chemotherapeutics
Edema (>eyes & ankles), pigmentation changes	Imatinib (edema is thru PDGFR)
Conjuctivitis	Cytarabine
Excessive lacrimation	Docetaxel
Blue sclera	Mitoxantrone
Pseudolymphoma	Gemcitabine (also erysipelas-like reaction)
Baboon syndrome	Hydroxyurea (also amoxicillin, ampicillin, nickel, heparin, mercury)
Neutrophilic eccrine hidradenitis	Cytarabine, bleomycin, GCSF
Acral erythema = hand-foot; Syndrome = Burgdorf's; Syndrome = "Palmar-plantar erythrodysesthesia"	Cytarabine, doxorubicin, fluorouracil, sorafenib (bullous variant: cytarabine, methotrexate, tegafur (PPK))
Radiation recall	Dactinomycin, doxorubicin, docetaxel, etoposide gemcitabine, methotrexate
Radiation enhancement	Doxorubicin, dactinomycin, 5-bromodeoxyuridine
Extravasation	
Necrosis (vesicant)	Doxorubicin, daunorubicin (large ulcerations), bleomycin, doxorubicin, vinblastine, vincristine
Rx: aspiration, cold packs, except vinca alkaloids require heat. Otherwise specific antidotes as below	

Antidote to extravasation of chemotherapeutic agents

Antidote	Specific drug
Sodium thiosulfate (neutralizes vesicant)	Mechlorethamine cisplatin
Dimethlysulfoxide (free radical scavenger), dexrazoxane	Anthracyclines, mitomycin C
Vinca alkaloids	Hyaluronidase

Adapted from Sanborn and Sauer. Cutaneous reaction to chemotherapy: commonly seen, less described, little understood. *Dermatol Clin.* 2008; 26:103–19; Guillot et al. Mucocutaneous side effects of antineoplastic therapy. *Expert Opin Drug Saf.* 2004; 579–87; Bolognia, Jorizzo, and Rapini. *Dermatology.* St. Louis: 2003.

UV Light Treatment

UVA/UVB dosing

	UVA			UVB	
Skin type	**Initial dose (J/cm^2)**	**Increment (J/cm^2)**	**Max**	**Initial dose (mJ/cm^2)**	**Increment (mJ/cm^2)**
I	0.5	0.5	5	20	5
II	1.0	0.5	8	25	10

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III	2.0	0.5–1.0	12	30	15
IV	3.0	0.5–1.0	14	40	20
V	4.0	1.0–1.5	16	50	25
VI	5.0	1.0–1.5	20	60	30

Classify patient with erythroderma as Type I skin.

NBUVB dosing

Skin type	Initial dose (mJ)	Increase (mJ)	Estimated goal ~4× initial dose
I	130	15	520
II	220	25	880
III	260	40	1040
IV	330	45	1320
V	350	60	1400
VI	400	65	1600
Vitiligo	170	30	Unknown

PUVA

- *Absolute contraindication*: Photosensitivity (lupus, albinism, XP), porphyria, pregnancy, lactation.
- *Relative contraindication*: Melanoma or family history of melanoma, personal history of non-melanoma skin ca, prior radiation, arsenic, photosensitizing meds (simply note use then "start slow and go slow"), severe cardiac/liver/renal disease, pemphigus/pemphigoid, immunosuppression, inability to understand details of tx.
- *Photosensitizing meds*: Griseofulvin, phenothiazine, nalidixic acid, salicylanilides, sulfonamides, TCN, thiazides, MTX, retinoids.

Choosing appropriate patients

- Usually reserved for severe disease or patients unresponsive to UVB
- Good choice for patients whose disease will likely require maintenance (i.e. long history of severe psoriasis or CTCL).
- Good choice for thicker plaques, palmar/plantar disease, or erythematous/pustular disease due to deeper penetration.
- Better in darker skin (Type III or above).

General precautions

- *Eye protection*: It is absolutely necessary on day of treatment
- *General sun protection*: Patients need to be more cautious with sun exposure to avoid risk of burning, worsening photoaging, and

"hardening" their skin with natural sunlight which makes them less responsive to phototherapy
- *Genital coverage for men*: Wear athletic support or sock over genitals. No full coverage underwear as most psoriasis and CTCL patients have involvement of their buttocks

8-METHOXYPSORALEN = Oxsoralen Ultra 10 mg caps
Dose 0.6 mg/kg

Take 1.5–2 h before treatment with food/milk.

Side effects: Nausea, anorexia, dizziness, HA, malaise, phototoxic reaction

Nausea: decrease dose by 10 mg, take with food, rarely anti-emetics. *Treatment for nausea*: Divide dose, take with food.

PUVA Burns: UVB burns present within 12–24 h, PUVA burns are delayed 48 h but can be as late as 96 h. Prevent repeat burns by careful questioning of patients by phototherapy nurses, patient education, and always skipping a day between tx (i.e. MWF) to give a burn time to present itself.

PUVA Itch: It can be intractable and can last for weeks. Make sure patient's skin is hydrated and then back off on light as soon as patients complain (see below). This itch usually does NOT respond to anti-pruritic agents.

Long-term side effects: Photoaging, non-melanoma skin ca, potential for increase melanoma risk, cataracts (prevent with eye protection), genital cancer (shield)

Clearing schedule

- Usually takes 10 treatments to tell if responsive
- If no response, increase additional 0.5 J/tx
- If after 15 treatments and no response, increase dose by 10 mg
- Correctable causes for non-response: missed tx, inadequate oxsoralen concentration in the skin (patient not pigmenting), patient not taking med, or taking medication which increases liver enzyme (i.e. carbamazepine, phenytoin)
- Takes 25–30 treatments to achieve control (3 months)

Maintenance schedule

- Once clearance is achieved, maintain dose but space out visits (i.e. qwk $\times$ 4, then qow $\times$ 4, then q mo)

Missed treatment

Missed 1 tx	Hold dose as previous
Missed $>$1 tx	Decrease by 0.5 J for each tx missed
Missed $>$3 tx	May need to return to starting dose

Pruritus protocol (i.e. PUVA itch)

Mild	Use moisturizer, increase UVA by 0.5 J
Severe	Stop UVA for a few days to see if light induced. (If yes, then decrease by 2–3 J)
Intractable	Localized: shield area, keep UVA constant Generalized: Stop tx until clear, then resume 2–3 J below pruritic dose

Erythema protocol

None	Increase per skin type
Minimal	(Erythema occurs but resolves by next appointment) Hold UVA dose content, do not increase until resolve
Marked	(Erythema occurs and does not resolve by next appointment) Stop tx until erythema resolve
Edema	Do not treat

Washington University Dermatology Toxic Epidermal Necrolysis (TEN) Protocol

Based on current published data and reviews on the treatment of TEN. Courtesy of Dr. Amy Cheng and Dr. Grace Bandow

Diagnosis of TEN

History

- Fever, cough, sore throat, constitutional sxs may occur 1–3 days prior to rash.
- Burning eyes, photophobia, burning/painful skin starts on torso/face.
- Drug exposure 1–3 weeks prior.

Physical Exam

- Initial lesions are poorly defined macules with dusky centers/bullae with surrounding erythema, that is two zones of color, not a classic target with three zones.
- Full thickness necrosis leads to Nikolsky sign (lateral shearing) and wrinkled paper skin. Detachment occurs in areas of pressure (palms/soles). Denuded areas are oozing dark red.
- Mucosal involvement: urethra, GI, vulva, anus, eyes, mouth, tracheobronchial tree.

Common culprits: Sulfa, PCN, quinolones, cephalosporins, carbamazepine, phenobarbital, phenytoin, valproic acid, NSAIDs, allopurinol, lamotrigine, HAART.

Workup for suspected TEN

- CBC, CMP, LFTs, albumin, lytes, baseline CXR.
- Skin biopsy for frozen section and H&E, IgA.
- Do not need to culture the skin unless you think they are septic.

Triage algorithm for TEN patients

1. What is the total body surface area affected?
   A. <10% TBSA (including areas of erythema) →Continue to Step 2
   B. >10% TBSA →Continue to Step 4

2. Is the patient:
   A. <10 year old or >50 year old →Continue to Step 4
   B. Between 11 and 49 year old →Continue to Step 3

3. Does the patient have underlying medical problems?
   A. Yes (CHF, Renal, Pulm, Diabetes, Others) →Continue to Step 4
   B. No → OK To: Manage on the Floor with Wound Care Consult
   Reevaluate Daily: If progresses or needs more extensive wound care, then transfer to ICU for care. Wound care alone justifies ICU transfer

4. ICU Care: (If no Burn Unit is readily available) Transfer to Unit based on underlying concerns
   A. Significant Medical Co-morbidities:
      – MICU
      – Wound Care Consult
   B. No-Significant Medical Co-morbidities:
      – SICU
      – Wound Care Consult

Treatment for all TEN patients

1. Start IVIg immediately. Check IgA levels first, but do not wait for results to start treatment because it can take several days. See Appendix I below for starting IVIg.
2. Identify and STOP ALL non-vital medications.
3. Consider additional dialysis if needed for patients with ESRD.
4. Consultations:
   a. Ophthalmology. 40% of TEN survivors have disabling ocular symptoms including scarring and blindness.
   b. Nutrition. Massive protein loss may require enteral or parenteral feeding.
   c. Consult additional services (pulmonary, GI, urology, OB-GYN for mucosal involvement) prn system involvement.
5. Evaluate percentage of TBSA affected daily.
6. Evaluate mucosal involvement daily: eyes, GU, pulmonary.
7. Wound care:
   a. Swab mouth, nose, involved orifices with saline daily. Apply mupirocin ointment. Non-sulfa antibiotic ointments and eye drops

are usually recommended by ophtholmology. They should follow daily to break up synechiae.

b. Vaseline with vaseline gauze to denuded skin (alternatives: Exudry, Telfa or Acticoat dressings, kept wet with sterile saline). Vaseline on intact blisters. Leave necrotic intact epidermis in place. Leave normal skin alone. Do not use Silvadene! (It has a sulfa moiety.)

8. Monitor electrolytes, albumin, fluids and replace accordingly – patients lose a lot transdermally but can get overloaded with high volume of IVIg if CHF or renal failure.
9. Warming to combat massive heat loss.
10. Avoid taping, debridement, or skin trauma.
11. Prophylactic antibiotics are not recommended: may cause worsening drug reactions and increase resistance.
12. Prednisone is controversial. Questionable benefit of short course in early TEN. Most do not recommend because of increased infections and mortality in septic patients.
13. Output follow up: ophtho, GI, GYN, urology, etc. based on involvement for evaluation and tx of strictures, phimosis, synechiae, etc.

Appendix I: American Burn Association Burn Center Referral Criteria

1. second or third degree burns >10% body surface area in patients <10 year old or >50 year old.
2. second and third degree burns >20% TBSA any age group.
3. Significant burns of face, hands, feet, genitalia.
4. Full-thickness burns that involve more than 5% of TBSA in other age groups.
5. Significant electric injury, including lightning injury.
6. Significant chemical injury.
7. Lesser burn injuries w/ associated inhalation injury, concomitant mechanical trauma or significant pre-existing medical disorders.
8. Burn injury in patients who will require special social, emotional, or long-term rehab support.

Appendix II: SCORTEN Score (Risk factors for death in both SJS and TEN)
One point for each factor:

Age > 40
Malignancy
Heart rate > 120
BUN > 10 mmol/l
Serum glucose > 250 mg/dl
Bicarb < 20 mEq/l
Initial BSA involved with epidermal detachment > 10%

Mortality rates are as follows:

SCORTEN 0–1 = 3.2%
SCORTEN 2 = 12.1%
SCORTEN 3 = 35.3%
SCORTEN 4 = 58.3%
SCORTEN > 5 = 90%

Appendix III: IVIg

Avoid in patients with known IgA deficiency and anaphylaxis to previous IVIg infusions.

Need monitored bed for administration (especially if IgA levels not available, frequently test not available over the weekend at many hospitals).

Gammagard is the IgA-deficient brand that needs to be specially ordered for IgA deficient or unknown status patients.

Dose 3 g/kg/total over 3–4 days as tolerated (slow infusion rate if necessary for ESRD or CHF patients; some cases demonstrated benefit w/2 g or 1.5 g)
Write orders to dose the infusion rate at

30 cc per hour × 1 h
60 cc per hour × 2nd h
120 cc per hour after that
For example 70 kg patient would get 70 g/d × 3 days
70 g is about 1600 cc of Gammar P
This would take ~12.5 h to infuse.

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COMMONLY USED MEDICATIONS

Cr = Cream, F = Foam, G = Gel, L = Lotion, O = Ointment, S = Solution, e=emollient

Acne Vulgaris / Rosacea

Accutane 0.5 – 1 mg/kg/day divided qd-bid. 10,20,30,40 mg
Azelex 20% Cr – 30, 50 g
Benzaclin (BP 5%, clinda 1%) G – 25, 50 g
Benzamycin (BP 5%, erythro 3%) G – 23, 46g
BP LQ 2.5,5,10%; bar 5, 10%; L &Cr 5, 10%; G 2.4,4,5,6,10,20%
Cleocin T 1% S, L – 60 ml, 1% G – 30, 60 g, 1% pledgets – 60/box
Differin 0.1% Cr, G – 45 g; 0.3% G – 45 g
Duac (BP 5%, clinda 1%) G – 45 g
Erythromycin 2% O – 25 g; 2% G – 27, 50 g
Evoclin 1% F – 50, 100 g
Finacea 15% G – 30 g
Klaron L– 59 ml
Metronidazole 1%Cr – 30 g; 0.75%Cr – 30,45 g; 0.75%G – 29 g; 0.75%L – 59 ml
Retin-A Micro 0.04%, 0.1% G – 20, 45 g; generic 0.025%, 0.05%, 0.1% Cr –20, 45 g; generic 0.025%, 0.1% G – 15, 45 g
Sulfacet R L – 25 ml
Tazorac 0.05%, 0.1% Cr – 15, 30, 60 g
Ziana (clinda 1.2%, tretinoin 0.025%) G – 30, 60 g

Antibiotics – Topical

Mupirocin/Bactroban bid/tid 2% Cr, O–15, 30 g
Polysporin – (bacitracin + polymyxin) – OTC
Silvadene 1% Cr – 20, 50, 400, 1000 g

Antibiotics – Systemic

Bactrim DS BID
Keflex 500 mg BID-QID; 250, 500 mg tab
Tetracycline 500 mg BID; 250, 500 mg tab
Doxycycline 100 mg BID; 50, 100 mg tab
Minocycline 100 mg BID; 50,100 mg tab

Antibiotic Preoperative Prophylaxis

1 hr prior to surgery
Amoxicillin: 2 g; 500 mg tab
Cephalexin: 2 g; 500 mg tab
If allergic to penicillin:
Clindamycin: 600 mg; 300 mg tab
Azithromycin/Clarithromycin: 500 mg; 500 mg tab

Antifungal

Ciclopirox (Penlac) 8% nail S – 6.6 ml
Diflucan/Fluconazole 150–300 mg Qwk; 150 mg
Griseofulvin 20 mg/kg/d; 250, 500 mg, 125 mg/5 ml
Lamisil/Terbinafine 250 mg po qd, 250 tab; OTC 1% C, S, spray
Loprox/ Ciclopirox 1% Cr, L – 15, 30, 90 g
Mentax/ Butenafine1% Cr– 15, 30 g
Micatin/Miconazole 2% Cr– 15, 30, 90 g
Nizoral/Ketoconazole 400 mg, 200 mg tab; 2% Cr–15, 30, 60 g; 2% wash – 120 ml
Specatazole/Econazole 1% Cr– 15, 30, 85 g
Sporanox/Itraconazole 200 mg qd or pulse dose 200 mg BID × 7 days Q month
Thymol 4% in alcohol: 30cc Disp c dropper.
Naftin1% G, Cr – 15, 30, 60 g
Zeasorb – AF Powder/Miconazole 2%

Antiparasitics

Elimite/Permethrin – Cr 5% – 60 g
Ivermectin 0.2 mg/kg × 1; 6 mg tab

Antivirals

Aldara/Imiquimod 3×/wk qhs; Cr 5%-1 box=12 or 24 pks
Abreva/docosanol 5×/d OTC Cr 10% – 2 g
Denavir/Penciclovir Q2h × 4d; Cr 1% – 2 g
Valtrex 2 g BID × 1d; 500, 1000 mg tab
Zovirax/Acyclovir Q3h × 5–7d; O 5%- 2, 10 g

Antihistamines

Allegra/Fexofenadine 60 mg BID or 180 mg QD; 60, 180 mg tab
Atarax/Hydroxyzine 10–50 mg q4-6h; 10, 25 mg, 10 mg/5 ml
Clarinex/Desloratadine 5 mg QD; 5 mg tab
Claritin/Loratadine 10 mg QD; OTC 10, 5/5 ml
Doxepin 10–75 qhs; 10, 25, 50 mg tab
Zyrtec/Cetirizine 5–10 mg; 5, 10, 5/5 ml

Bleaching agents

Azelex 20% Cr – 30, 50 g
Hydroquinone BID. 4% Cr – 30, 60 g

Chemotherapy

Aldara/Imiquimod. For AK, BCC qhs × 8–12wks. Cr 5% – 1 box = 12 or 24 single use 250 mg packets
Efudex/Fluorouracil. For AK qd-bid × 2–6wks. 5% Cr– 25 g; 2%, 5% S – 10 ml
Solaraze/diclofenac bd × 3mo; Cr 5% – 30, 45 g

CTCL

Bexarotene Tabs 200–300 mg/m2 qd; 75 tab
Nitrogen Mustard BID.10 mg% in Aquaphor
Targretin/Baxarotene Gel qd-bid. 1% G – 60 g

Psoriasis

Dovonex/Calcipotriene bid. 0.005% O, Cr – 30, 60, 100 g; scalp S – 60 ml
Dermazinc with Clobetasol Spray. Write Dermazinc 4 oz. compound with 50 mcg micronized clobetasol, disp 4 oz.
Liquor Carbonis Detergens (LCD): Must be compounded: TMC 0.1% oint compounded with 10% LCD, Disp.1 lb.
Oxsoralen Ultra 0.4–0.6 mg/kg 1–2 h prior to PUVA. 10 mg tab
Tazorac/Tazorotene qd. Cr 0.05%, 0.1% – 15, 30, 60 g, G 0.05%, 0.1% – 30, 100 g

Miscellaneous

Biotin 2.5 mg qd
Colchicine 0.3 mg, titrate to diarrhea; 0.6 mg tab
Drysol 20% Solution; QHS until effective then spaced out; S – 35, 37.5, 60 ml
Folic Acid 1 mg qd; 1 mg tab
Lac-hydrin (lactic acid) bid; Cr 12% – 140, 385 g;L 12% – 150, 360 ml
Niacinamide 500 mg tid; 500 mg tab
Propecia/finesteride 1 mg qd; 1 mg tab
Robinul 1 mg qd, titrate to effect; 1 mg tab
Trental 400 mg tid; 400 mg tab
Vaniqa/eflornithine bid. Cr 13.9% – 30 g

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