Neelam A. Vashi *Editor*

The Dermatology Handbook

A Clinician's Guide

Springer

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Contents

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Chapter 1
The Basics: Skin Types, Definitions, and Differentials

Elizabeth R. Rae, Mayra B. C. Maymone, and Neelam A. Vashi

Table 1.1 Skin types

Skin type	History/physical examination
I	Always burn, never tan
II	Always burn, but sometimes tan
III	Sometimes burn, but always tan
IV	Never burn, always tan
V*	Moderately pigmented
VI*	Deeply pigmented dark brown to darkest brown/black

*Patients with natural pigmentation of these types may be classified into a lower skin-type category if the sunburning history so indicates. Adapted from Fitzpatrick TB. Soleil et peau. Journal de Medecine Esthetique. 1975;2(33)

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Skin Lesion Description

Describing skin lesions and findings is an important skill in order to effectively communicate with colleagues. The description should include primary lesion terminology with information in regards to color, distribution, color, configuration, borders, and shape along with any secondary lesions if present. The tables below define terms that are used to describe lesions.

Table 1.2 Primary Lesions

Term	Size	Description
Macule	<1 cm	Flat spot that can only be noticed visually; without elevation
Papule	<1 cm	Dome-shaped, flat-topped, may be umbilicated or with a dell
Vesicle	<1 cm	Raised bump filled with air or clear liquid[a]
Pustule	<1 cm	Raised bump filled with pus
Nodule	<1 cm	Elevated bump on the skin that can occur in all layers of the skin[a]
Cyst	Varies	Nodule filled with liquid or semi-liquid
Plaque	>1 cm	Flat-topped but raised lesion; with elevation
Patch	>1 cm	Large flat spot (macule)
Bulla	>1 cm	Fluid-filled sacs that occur when fluid becomes under the skin[a] - Flaccid (more likely epidermal) vs tense (more likely dermal) - Epidermal bullae can appear tense on acral sites because the overlying stratum corneum is thicker - Although tense blisters can evolve to flaccid, flaccid blisters will not become tense
Tumor	>1 cm	Firm, solid mass on the skin or subcutaneous tissue[a]

[a]Primary Skin Lesions. SkinVision. https://www.skinvision.com/library/primary-skin-lesions. Published July 10, 2017

Table 1.3 Terminology of other descriptive lesions

Term	Description
Wheal	Red, swollen plaque, often itchy and changes shape, aka hives or welts
Telangiectasia	Dilated blood vessels near the skin surface that cause threadlike lines
Petechiae	Non-blanching red spot that is typically <1 cm
Purpura	Non-blanching red spot that is typically >1 cm
Comedones	Dilated hair follicles filled with keratin, bacteria, and sebum Closed comedones (whiteheads) have an obstructed opening to the skin Open comedones (blackheads) have an opening to the skin filled with dark appearing (oxidized) skin debris
Milium or Milia (plural)	Small, superficial epidermoid cysts, appear as small, white bumps
Burrow	Tunnels formed in the skin, appear as linear lines (from parasitic infestation)
Boil (furuncle)	Pus-filled bump that forms under the skin when bacteria infect or inflame one or more hair follicles; begin as red, tender bumps; painful Carbuncles are clusters of boils that form connections under the skin

Table 1.4 Terminology for describing color, shape, texture, and pattern of lesions

Color

Although describing color can be somewhat subjective, the description should be made with the specific color. It is important to also distinguish certain features of colors with specific terms as described in the below table.

Term	Description
Depigmented	No color/white; Wood's lamp will fluoresce
Hypopigmented	Decrease of skin pigment or color
Hyperpigmented	Increase in skin pigment or color
Erythematous	Red and blanches on palpation (or diascopy)
Violaceous	Purple
Purpuric	Red/purple that does not blanch
Dusky	Dark purple/gray; can be difficult to distinguish purpura vs early necrosis

Shape

The outline of an area, or shape, tells important information about the underlying lesion and helpful when communicating through medical records.

Term	Description
Annular	Round with central clearing
Round/nummular/discoid	Round without central clearing
Ovoid	Oval-like
Serpiginous	Having a wavy margin (snake-like)

Table 1.4 (continued)

Targetoid	Like a target, with three zones: dusky (or blistered) center, surrounded by white ring, and then erythema; often refers specifically to erythema multiforme lesions
Polycyclic	Multiple overlapping annular lesions
Arcuate	Incomplete annular arc
Polymorphous	Many different shapes

Texture

Texture refers to the feel and/or consistency of a surface or substance.

Term	**Description**
Soft	Easily compressible, like fat
Firm	Not easily compressible or movable, hard; such as when feeling calcium filled lesions that are very hard on palpation
Indurated	Firm and bound-down
Boggy	Edematous, suggesting fluid between collagen in the dermis
Fleshy	Implies exophytic or pedunculated with a soft, squishy texture
Horny	Has thick pointy hyperkeratotic elements, an example is a cutaneous horn
Vegetative	Layered extension of a plaque/tumor, appears to be growing upon itself

(continued)

Table 1.4 (continued)

Juicy	An edematous/fluid-filled appearance

Patterns

Patterns can be thought of as the configuration, groupings, distribution of lesions and also provide diagnostic information.

Term	**Description**
Follicular/folliculocentric	Arising from and associated with hair follicles
Morbilliform	Multiple macules and papules 2 mm to 1 cm
Reticular/reticulated	Net-like
Retiform	Branching and/or angulated
Guttate	Small spots or "drops"
Monomorphic/monomorphous	All lesions appearing identical and in the same stage

Table 1.5 Secondary lesions

Term	**Description**
Erosions	Epidermal breaks in skin (superficial, do not appear deeper than top layer of skin)
Ulcers	Deeper breaks in skin involving the dermis; may appear "punched out" or with "undermined borders"
Crust	Dried exudates or plasma from vesicle, pustule, trauma (aka scab)
Scale	Compacted stratum corneum appearing as flakes "Branny" scale is exfoliating scale (bran-flake like)

Table 1.5 (continued)

Term	Description
Eschars	Thick black/necrotic crusts (can be associated with infections such as rickettsialpox, anthrax, brown recluse spider bites, ecthyma gangrenosum)
Dermal Atrophy	Wrinkled
Epidermal Atrophy	Shiny
Poikiloderma	Appearance with 3 components: atrophy, hypo/hyperpigmentation, and telangiectasia
Collarette of Scale	Small circle of scaling (from ruptured/evolved vesicle or pustule)
Trailing Scale	Scale at inner edge of erythema; occurs in pityriasis rosea and erythema annulare centrifugum
Leading Scale	Scale at edge of erythema (such as in tinea corporis)
Exfoliation	Peeling of topmost skin layer (stratum corneum)
Desquamation	Scaling and loss of topmost skin layer (stratum corneum)
Denudation	Loss of entire epidermis including basement membrane
Epidermal Change	Scale, pigmentation alteration, vesiculation, fissures, lichenification/thickening, epidermal atrophy, verrucous/papillomatous change
Dermal Change	Dermal atrophy, loss of elastic tissue (termed anetoderma), erythema, papules, plaques, nodules, cysts, sclerosis/scar/keloid, peau d'orange (dimpled appearance)

Differential Diagnoses Based on Primary Lesions

Primary Lesions

Macules and Patches

White/Hypopigmented Macules

Alezzandrini's syndrome (vitiligo)
Amelanotic melanoma or melanoma with regression
Amino acid disorders (e.g. Phenylketonuria)
Atrophic lichen planus
Chediak-Higashi syndrome
Chemical leukoderma (i.e. phenols)
Halo nevus without nevus
Hypomelanosis of Ito
Hypopigmented mycosis fungoides
Idiopathic guttate hypomelanosis
Incontinentia pigmenti – fourth stage
Lichen sclerosis et atrophicus
Morphea
Nevus anaemicus
Nevus depigmentosus
Oculocutaneous albinism
Partial albinism (piebaldism)
Pityriasis alba
Pityriasis Lichenoides chronica
Progressive macular hypomelanosis
Post inflammatory hypopigmentation
Radiation dermatitis
Scarring discoid lupus erythematosus
Syphilis, yaws, pinta
Thyroid disease
Tinea versicolor
Tuberculoid leprosy

Tuberous sclerosis
Vitiligo
Vogt-Koyanagi syndrome (vitiligo)
Waardenburg's syndrome (piebaldism)

Brown Macules

Acanthosis nigricans
Adrenocorticotropic hormone (ACTH) administration
Addison's disease
Agminated Nevus
Albright's syndrome
Ataxia-telangiectasia
Becker's nevus
Berloque dermatitis
Bloom's syndrome
Cafe au lait spots
Congenital nevus
Drug (i.e. arsenic, psoralen, chlorpromazine, minocycline)
Dyskeratosis congenita
Ephelides
Erythema dyschromicum perstans (initial lesions)
Erythromelanosis follicularis faciei et colli
Exogenous Ochronosis
Fanconi's syndrome
Fixed drug eruption
Galli-Galli disease
Hemochromatosis
Junctional nevus
Lentigo maligna
Lentigo
Lichen amyloidosis
lncontinentia pigmenti - third stage
Macular amyloidosis
Melasma
Mongolian spot
Moynahan's syndrome (LEOPARD)

Nevus of Ota/Ito
Nevus spilus
Peutz-Jeghers syndrome
Pigmented contact dermatitis (Riehl's melanosis)
Phytophotodermatitis (i.e. limes, celery, fig)
Postinflammatory hyperpigmentation
Seborrheic keratosis (early)
Speckled lentiginous nevus
Traumatic tattoo
Tuberous sclerosis
Urticaria Pigmentosa
Von Recklinghausen's Neurofibromatosis

Erythema/Red Macules

Acral erythema (palms and soles – due to chemotherapy)
Carcinoid
Drug hypersensitivity syndrome (sulfa, anticonvulsants, allopurinol, minocycline)
Erysipelas
Figurate erythemas –

- Erythema multiforme
- Erythema annulare centrifugum
- Erythema marginatum
- Erythema chronica migrans
- Erythema gyratum repens
- Erythema dyschromicum perstans

Fixed drug eruption
Necrolytic migratory erythema (glucagonoma)
Physical agents –

- Heat (erythema ab igne, first degree burn)
- Cold
- Trauma

Postinflammatory erythema
Scarlet fever
Staph/strep toxic shock syndrome
Toxic erythema (drug, infection, systemic disease)
Ultraviolet exposure
Urticaria
Urticaria pigmentosa
Vascular nevi
Viral exanthems (i.e. nterovirus, hepatitis, mononucleosis, measles, roseola, erythema infectiosum)

Atrophic Patches

Acrodermatitis chronica atrophicans
Anetoderma
Aplasia cutis congenita
Atrophic lichen planus
Atrophie blanche
Atrophoderma of Pasini and Pierini
Chronic graft vs. host reaction
Extramammary Paget's
Focal dermal hypoplasia
Follicular atrophoderma
Leprosy
Lichen sclerosus et atrophicus
Lupus erythematosus
Macular atrophy
Malignant atrophic papulosis (Degos disease)
Meischer's granuloma (giant cell elastophagocytosis)
Morphea
Necrobiosis lipoidica diabeticorum
Nevus lipomatosus
Sarcoidosis
Steroid application or injection
Striae
Syphilis, tertiary

Papules and Plaques

Red Papules

Arthropod reaction
Bacteremia (i.e. meningococcal, gonococcal)
Disseminated candidiasis
Eruptive xanthomas
Folliculitis (i.e. bacterial, candidal, eosinophilic, fungal, viral)
Gianotti-Crosti syndrome (children-acral only; hepatitis B, EBV)
Guttate Psoriasis
Hot tub folliculitis (*Pseudomonas*)
Lymphomatoid papulosis
Miliaria rubra/profunda
Papular drug eruption
Pityriasis lichenoides et varioliformis acuta
Scabies
Secondary Syphilis
Viral exanthem

Annular Papules

Alopecia mucinosa
Arthropod reaction
Basal cell carcinoma
Contact dermatitis
Dermatophyte infections
Elastosis perforans serpiginosa
Erythema elevatum diutinum
Granuloma annulare
Leiomyoma
Lichen planus
Lymphocytic infiltrate of Jessner
Lymphocytoma cutis
Lymphoma/leukemia cutis

Leishmaniasis
Mastocytoma
Meischer's granuloma (giant cell elastophagocytosis)
Necrobiosis lipoidica diabeticorum
Nummular eczema
Sarcoidosis
Syphilis, secondary or tertiary

Hyperkeratotic Papules

Acquired perforating dermatosis (Kyrle's disease)
Acrokeratosis verruciformis of Hopf
Actinic keratosis
Arsenic ingestion
Confluent reticulate papillomatosis (Gougerot-Carteaud)
Cutaneous horn
Darier's disease
Elastosis perforans serpiginosa (elastic fibers)
Epidermal nevi (Inflammatory Linear Verrucous Epidermal Nevus – ILVEN)
Follicular lichen planus
Incontinentia pigmenti (verrucous stage)
Keratoacanthoma
Keratosis pilaris
Keratosis punctata
Lichen spinulosus
Lichen striatus
Lithium ingestion
Localized epidermolytic hyperkeratosis
Perforating folliculitis
Phrynoderma
Pityriasis rubra pilaris
Porokeratosis
Psoriasis
Reactive perforating collagenosis (collagen fibers)
Seborrheic keratosis
Verruca vulgaris/plana

Lichenoid Papules

Bowenoid papulosis (genitals)
Cowden's disease (lichenoid papules on the face)
Gianotti-Crosti (acral lichenoid papules)
Lichen amyloidosis
Lichen myxedematosus
Lichen nitidus
Lichen planus
Lichen sclerosus et atrophicus
Lichen simplex chronicus
Lichen spinulosus
Lichen striatus
Lichenoid actinic keratosis
Lichenoid drug eruption
Lichenoid seborrheic keratosis
Papular granuloma annulare
Sarcoidosis
Secondary syphilis
Tuberculosis cutis lichenoides (lichen scrofulosorum)
Verruca plana

Linear Papules

Contact dermatitis
Granuloma annulare
Herpes zoster (usually vesicular)
Ichthyosis hystrix
Insect bites
Jellyfish stings (usually vesicular)
Koebnerization (i.e. lichen planus, psoriasis, verruca vulgaris)
Linear epidermal nevus
Lichen planus
Linear porokeratosis
Lichen nitidus
Lichen striatus

Linear verruca vulgaris/plana
Nevus unius lateris
Nevus verrucosus
Sporotrichosis

Red Plaques

Actinic keratosis
Acute hemorrhagic edema of infancy
Alopecia mucinosa
Amelanotic melanoma
Bowen's disease
Discoid lupus
Eosinophilic granuloma
Erysipelas
Erythema elevatum diutinum
Fixed drug eruption
Granuloma annulare
Granuloma faciale
Kaposi's sarcoma
Langerhan's cell histiocytosis (intertriginous areas)
Leishmaniasis
Leprosy
Leukemia/lymphoma cutis
Lupus vulgaris
Lymphocytic infiltrate of Jessner
Malignant angioendotheliomatosis
Mycosis fungoides
Polymorphous light eruption
Pseudolymphoma of Spiegler-Fendt
Psoriasis
Rosacea
Sarcoidosis
Seborrheic dermatitis
Superficial basal cell carcinoma
Sweet's syndrome

Annular Plaques

Actinic granuloma (annular elastolytic giant Cell Granuloma)
Alopecia mucinosa
Basal cell carcinoma
Bowen's disease
Cutaneous larva migrans
Deep fungal infection
Discoid lupus erythematosus
Eosinophilic annular erythema
Erysipeloid
Erythema annulare centrifugum
Erythema chronicum migrans (Lyme disease)
Erythema multiforme
Factitial dermatitis
Fixed drug eruption
Granuloma annulare
Granuloma faciale
Leprosy
Leukemia/lymphoma cutis
Lichen planus
Lichen sclerosus et atrophicus
Lichen simplex chronicus
Lupus vulgaris
Lymphocytic infiltrate of Jessner
Lymphocytoma cutis
Morphea
Mycosis fungoides
Necrobiosis lipoidica diabeticorum
Necrolytic migratory erythema
Nummular eczema
Papular mucinosis
Parapsoriasis
Polymorphous light eruption
Porokeratosis of Mibelli
Psoriasis
Sarcoidosis
Seborrheic dermatitis

Syphilis, secondary
Tinea
Urticaria

Nodules and Tumors

Table 1.6 Dermal tumors and nodules

Dermal tumor/nodule	Diseases
Appendageal	Adenoma sebaceum
	Chondroid syringoma
	Clear cell acanthoma
	Clear cell hidradenoma
	Cylindroma
	Eccrine acrospiroma
	Eccrine poroma
	Eccrine spiradenoma
	Eruptive vellus hair cyst
	Hydrocystoma
	Nevus sebaceous
	Pilomatrixoma
	Sebaceous adenoma (consider Muir-Torre syndrome)
	Sebaceous epithelioma (consider Muir-Torre syndrome)
	Sweet's syndrome
	Syringoma
	Trichoepithelioma
	Trichofolliculoma
	Tricholemmoma
Malignancy	Cutaneous metastases
	Kaposi's sarcoma
	Keratoacanthoma
	Keratoacanthoma/squamous cell carcinoma
	Leukemia/lymphoma cutis
	Mycosis fungoides
	Nodular basal/squamous cell carcinoma
	Nodular melanoma
	Various soft tissue sarcomas

(continued)

Table 1.6 (continued)

Dermal tumor/nodule	Diseases
Cysts	Dermoid cyst Digital mucous cyst Epidermoid cyst Ganglion cyst Median raphe cyst Phaeohyphomycotic cyst Pilar (trichilemmal) cyst Steatocystoma multiplex
Granulomas	Foreign body granuloma Infectious granuloma (atypical mycobacteria, fungal) Juvenile xanthogranuloma Lupus vulgaris Reticulohistiocytoma Rheumatoid nodule Sarcoidosis Subcutaneous granuloma annulare
Histiocytomas	Dermatofibroma Dermatofibrosarcoma protuberans Fibrous histiocytoma Progressive nodular histiocytosis Sclerosing hemangioma
Neural	Neurilemmoma, schwannoma, neurothekeoma Neurofibroma Neuroma

Table 1.6 (continued)

Dermal tumor/nodule	Diseases
Vascular	Acquired tufted angioma Angiolymphoid hyperplasia with eosinophilia Angiosarcoma A-V malformation Erythema elevatum diutinum Glomus tumor Hemangiopericytoma Hemangioma Kaposi's sarcoma (classical and HIV) Nodular vasculitis Polyarteritis nodosa Superficial thrombophlebitis Thrombosed varicosity
Infectious Nodules	Abscess Anthrax Atypical mycobacteria Bacterial lymphangitis Blastomycosis Cat scratch disease Cutaneous Tuberculosis Deep fungal infection Furunculosis Giant Molluscum Glanders Leishmaniasis Lepromatous leprosy Melioidosis Milker's nodule Mycetoma Nocardia Orf Primary inoculation blastomycosis Primary inoculation tuberculosis Sporotrichosis Superficial Thrombophlebitis Trichophyton granuloma Tularemia

(continued)

Table 1.6 (continued)

Dermal tumor/nodule	Diseases
Inflammatory Nodules (not otherwise specified)	Calcinosis Cutis Clear cell acanthoma Digital fibrokeratoma Gottron's papules (dermatomyositis) Subcutaneous fat necrosis Sweet's syndrome
Other	Atypical fibroxanthoma Calcinosis/osteoma cutis Eruptive/tuberous xanthoma Erythema nodosum Foreign body Hypertrophic scar/keloid Leiomyoma Lipoma/hibernoma Seroma/hematoma Spitz nevus Tophus

Red Nodules

Table 1.7 Red Nodules

Nodule	Diseases
Malignancy	Amelanotic melanoma
	Basal/squamous cell carcinoma
	Cutaneous endometriosis
	Keratoacanthoma
	Leukemia cutis
	Lymphoma cutis
	Metastatic carcinoma
Histiocytic	Atypical fibroxanthoma
	Dermatofibroma
	Dermatofibrosarcoma protuberans
	Eosinophilic granuloma
	Eruptive xanthoma
	Foreign body granuloma
	Nodular granuloma annulare
	Sarcoidosis
Infectious	Anthrax
	Atypical mycobacteria
	Bacterial abscess, furuncle
	Leishmaniasis
	Milker's nodule
	Nodular scabies
	Orf
	Tularemia
Inflammatory	Erythema induratum
	Erythema nodosum
	Insect bites
	Sweet's syndrome
	Weber-Christian panniculitis

(continued)

Table 1.7 (continued)

Nodule	Diseases
Vascular	Angiokeratoma (consider Fabry's disease) Angiosarcoma Arterious-Venous malformation Bacillary angiomatosis Cutaneous polyarteritis nodosa (especially wrists and ankles) Hemangioma Hemangiopericytoma Kaposi's sarcoma Leukocytoclastic vasculitis Pyogenic granuloma
Miscellaneous	Appendageal tumors (clear cell acanthoma, clear cell hidradenoma, eccrine poroma) Clear cell acanthoma Cutaneous myiasis Leiomyoma Lymphomatoid papulosis Neurothekeoma Spitz nevus

Subcutaneous Nodules without Epidermal Changes

Table 1.8 Subcutaneous nodules without epidermal changes

Nodule	Diseases
Appendageal	Spiradenoma, hidrocystoma, acrospiroma, mixed tumor, pilar tumors, etc.
Calcified	Calcified epidermoid and pilar cysts Calcinosis cutis (consider CREST) Osteoma cutis Pilomatrixoma Primary and metastatic calcification

Table 1.8 (continued)

Nodule	Diseases
Cysts	Embryologic (branchial cleft, bronchogenic cyst, cystic hygroma, thyroglossal duct cyst) Epidermal inclusion cyst Ganglion Mucous Pilar (trichilemmal) Seroma Steatocystoma multiplex Vellus hair cysts
Histiocytomas	Dermatofibroma Dermatofibrosarcoma protuberans Fibrous histiocytoma Sclerosing hemangioma
Neural	Neurofibroma Neurolemmoma, schwannoma, neurothekeoma Neuroma
Sarcomas	Angiosarcoma Fibrosarcoma Leiomyosarcoma Liposarcoma Malignant fibrous histiocytoma
Other	Angiolipoma Cutaneous myiasis Erythema elevatum diutinum Foreign body granuloma Glanders (“Farcy buds” - Burkholderia Malleli) Gouty tophi Leiomyoma Lipoma Metastatic carcinoma Nodular pseudosarcomatous fasciitis Rheumatoid nodule Subcutaneous granuloma annulare Synovial tumor Thrombosed varicosity

Painful Tumors

Adiposis dolorosa (Dercum's disease)
Angiolipoma
Blue rubber bleb nevus
Chondrodermatitis nodularis helicis
Cutaneous endometriosis
Eccrine spiradenoma
Endometriosis
Foreign body granuloma
Glomus tumor
Granular cell tumor
Leiomyoma
Neurilemmoma
Neuroma
Osteoma cutis

Pustules

Acne vulgaris
Acute febrile neutrophilic dermatosis
Anthrax
Atypical mycobacteria
Benign familial pemphigus (Hailey-Hailey disease)
Cellulitis
Cowpox
Deep fungal infections (i.e. actinomycosis, nocardia, sporotrichosis)
Dermatitis herpetiformis
Disseminated candidiasis
Ecthyma
Erysipeloid
Erythema toxicum neonatorum
Folliculitis (bacterial, candidal, eosinophilic, fungal, steroid use)
Furuncle, carbuncle
Gonococcemia
Herpes simplex/zoster

Hot tub folliculitis (*Pseudomonas*)
Impetigo
Impetigo herpetiformis
Infected contact dermatitis
Infected dyshidrotic eczema
Intertrigo
Miliaria
Miliaria rubra
Monkeypox
Multiple arthropod bites
Pemphigus foliaceus, IgA pemphigus
Perleche
Pustular psoriasis
Rhinoscleroma
Scabies
Smallpox
Steroid acne
Subcorneal pustular dermatosis (Sneddon-Wilkinson)
Sycosis barbae
Tinea
Transient neonatal pustular melanosis
Varicella

Vesicles and Bullae

Arthropod reaction
Behçet's syndrome
Benign familial pemphigus (Hailey-Hailey disease)
Benign mucous membrane pemphigoid
Bullosa diabeticorum
Bullous fixed drug eruption
Bullous impetigo
Bullous lichen planus
Bullous pemphigoid
Burn, second degree
Cat scratch disease
Chronic bullous dermatosis of childhood
Coma blisters

Congenital ichthyosiform erythroderma
Contact dermatitis
Dermatitis herpetiformis
Discoid lupus erythematosus
Drug reaction (bullous)
Dyshidrotic eczema (pompholyx)
Epidermolysis bullosa
Erythema elevatum diutinum
Erythema multiforme
Erythema toxicum neonatorum
Factitial
Factitial dermatitis
Friction blister
Gonococcemia, meningococcemia
Gunther's disease
Hand, foot, and mouth disease
Herpes gestationis
Herpes simplex/zoster
Hydroa vacciniforme
Incontinentia pigmenti
Lymphangioma/seroma
Miliaria
Necrolytic migratory erythema (glucagonoma)
Neonatal pustular melanosis
Pemphigus vulgaris, foliaceus, lgA
Photoallergic drug eruption
Polymorphous light emption
Porphyria cutanea tarda
Pressure urticaria
Pseudoporphyria
Pyoderma gangrenosum
Rickettsialpox
Rocky mountain spotted fever
Scabies
Smallpox
Smallpox (variola)
Staph scalded skin syndrome
Stevens-Johnson syndrome
Subcorneal pustular dermatosis (Sneddon-Wilkinson)

Sweet's syndrome
Tinea corporis
Tinea manuum/pedis
Toxic epidermal necrolysis
Transient acantholytic dermatosis (Grover's disease)
Urticaria pigmentosa/mastocytoma
Varicella
Vesicular id reaction
Viral infection (simplex, zoster, varicella, smallpox)
Weber-Cockayne syndrome

Ulcers

Table 1.9 Ulcers and associated diseases

Ulcers	Diseases	Lymphadenitis
Bacterial	Anthrax	+
	Chancroid	+
	Cutaneous diphtheria	
	Ecthyma	
	Glanders	+
	Granuloma inguinale	
	Leprosy	
	Melioidosis	+
	Phagedenic ulcer	
	Scrofuloderma	
	Syphilis	+
	Tuberculosis and atypical mycobacteria	
	Tularemia	+
	Yaws	

(continued)

Table 1.9 (continued)

Ulcers	Diseases	Lymphadenitis
Bites	I.e. brown recluse spider	
Blood element pathology	Cold agglutinins	
	Congenital hemolytic anemia	
	Polycythemia	
	Sickle cell ulcer	
Burns	Chemical, electrical, thermal	
Circulatory disorders	Decubitus (pressure)	
	Hypertensive	
	Stasis	
	Sickle cell ulcer	
	Thromboangiitis	
	Thrombosed varicosity	
	Vasculitis	
Deep Fungal	Actinomycosis	
	Blastomycosis	
	Candida	
	Chromoblastomycosis	
	Coccidioidomycosis	
	Histoplasmosis	
	Murcomycosis	
	Sporotrichosis	+
Factitial	Delusions of parasitosis	
	Neurotic excoriations	

Table 1.9 (continued)

Ulcers	Diseases	Lymphadenitis
Malignancy	Basal cell	
	Lymphoproliferative malignancies	
	Melanoma	
	Metastases	
	Mycosis fungoides	
	Squamous cell	
Miscellaneous	Antiphospholipid syndrome	
	Crohn's disease	
	Intravenous drug abuse	
	Necrobiosis lipoidica diabeticorum	
	Pyoderma gangrenosum	
	Radiation dermatitis	
Parasitic	Amebiasis	
	Leishmaniasis	
Traumatic		

Necrotic Lesions

Bromoderma
Behçet's disease
Calciphylaxis
Chemical agents - coumadin, intravenous adrenergics, chemotherapeutic agents, cocaine levamisole
Disseminated intravascular coagulation
Dysproteinemias – cryoglobulins, cryofibrinogens
Embolization –thrombus, fat

Envenomation – brown recluse spider, snakes, scorpion
Factitial
Granulomatosis with polyangiitis
Infection – bacterial (i.e. anthrax, streptococcus, atypical mycobacteria, mengiococcus, rickettsial, treponemal), fungal (i.e. nocardia, actinomycosis, sporotrichosis, histoplasmosis, cryptococcus, blastomycosis, tuberculosis), viral (i.e. smallpox, varicella)
Physical agents – heat, cold, trauma, pressure, electrical, radiation
Primary vascular – artetiosclerosis, thromboangiitis, diabetes
Pyoderma gangrenosum
Vasculitis secondary to connective tissue disease – SLE, polyarteritis, rheumatoid arthritis, temporal arteritis, Wegener's, CREST
Vasospastic – Raynaud's, hypertensive ulcer, ergot poisoning, arterial or venous drug extravasation

Vascular Lesions

Non-palpable Purpura (Petechial and Ecchymotic)

Capillaritis

- Schamberg's purpura- "cayenne pepper" pattern on legs
- Majocchi's purpura (purpura annularis telangiectoidess)
- Gougerot-Blum – purpuric lichenoid dermatitis
- Ducas and Kapetanakis – eczematoid purpura

Coagulopathies – disseminated intravascular coagulation, liver disease, anticoagulant therapy
Drug – anticoagulants, phenacetin, steroids, NSAIDs
Hypersensitivity vasculitis
Infections – Subacute Bacterial Endocarditis, Rock Mountain Spotted Fever (RMSF), meningococcemia, gonococcemia, Weil's disease (leptospirosis), various hemorrhagic fevers including Ebola and Marburg, congenital rubella, echovirus, toxoplasmosis, cytomegalovirus

Livedo reticularis
Resolving erythemas
Scurvy (perifollicular)
Senile purpura
Systemic disease – diabetes, Cushing's disease, uremia
Thrombocythemia
Thrombocytopenia – ITP, TIP, bone marrow depression
Toxic venoms
Traumatic purpura
Waldenström's hyperglobulinemic purpura

Palpable Purpura (Cutaneous Vasculitis)

I. **Primarily Cutaneous**

Cutaneous polyarteritis nodosa
Erythema elevatum diutinum
Hypersensitivity vasculitis/idiopathic allergic vasculitis/anaphylactoid purpura (all likely the same entity) – usually due to infection, drug, or systemic disease
Pityriasis lichenoides et varioliformis acuta (PLEVA) (lymphocytic as opposed to leukocytoclastic)
Sweet's syndrome
Urticarial vasculitis/erythema multiforme

II. **Cutaneous and systemic – usually leukocytoclastic unless noted**

Abnormalities in blood viscosity

- *Cold agglutinins* – viral pneumonia, SLE, lymphoma
- *Cryofibrinogens* – abnormality in clotting and degradation – seen in viral diseases (especially hepatitis)
- *Cryoglobulinemia* – cold exposure, multiple myeloma, SBE, leukemia, RA, liver disease, hepatitis, disseminated cancer, syphilis, mononucleosis, primary idiopathic
- *Hypergammaglobulinemic purpura*

Carcinoma: lymphoma, leukemia, lung and bowel cancer, Hodgkin's disease, multiple myeloma

Collagen vascular diseases (usually a livedo pattern): rheumatoid arthritis, SLE, dermatomyositis, Sjörgen's, inflammatory bowel disease
Drug (usually lymphocytic): ASA, NSAIDs, sulfa, chloroquine, penicillin, quinidine, thiazides, TB drugs, phenothiazines
Infection: streptococcus, Rock Mountain Spotted Fever, GC, meningiococcemia, Tuberculosis, syphilis, viruses (especially hepatitis)
Other:

- *Henoch-Schöenlein purpura* – abdominal pain, mucosal bleeding, hematuria, arthralgias, headache
- *Polyarteritis nodosa and other related granulomatous arteritides* – allergic granulomatosis, Wegener's

Telangiectasia

Primary

Ataxia telangiectasia
Essential telangiectasia
Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu)
Nevus telangiectaticus
Poikilodermatous diseases (Bloom's syndrome, Cockayne's syndrome, Dyskeratosis congenita
Poikiloderma atrophicans vasculare, Rothmund-Thomson syndrome)
Spider angioma
Telangiectasia macularis eruptiva perstans
Xeroderma pigmentosum

Secondary

Actinic damage
Basal cell carcinoma
Chronic topical steroid application
Collagen vascular disease

Drugs (estrogen, corticosteroids)
Keloid
Liver disease
Melasma
Necrobiosis lipoidica
Poikiloderma of Civatte
Pregnancy
Radiation dermatitis
Rosacea

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Chapter 2
Dermoscopy Basics

Sarah Kam and Neelam A. Vashi

Dermoscopy: The 2 Step Algorithm [1–3] (Fig. 2.1)

The first part of the 2-Step Algorithm (Fig. 2.1) involves determining if a cutaneous lesion is a pigmented lesion or not (Table 2.1). A pigmented lesion typically presents with one or more pigment pattern(s) as described in Tables 2.2 and 2.3. The only exception to this rule is if the lesion is unequivocally a dermatofibroma. If the lesion contains at least one pigment pattern, then proceed to Step 2 for melanocytic lesions. If the cutaneous lesion does not contain at least one pigment pattern, then proceed to Step 2 for non-melanocytic lesions.

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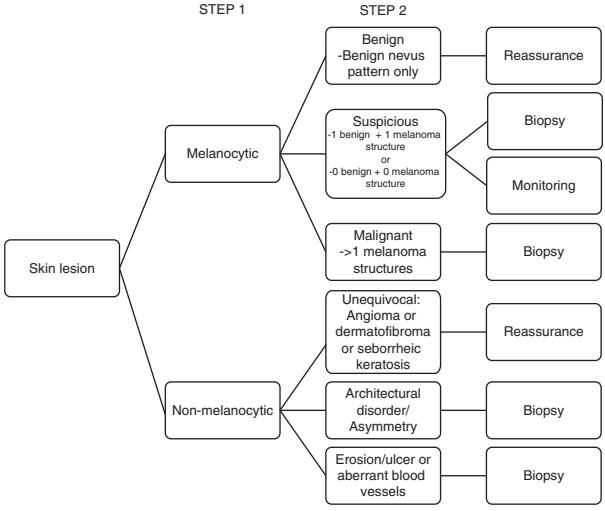


FIGURE 2.1 The 2-Step Algorithm

Step 1 (Table 2.1):

TABLE 2.1 Dermoscopic Findings of Common Cutaneous Lesions

Melanocytic lesions	Pigment network 	Streaks 	Aggregated globules 	Uniform blue pigment 	Pseudonetwork 	Parallel pattern 
Dermatofibroma	Delicate, peripheral pigment network with central scar-like structure and dimple sign 					
Basal cell carcinoma	Arborizing blood vessels 	Leaf-like structures	Blue-gray globules/ovoid nests	Pearly areas/ulceration 		
Seborrheic keratosis	Milia-like cysts 	Comedo-like openings	Crypts 	Moth-eaten borders	Cerebriform pattern	

Angioma or angiokeratoma	Red/blue/black lacunae 				
Blood vessels in non-melanocytic tumors	Glomerular vessels at periphery: SCC 	Crown vessels: Sebaceous hyperplasia/ Molluscum 	"Pearls on a string" Clear cell acanthoma 	Hairpin: Keratoacanthoma 	
Blood vessels in melanocytic tumors	Comma-shaped: Intradermal nevus 	Dotted 	Linear 	Hairpin 	Polymorphous >2 types 
Structureless	Structureless lesions are concerning for amelanotic melanoma				

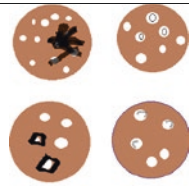
TABLE 2.2 Dermoscopic Features of Benign Nevi

Pattern	Illustration
Reticular - Diffuse reticular - Patchy reticular - Peripheral reticular with central hypopigmentation - Peripheral reticular with central hyperpigmentation	
Homogeneous	
Peripheral globules	
Starburst Globular 2 Components - Peripheral reticular + central globules - ½ reticular + ½ globules	  
Symmetrical multi-component	
Parallel furrow pattern in volar/acral skin	

Table 2.3 Dermoscopic features of melanoma

Features	Description	Image
Atypical pigment network and angulated lines	Significant variability in distribution and organization of pigment and lines	
Negative network	Serpiginous hypopigmented lines between hyperpigmented elongated lines	
Atypical dots or globules	Disorganized dots or globules of varying size, color, distribution	
Irregular streaks or pseudopods	Radiating linear pigment at periphery. Pseudopods are streaks with knobs at the end of the projections.	
Regression structures	Non-palpable depigmented areas	
Blue-white veil	Palpable area with blue-black area with overlying white ground-glass appearance	
Shiny white lines	Bright white lines in parallel or perpendicular orientation under polarized light	
Atypical blotch	Asymmetrical area of hyperpigmentation obscuring other structures	
Polymorphous vessels	2 or more type of blood vessels in disorganized distribution	

Table 2.4 Melanoma of special sites

Site	Description	Illustration
Face	- Blotches of pigment with obliteration of follicles - Concentric rings of pigment surrounding another circle - Gray circles in follicular openings - Incomplete circles in follicles - Angulated lines in adnexal openings	
Mucosa	Structureless areas with blue/gray/white	
Volar/acral surfaces	Parallel ridge pattern: Thick lines of pigmentation on ridges	
Nail apparatus	Irregular pigmented bands with multiple colors, varying thickness and loss of parallelism	

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Chapter 3
Diagnosing Bedside: Common Laboratory Techniques

Catherine Higham and Neelam A. Vashi

When performed:
To identify superficial fungal infections.

Technique:

- Wipe area with alcohol prior to scraping to ensure better control of the scale [1]. Scrape scale onto slide. Specific technique depends on type and location of lesion, as below. Use blade or slide cover to focus scale into one area of the slide.
  - **Scaly plaque:** scrape firmly with a #15 blade over the scaly portion. If no clearly advancing border (i.e., tinea pedis), scrape entire affected area [2, 3].
  - **Nails**: scrape the subungual debris. Curette may be easier than #15 blade. If superficial onychomycosis is suspected, can scrape nail plate itself [1, 4].

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  - **Pustule or vesicle:** Use a #15 blade to un-roof the lesion. Examine roof of lesion for fungal elements [2].
  - **Suspected tinea capitis:** Pluck several hairs and place on slide. Also try to collect scale from and broken hairs from affected area [5].

- Add one drop of KOH to the scale collection [1].
- Place cover slip over specimen.
- Gently heat as heating will accelerate keratinocyte degradation. Be careful not to overheat. Specimen should not reach a boil. (note: if using KOH that contains DMSO, do **NOT** heat) [1]. If unable to heat, may need to let specimen sit for 20–30 min prior to examining.
- To increase contrast of fungal elements, microscope condenser should be lowered [1].
- First scan specimen at low power to identify cells. Then examine for fungal elements at higher power [1, 6].

Diagnosis:
- **Dermatophyte:** long, slender branching hyphae that extend across cell walls [1, 2].
- **Tinea versicolor:** short hyphae and spores (spaghetti and meatballs) [1].
- **Candida:** yeast and pseudo-hyphae [1].

Scabies Preparation

Technique:
- Look for an un-excoriated burrow. Classic locations: webbing of fingers/toes, wrists, elbows, umbilicus, axillae, waistline, buttocks, glans penis, nipples/areolae [7].
- Can use dermatoscope to look for small triangles ("delta wing sign") representing mites [7, 8].
- Dip tip of #15 blade in mineral oil and firmly scrape an un-excoriated burrow [7, 9]. Note: can use a 3 mm disposable curette in pediatric population [7, 10].
- Scrape debris onto slide [7].

- Scrape multiple potential burrows to increase likelihood of finding evidence of scabies.
- Tip: for crusted scabies with substantial scale, can be helpful to add drop of KOH to reduce keratinocyte debris [7].
- Examine first with scanning power [1].

Identification
- Look for mites, eggs, and/or scybala (feces) in specimen.
- **Mite:** round, 8 legs
- **Eggs:** oval structure
- **Scybala:** dark brown pellets

Tzanck Smear

When performed:
To identify varicella zoster virus or herpes simplex virus infections at the bedside.

Technique:
- Identify intact vesicle or pustule, not a crusted or excoriated one [1, 11].
- Unroof intact vesicle or pustule. Use #15 blade to scrape base and inner roof of lesion. Smear onto glass slide and allow to air dry [1, 11].
- Fixation depends on specific stain used. Wright or Giemsa stains are commonly used [1].

Diagnosis:
- Will see multinucleated giant cells, ballooning keratinocytes, enlarged keratinocyte nuclei, and intranuclear inclusion bodies. Intranuclear inclusion bodies are often difficult to visualize [1, 11].
- Can send additional specimen for culture and/or viral PCR to confirm diagnosis. Use same collection technique, as described above and place in appropriate media.

Fungal cultures:
- Commonly obtained for suspected tinea capitis and onychomycosis
- Nail clippings should be as proximal as possible and include subungual debris. If there is concern for superficial onychomycosis, overlying scale should also be scraped and included [1, 4].
- Hair shafts should include root.
- Place in appropriate fungal media.

Histopathologic analysis of nails with PAS stain:
- Commonly obtained for suspected onychomycosis.
- Nail clippings should be as proximal as possible and include subungual debris. If there is concern for superficial onychomycosis, overlying scale should also be scraped and included [1, 4].
- Nail specimen can be put in formalin or by itself in a specimen cup.

Gram Stain

When performed:
To identify cutaneous bacterial infections.

Technique [1]**:**
- Smear purulent material onto glass slide.
- Can let specimen air-dry or gently heat.
- Stain with crystal violet for 30–60 s, then wash off gently with tap water.
- Stain with gram iodine for 30–60 s, then wash off gently with tap water.
- Rinse with decolorizer (acetone or alcohol) until run-off fluid is clear.
- Stain with safranin for 30–60 s, then rinse off gently with tap water.
- Let specimen air-dry or gently blot.

Diagnosis:
- Gram positive organisms: stain purple by crystal violet [1]
- Gram negative organisms: stain pink by safranin [1]
- Staph: gram positive cocci in clusters [12]
- Strep: gram positive cocci in chains [12]

Special Biopsy Techniques:
- Direct immunofluorescence:
  - For bullous disease: 3–4 mm punch of adjacent, non-lesional skin
  - For vasculitis processes: 3–4 mm punch of lesional skin
- Scalp biopsy: Try to get at least a 4 mm punch. Request horizontal sectioning, if possible.

Wood's Light Examination

When performed:
To identify a variety of skin disorders including vitiligo, melasma, tinea versicolor, and erythrasma.

Technique:
- Best performed in a dark room.
- Light source should be held a minimum of 10 cm from patient's skin [13].
- Note: Topical products and scale can alter fluorescence patterns [5].

Identification:
- **Vitiligo:** lesions appear as sharply demarcated, bright white macules and patches [13].
- **Melasma** (with increased epidermal melanin): lesions appear darker and with greater contrast with normal skin than in natural light [13].
- **Erythrasma:** lesions appear as coral-red patches [13].

- **Tinea versicolor:** lesions appear as yellow-orange patches [13].
- **Porphyria cutanea tarda:** urine fluoresces pink or orange-red [13].
- **Progressive macular hypomelanosis:** lesions fluoresce orange-red follicularly [5].

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Chapter 4
An approach to Dermatopathology: Immunohistochemical and special stains

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When viewing pathology specimens under the microscopic, it is important to first orient yourself to the specimen and then:

1. Be able to differentiate whether it was a shave or punch biopsy
2. Decipher the location based on what you see
   (a) Thick stratum corneum and presence of stratum lucidum: acral

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(b) Thin skin with loose connective tissue: eyelid
(c) Terminal hair follicles: scalp, axilla vs. vellus hair follicles: face
(d) Sebaceous glands: face
(e) Absent stratum corneum or granulosum: mucosa

3. Visualize all layers present including the epidermis, dermis, subcutaneous fat
4. Locate areas with main pathology

Descriptive Terms

Term	Description
Acantholysis	Separation of epidermal keratinocytes due to destruction of desmosomes
Acanthosis	Hyperplasia of epidermis
Atrophy	Chronic degeneration of the epidermis or dermis resulting in thinning and fragility of structure
Dyskeratosis	Abnormal keratinization of a keratinocyte while the cell is still in the epidermis
Epidermotropism	The propensity of malignant lymphocytes to migrate into the epidermis without significant spongiosis
Exocytosis	The presence of inflammatory cells, such as benign lymphocytes, neutrophils or eosinophils, within the epidermis during an inflammatory reaction
Fibrosis	An increase in both individual collagen fiber thickness and in overall collagen density within the dermis

Hyperkeratosis	An increase in the thickness of the stratum corneum
Interface changes	Constellation of changes seen at the dermoepidermal junction in interface dermatitis, including formation of vacuoles in the basal keratinocytes, dying individual keratinocytes, and lymphocyte exocytosis
Interstitial	Located in the spaces between the collagen and elastic fibers of the dermis
Lichenoid	Having a band-like infiltrate of inflammatory cells (usually lymphocytes) directly beneath the epidermis and masking the dermoepidermal junction
Papillomatosis	Undulating epidermal projections resembling fingers or church spires
Parakeratosis	Retention of the nucleus within the stratum corneum cells instead of loss of the nucleus
Pigment incontinence	Loss of melanin, which is normally found in epidermal keratinocytes and melanocytes, into the dermis where it is phagocytosed by melanophages
Pseudoepitheliomatous hyperplasia	Marked irregular acanthosis of the epidermis that is so severe as to mimic squamous cell carcinoma
Psoriasiform	Having epidermal hyperplasia featuring long, thin, regular rete ridges that resemble those seen in classic plaque-type psoriasis

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Solar elastosis	Gray-blue discoloration of superficial dermal elastic fibers secondary to sun damage
Spongiosis	Edema between epidermal keratinocytes, pushing them apart and straining intercellular bridges
Vasculitis	Endothelial cell swelling, fibrinoid necrosis of the vessel wall, and infiltration of the vessel wall by inflammatory cells
Vasculopathy	Any abnormality of the vessel wall that does not meet the criteria of vasculitis

Melanocytic Markers

Marker	Pattern of Staining	Cell Types Positive	Common Uses in Dermpath
S-100	Nucleus & cytoplasm	Melanocytes, nerve sheath cells, some histiocytes	Melanocytic nevi and melanoma, neural tumors, Langerhans cells, granular cell tumors, Rosai-Dorfman disease
MART-1 (Melan-A)	Cytoplasm	Melanocytes	Melanocytic nevi and melanoma
SOX-10	Nucleus	Melanocytes, nerve sheath cells	Melanocytic nevi and melanoma, neural tumors
MiTF	Nucleus	Melanocytes, nerve sheath cells	Melanocytic nevi and melanoma
HMB-45	Cytoplasm	Melanocytes	Melanocytic nevi and melanoma

Epithelial markers

Marker	Pattern of staining	Cell types positive	Common uses in Dermpath
High Molecular Weight Cytokeratins	Cytoplasm	Epithelial cells of epidermis, hair follicle, sebaceous gland, eccrine and apocrine ducts	BCC and SCC (+), adnexal tumors variable
Low Molecular Weight Cytokeratins	Cytoplasm	Epithelial cells of epidermis, hair follicle, sebaceous gland, eccrine and apocrine glands	Adnexal tumors (+), metastatic carcinoma usually (+)
CAM5.2	Cytoplasm	Epithelial cells of epidermis, hair follicle, sebaceous gland, eccrine and apocrine glands	Eccrine and apocrine secretory coils (+), Paget's disease (+), SCC (−)
Epithelial Membrane Antigen (EMA)	Cytoplasm	Epithelial cells and ducts of sebaceous gland, eccrine and apocrine glands	(+) in SCC, sebaceous tumors, and eccrine and apocrine adnexal tumors, (−) in BCC
Carcinoembryonic Antigen (CEA)	Ductal/luminal cytoplasm	Ductal/luminal surfaces of eccrine and apocrine ducts and glands	Identifying ductal differentiation in tumors such as microcystic adnexal carcinoma (+)

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BerEP4	Cell membrane	Epithelial cells of some vellus hair follicles, eccrine and apocrine coils	Distinguishing BCC (+) from SCC (−) and microcystic adnexal carcinoma (−)
P63	Nucleus	Epithelial cells of epidermis, hair follicle, myoepithelial cells of eccrine and apocrine glands and ducts	SCC (+), distinguishing primary skin adnexal tumors (+) from metastatic adenocarcinoma (−)

Mesenchymal markers

Marker	**Pattern of staining**	**Cell types positive**	**Common uses in Dermpath**
Factor XIIIa	Cytoplasm	Dermal dendritic cells, fibroblasts	Dermatofibroma (+) vs. dermatofibrosarcoma protuberans (−)
CD34	Cytoplasm	Endothelial cells, dermal dendritic cells	Vascular tumors, dermatofibrosarcoma protuberans, spindle cell lipoma
CD31	Cytoplasm	Endothelial cells	Vascular tumors
D2–40	Cytoplasm	Endothelial cells of lymphatics	Lymphatic tumors
SMA	Cytoplasm	Smooth muscle, myofibroblasts	Smooth muscle tumors, nodular fasciitis, glomus tumor

Desmin	Cytoplasm	Smooth and skeletal muscle	Tumors of smooth and skeletal muscle
Vimentin	Cytoplasm	All cell types of mesenchymal derivation	Usually carcinoma (−), sarcoma (+)
Neuron-specific Enolase	Cytoplasm	Nerves and neuroendocrine cells	Identifying neural and neuroendocrine tumors such as granular cell tumor (+)

Hematopoietic markers

Marker	**Pattern of staining**	**Cell types positive**	**Common uses in Dermpath**
CD45/LCA	Membrane/ cytoplasm	Lymphocytes, neutrophils, eosinophils, histiocytes, plasma cells	Establish the hematopoietic origin of a tumor/infiltrate
CD3	Membrane/ cytoplasm	T-lymphocytes	Identifying T-lymphocytes
CD20	Membrane/ cytoplasm	B-lymphocytes	Identifying B-lymphocytes
CD4	Membrane/ cytoplasm	Helper T-lymphocytes	Identifying helper T-lymphocytes
CD5	Membrane/ cytoplasm	T-lymphocytes	T cell marker, loss of CD5 can indicate possible malignancy

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CD7	Membrane/ cytoplasm	T-lymphocytes	T cell marker, loss of CD7 can indicate possible malignancy
CD8	Membrane/ cytoplasm	Cytotoxic T-lymphocytes	Identifying cytotoxic T-lymphocytes
CD30	Membrane/ cytoplasm	Activated T-lymphocytes and neoplastic T-lymphocytes	Increased expression in lymphomatoid papulosis and anaplastic large T-cell lymphoma
CD68	Membrane/ cytoplasm	Histiocytes/ macrophages	Identifying histiocytes
CD38/138	Membrane/ cytoplasm	Plasma cells	Identifying plasma cells
CD56	Membrane/ cytoplasm	NK/T cells, neuroendocrine cells	Identifying NK-cell differentiation, also in neuroendocrine tumors
BCL-2	Cytoplasm	T-lymphocytes, B-lymphocytes outside of germinal centers	Marginal zone lymphoma, diffuse large B-cell lymphoma, absent in most cases of primary cutaneous follicle center lymphoma vs. strong positive reaction in nodal follicular lymphoma

BCL-6	Nucleus	B-lymphocytes within germinal centers, some T-lymphocytes	Follicle center lymphoma
CD10	Membrane/ cytoplasm	Germinal center B-cells, sebaceous glands	Follicle center lymphoma (+), also (+) in atypical fibroxanthoma and clear cell renal cell carcinoma
MUM-1	Nucleus	Plasma cells and post-germinal center B-lymphocytes	Diffuse large B-cell lymphoma, myeloma
Kappa light chain	Cytoplasm	Plasma cells	Marginal zone lymphoma
Lambda light chain	Cytoplasm	Plasma cells	Marginal zone lymphoma
ALK-1	Nucleus and cytoplasm	Anaplastic large T-cell lymphoma (ALCL) cells	Usually systemic ALCL (+) vs. primary cutaneous ALCL (–)

Miscellaneous IHC markers

Marker	**Pattern of staining**	**Cell types positive**	**Common uses in Dermpath**
CK7	Cytoplasm	Tissue of breast, lung, upper GI tract and bladder	Identifying adenocarcinomas of breast, lung, upper GI tract and bladder, (+) in Toker cells, mammary and extramammary Paget's disease

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CK20	Cytoplasm	Merkel cells, adenocarcinomas of colon, bladder and bile ducts	Merkel cell carcinoma, identifying adenocarcinomas of colon, some cases of extramammary Paget's disease secondary to underlying carcinomas
CD1a	Membrane/ cytoplasm	Langerhans cells	Identifying Langerhans cells
CD117 (c-kit)	Membrane/ cytoplasm	Mast cells	Identifying mast cells
TTF-1	Nuclear	Lung carcinoma, thyroid carcinoma	Thyroid cancer, distinguishing between small cell carcinoma of the lung and Merkel cell carcinoma
Adipophilin	Perivacuolar	Sebaceous gland cells	Establishing sebaceous differentiation in a tumor, sebaceous tumors
GCDFP-15	Cytoplasm	Breast ducts	Identifying breast carcinoma, mammary and extramammary Paget's disease
Chromogranin	Cytoplasm	Neuroendocrine cells and tumors	Identifying neuroendocrine tumors such as Merkel cell carcinoma

Synaptophysin	Cytoplasm	Neuroendocrine cells and tumors	Identifying neuroendocrine tumors such as Merkel cell carcinoma

Special stains

Marker	**Material staining**	**Color of positive stain**	**Common uses in Dermpath**
PAS	Fungal structures, basement membrane, glycogen, epithelial mucins	Dark pink/red	Dermatophytes and deep fungal infections
GMS	Fungal structures	Black	Fungal infections
Alcian Blue	Stromal/ mesenchymal mucin	Bright blue	Dermal mucin deposition
Colloidal Iron	Mucins, some stromal and some epithelial	Blue	Dermal mucin deposition
Masson Trichrome	Stain that highlights collagen and muscle	Collagen: blue/ green, muscle fibers/keratin: red	Identifying collagen and fibrosis
Fontana Masson	Melanin	Black granules	Distinguishing between hemosiderin (−) and melanin pigment (+)
Perl's Prussian Blue	Iron/ hemosiderin	Blue granules	Distinguishing between hemosiderin (+) and melanin pigment (−)

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Chloroacetate esterase (Leder stain)	Mast cell granules	Purple	Identifying mast cells
Gram	Bacteria	Gram+ organisms: dark blue/ purple, Gram- organisms: red	Identifying bacteria
Fite	Mycobacteria	Red	Identifying mycobacteria
Warthin Starry	Spirochetes, some bacteria	Black	Syphilis, bacillary angiomatosis
Toluidine Blue	Mast cells, mucin	Mast cells: purple, mucin: purple/red	Identifying mast cells
Congo Red	Amyloid	Red/orange	Identifying amyloid
Crystal Violet	Amyloid	Violet/purple	Identifying amyloid
Verhoeff-Van Gieson	Elastin	Black	Identifying elastic fibers
Von Kossa	Calcium	Black	Identifying calcium, calciphylaxis, pseudoxanthoma elasticum
Oil Red O	Lipid (fresh or frozen tissue only)	Red	Identifying lipids and fat
Sudan Black B	Lipid	Black	Identifying lipids and fat
Giemsa	Mast cells	Dark blue/ purple	Identifying mast cells

Immunofluorescence Studies

Direct immunofluorescence (DIF): An antibody directly detects presence of a pathologic antibody in the skin

Indirect immunofluorescence (IIF): Serum is introduced to a substrate in order to detect circulating antibodies

Salt-split skin test: with NaCl, skin is cleaved at lamina lucida at BMZ – Allows separation of roof/floor fluorescence

Biopsy sites for DIF: autoimmune blistering diseases – inflamed but unblistered perilesional skin, autoimmune and inflammatory diseases other than blistering diseases – lesional skin, vasculitis- 1 to 2 day-old fresh lesional skin

Disease	Pattern of DIF Staining	Salt Split IF
Pemphigus vulgaris	IgG and occasional C3 in the intercellular region of the epidermis	
Pemphigus foliaceus	IgG and occasional C3 in the intercellular region of the epidermis	
Pemphigus erythematosus	Intercellular and basement membrane staining with IgG and/or C3	
Paraneoplastic pemphigus	Intercellular and basement membrane staining with IgG and/or C3	
IgA pemphigus	Intercellular deposition of IgA in the epidermis	
Bullous pemphigoid	Linear, homogeneous deposition of IgG and/or C3 at the BMZ	Roof
Epidermolysis bullosa acquisita	Linear deposition of IgG (les commonly C3, IgA or IgM) at the BMZ	Floor

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Disease	Pattern of DIF Staining	Salt Split IF
Bullous SLE	IgG (less commonly IgA, IgM) and complement at the BMZ	Floor
Mucous membrane pemphigoid	Linear deposit of IgG (and sometimes IgA) and C3 at the BMZ	Roof/ Floor
Linear IgA bullous dermatosis	Homogeneous linear pattern of IgA deposition at the BMZ	Roof/ Floor
Dermatitis herpetiformis	Granular deposits of IgA in the dermal papillae	
Porphyria cutanea tarda	Ig, complement and fibrinogen at the BMZ and around blood vessels	
Henoch-Schönlein purpura	IgA (usually fibrinogen and C3 as well) deposition in blood vessels	
Lichen planus	Shaggy deposits of fibrin at the BMZ	

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Chapter 5
Dermatologic Emergencies

Caroline LaRosa, Andrew Chen, and Amy Y.-Y. Chen

Stevens-Johnson Syndrome (SJS) and Toxic-Epidermal Necrolysis (TEN) [1, 2]

Key Points:

- Rare, severe, acute, most often drug-related, skin reactions characterized by significant epidermal and mucosal loss.
  - SJS < 10% body surface area (BSA)
  - SJS/TEN overlap 10–30% BSA
  - TEN >30% BSA

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Signs and symptoms:

- Suspect in patients with fever, flu -like symptoms preceding severe mucocutaneous involvement typically occurs 7–10 days following initiation of inciting drug.
- Skin involvement classically starts on the face and trunk and rapidly spread over the course of a few days to their maximum extent. Skin lesions may be macular or targetoid, coalesce, and desquamate over time.
- + Nikolsky sign
- Erosions of any mucosal surface (eyes, nose, mouth, gastrointestinal tract, vagina, penis, urinary tract)
  - Oral mucosa and conjunctiva are most commonly affected.
  - If any concern of involvement, needs evaluation by appropriate specialist as soon as possible (ophthalmology, ENT, GYN, urology etc.)

Before you see the patient suspected of SJS/TEN:

1. Call pathology lab. Find out how and where to bring the frozen section specimen
2. Call pathology attending and inform his/her about a potential need for reading of a frozen section
3. If you work in a hospital system with a burn unit, you should touch base with the burn unit team regarding such a potential patient. If there is no burn unit in your hospital, medical or surgical intensive care unit will be your best option.

Diagnostic work up:

- Skin biopsy with frozen sections for rapid diagnosis.
  - Obtain two 4 mm perilesional punch biopsy specimens, one for frozen section and one for permanent section.
  - Histology shows full-thickness necrosis of keratinocytes, subepidermal split, and sparse or absent inflammatory infiltrate.
- Baseline CBC, LFTs, BMP, stat IgA level (for IVIG) and cultures.

Table 5.1 Potential causative agents

Medications/class commonly associated with SJS and TEN
Allopurinol
Aminopenicillins
Amithiozone
Antiretrovirals (especially non-nucleoside reverse transcriptase inhibitors)
Barbiturates
Carbamazepine
Chlormezanone
Phenytoin anticonvulsants
Lamotrigine
Phenylbutazone
Piroxicam
Sulfadiazine
Sulfadoxine
Sulfasalazine
Trimethoprim-sulfamethoxazole

Intervention:

- Identify and stop potential causative agents: medication (antibiotics, anticonvulsants or anti-inflammatories) or infection (Table 5.1)
- Correct fluid and electrolyte imbalances; watch for hypercatabolism, and acute respiratory distress syndrome
- Watch out for infection, bacteremia. Low threshold to reculture and treat any suspected infection
- Avoid manipulation of skin and use of adhesive dressings; erosions can be managed with xeroform dressings or vaseline embedded gauze or saline soaked gauze. Many burn units have their own specific wound dressing preference.

- Viscous lidocaine for oral erosions
- Pain management as per primary team
- IV/NG tube for nutrition
- Calculate SCORTEN Severity score for prognosis. One point for each item below (Table 5.2).
  - Age ≥ 40
  - HR ≥ 120 bpm
  - Malignancy
  - BSA detachment ≥ 10% at day 1
  - Serum BUN > 10 mmol/L
  - Serum bicarbonate level < 20 mmol/L,
  - Serum glucose level > 14 mmol/L
- IVIG is frequently used to manage more severe patients. Depending on your hospital, you may need hematology consult to obtain IVIG and nephrology consult if impaired renal function (for dosing). Anti-TNF agents (mostly infliximab and etanercept but also adalimumab) and cyclosporine have shown some efficacy in a few case studies. Role of systemic corticosteroids and other non-steroid immunosuppressive medications is controversial.
- Average time for epidermal regrowth ~ 3 weeks. The most common sequelae are ocular scarring and visual loss. Overall morbidity ~ 5% SJS and ~ 30% TEN.
- The most frequent causes of death are sepsis and multiorgan failure

Table 5.2 SCORTEN Severity score for prognosis

SCORTEN	Mortality rate (%)
0–1	3.2
2	12.1
3	35.8
4	58.3
≥5	90

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) [3–5]

Key Points:

- Rare, idiosyncratic adverse drug reaction often related to reactivation of herpesviruses. Delayed onset, 2–6 weeks following drug ingestion.

Signs and symptoms:

- Fever
- Skin eruption (most often maculopapular morbiliform exantham)
- Multiorgan involvement. Any visceral organs can potentially be involved. Needs complete review of systems.
  - Liver (60- > 80% of cases), kidneys (10–30% of cases) and lungs (5–25% of cases)
  - Autoimmune thyroiditis is a late complication. Needs follow up with PCP after discharge.
- Hypereosinophilia
- Facial edema
- No mucosal involvement
- Lymphadenopathy (most common cervical lymph node)

Diagnostic work up:

- Skin biopsy often done but shows no diagnostic feature
- Labs: CBC, CMP, UA, viral hepatitis panel, thyroid function test
  - Hematologic abnormalities including high eosinophil counts (may be transient, need for frequent monitoring) and presence of atypical lymphocytes
  - No standardized protocol for herpes virus testing
- Two diagnostic criteria (Tables 5.3A and 5.3B):

Intervention:

- Identify and stop culprit medication: aromatic anticonvulsant (phenytoin, phenobarbital, carbamazepine); other drugs: sulfanamides, minocyclines, dapsone, sulfasalazine, and allopurinol.

Table 5.3A RegiSCAR criteria

RegiSCAR criteria (three out of four * required for diagnosis)
Hospitalization*
Reaction suspected to be drug-related*
Acute rash*
Fever >38 C*
Enlarged lymph nodes at minimum of 2 sites*
Involvement of at least 1 internal organ*
Blood count abnormalities*
Lymphocytes above or below normal limits
Eosinophils above the laboratory limits
Platelets below the laboratory limits

*Necessary for making the diagnosis

Table 5.3B Japanese group's criteria for the diagnosis of DRESS/DIHS

Japanese group's criteria for diagnosis of DRESS/DIHS (needs 7/10 for diagnosis)
Maculopapular rash developing >3 weeks after starting suspected drug
Prolonged clinical symptoms 2 weeks after discontinuation of suspected drug
Fever >38 C
Liver abnormalities (alanine aminotransferase>100 U/L)
Leukocyte abnormalities
Leukocytosis (>11 × 109/L)
Atypical lymphocytosis (>5%)
Eosinophilia (>1.5 × 109/L)
Lymphadenopathy
Humans Herpes 6 reactivation

- No evidence-based guidelinesfor management
  - Supportive measures.
  - Systemic corticosteroids are the first-line therapy. Most patients respond to moderate or high dose steroids of 40–60 mg prednisone equivalent daily, with long gradual dose-reduction given over 10 weeks. Treatments with non-steroids immunosuppressants, plasma exchange and IVIG depends on specific organ involvement.
- Potentially fatal drug reaction with a mortality rate of 10%.

Necrotizing Fasciitis [6]

Key Points:
- Aggressive, rapidly progressive inflammatory infection of the fascia leading to extensive necrosis of subcutaneous tissue and fascia with relative sparing of the muscle.

Signs and symptoms:
- Most common initial cutaneous findings are pain, swelling, and erythema (may be confused with cellulitis and other skin and subcutaneous infections).
- Think of necrotizing fasciitis if rapid progression of cutaneous lesion, necrosis, dusky appearance or cyanosis of the tissue, and extreme local tenderness that is out-of-proportion to the exam.
- Fever, tachycardia, hypotension, altered mental state + other signs of sepsis

Diagnostic work up:
- Imaging: CT is 80% sensitive, while MRI is 100% sensitive with 86% specificity.
  - Gas may be identified in tissue (most often seen in gas gangrene caused by clostridia).
  - Asymmetric fascial thickening, fat stranding, and gas tracking along fascial planes are the most important imaging findings on CT and MRI scans.
- Two types of necrotizing fasciitis, distinguished based on bacterial morphology. Type I: polymicrobial bacterial with both aerobic and anaerobic bacteria. Type II: monomicrobial, most common Group A Streptococcus.

- Intervention:
- Surgical Emergency
  - Surgical debridement and IV antibiotics.
  - Hyperbaric oxygen may be used as adjunctive therapy.

Staphylococcal Scalded Skin Syndrome (SSSS) [7–10]

Key Points:

- Systemic toxic disease resulting from exfoliative toxin (ET) produced by infection with Staphylococcus aureus.
  - Toxin cleaves demoglein 1 in the superficial epidermis, creating blisters and denuding of the skin.
- More often occurs in children younger than 5. Occasionally occurs in adults (especially those with impaired immune status or renal dysfunction).

Signs and symptoms:

- Infection may begin as sore throat and purulent conjunctivitis (alternatively, in neonates, the umbilical cord is often the source of infection)
- Within 48 h of symptom onset, development of
  - Fever, malaise
  - Erythematous tender areas on the face, neck, axilla, and perineum develop. Flaccid bullae develop in erythematous areas
  - + Nikolsky sign
  - Mucosal membranes typically spared

Diagnostic work up:

- Skin biopsy: detached superficial epidermis with separation at the granular layer
- Culture from: blood, urine, nasopharynx, umbilicus, or any suspected focus of infection. Culture of intact blister are sterile.

Intervention:

- Management: ICU or burn unit
  - Supportive care including NG tube, IV fluids

  - Early initiation of IV antibiotics (penicillinase-resistant penicillins recommended, clarithromycin or cefuroxime if penicillin-allergic)
  - Pain management
    - Avoid NSAIDS due to risk of impaired renal function
  - IVIG or fresh frozen plasma useful in some cases
  - Silicone or none-stick dressings over denuded skin
  - Monitor for sepsis and pneumonia
- Prognosis: re-epithelialization of denuded skin in 6–12 days
  - No scarring
- Mortality is less than 10% in children, but between 40–63% in adults.

Filler Emergencies [11–15]

Key Points:

- Intravascular injection of filler can lead to devastating complications such as skin necrosis or blindness.
- Preparation of filler crash kit
- Danger Zones/Risk Factors
  - Deep injections – especially nasal radix and lateral nasal wall
  - Upper lip philtrum injection – vessel is superficial
  - Large volume bolus (greater than 0.1 cc)
  - Prior rhinoplasty
  - High pressure injection
  - Small, sharp needles

Signs and Symptoms:

- Arterial injection – immediate, severe, and disproportionate pain and color changes (white spots)
- Venous injection – less severe, dull, or delayed pain (in some cases, no pain)
- Filler blindness [11] – mechanism of action through retrograde flow; also possible vascular compression
  - Injection of supratrochlear, supraorbital, angular and dorsal nasal arteries (all branches of the external carotid artery) will result in retrograde flow of the filler – emboli into the ophthalmic artery [12]

  - Central retinal artery occlusion for more than 60–90 min causes irreversible blindness

Diagnostic work up: This is a clinical diagnosis

- Patients may exhibit:
  - Severe pain (or no pain)
  - Blanching
  - Mottled skin discoloration (livedo reticularis)
  - Blindness

Supplies for Filler Emergency Kit: Nitropaste, Hyaluronidase, Aspirin, oxygen
Others: timolol, acetazolamide, nitroglycerin, mannitol

Interventions:

- Use warm compress and massage filler out of entry site
  - 5–10 min, every 1–2 h
- Apply topical nitropaste to the area
  - Half inch of 2%
- Give oral baby aspirin
- Give supplemental oxygen
- Administer hyaluronidase for hyaluronic acid based fillers
  - Available forumlations: hylase (derived from bovine testicular hyaluronidase), vitrase (derived from ovine hyaluronidase), hylenex (recombinant human hyaluronidase)
  - For intravascular infarction, high doses of hyaluronidase (200–300 U) have been recommended – repeated daily for 2 days [13].
  - In acute ischemia, consensus recommendations to treat the entire ischemic area with hyaluronidase. Repeat until clinical resolution is achieved (hourly or daily) [14].
  - Doses up to 1500 U may be required for reversal of vascular compromise
- Recommended medical treatment for filler blindness [15]:
  - Digital massage: start immediately while preparing the treatment and to continue once the drugs have been administered.
    - Place patient in supine position with eyes closed

    - Apply firm pressure (enough to ensure that the eyeball is indented about 2–3 mm) on the eyeball through the closed eyelids
    - Apply firm pressure for 5–15 s and quickly release.
    - Repeat this cycle for at least 5 min.
- One drop of topical timolol 0.5% and/or an acetazolamide 500 mg tablet (after excluding allergy to sulfonamides)
- Sublingual pill of aspirin (325 mg) or one of nitroglycerin (0.6 mg).
- Intravenous mannitol infusion, 100 mL over 30 min, of mannitol 20%.
- If despite these measures the patient does not recover vision in the first 15–20 min, the patient must be referred to ophthalmology for anterior chamber paracentesis to decrease intraocular pressure, and possible retro-bulbar injection of hyaluronidase

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Chapter 6
Common Skin Diseases: Quick Reference

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Condition
Contact dermatitis

ICD-10
L23.9 Allergic contact dermatitis (ACD)
L24.9 Irritant contact dermatitis (ICD)

Physical Exam Findings
Variable findings, but classically a characteristically localized grouping of erythematous macules/patches, vesicles, or bullae after an acute exposure. Lichenification may be seen in chronic exposure. If localized to the face, neck, upper chest, or eyelids, suspect an airborne allergen such as fragrances or nail polish.

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Pathophysiology/Symptoms
Allergic contact dermatitis (ACD) requires a history of previous exposure and sensitization. Intense pruritus 24–48 h following exposure, as it is a type IV hypersensitivity. In contrast, irritant contact dermatitis (ICD) causes direct toxicity to cells and can occur immediately following exposure, usually causing a burning sensation.

Differential Diagnosis
Allergic contact dermatitis, irritant contact dermatitis, atopic dermatitis, nummular dermatitis, dyshidrotic dermatitis, stasis dermatitis, seborrheic dermatitis, rosacea, dermatomyositis, cutaneous T-cell lymphoma (CTCL)

Diagnostic Tests
The diagnosis is generally clinical. If unable to discern an obvious potential trigger based on history or avoidance alone, consider patch testing. Biopsy is reserved for refractory cases or if diagnosis is unclear, as other concerning dermatoses (such as CTCL) can present similarly.

Management
Identification and avoidance of the offending agent and symptomatic management are the mainstays of treatment. Topical steroids are the primary pharmacologic modality for symptomatic control; low-potency for face and intertriginous areas and mid- to high-potency for the body and scalp. Advise patients not to exceed recommended use due to long-term side effects. Consider biopsy for consideration of other potential diagnoses if unresolving or if symptoms persist despite trigger avoidance or in cases of therapy recalcitrance.

Condition
Cellulitis

ICD-10
L03.90

Physical Exam Findings
Classic signs of inflammation including an ill-defined erythematous patch, tenderness, warmth, and swelling occurring in a unilateral extremity or face. May also see linear erythema suggestive of lymphangitis and/or regional lymphadenopathy. Vesicles, petechiae, bullous lesions, or purpura may be seen in severe cases. Red-flag findings include severe tenderness, dusky gray color, malodorous discharge, crepitus, significant edema, and/or rapid progression.

Pathophysiology/Symptoms
Bacterial infection of the deep dermis and subcutaneous tissue characterized by redness/erythema, warmth, swelling, and pain. Onset may be preceded by fevers, chills, or malaise. Patient may also have an inciting event such as puncture wound, trauma, or fissuring in web-spaces.

Differential Diagnosis
Very broad, but numerous vascular, inflammatory, and infectious etiologies can mimic cellulitis. This includes but is not limited to erysipelas, arthropod bite, erythema migrans, chemical cellulitis, Wells syndrome, atopic dermatitis, allergic and irritant contact dermatitis, phytophotodermatitis, panniculitidies, lymphedema, deep venous thrombosis, thrombophlebitis, lipodermatosclerosis, venous stasis, gout, fixed drug eruption, calciphylaxis.

Diagnostic Tests
The diagnosis is generally clinical. Purulent wounds should be sent for culture and sensitivity (C&S) studies. Venous ultrasound imaging should be performed if thrombosis is also suspected.

Management
Choice of therapy/management will be largely determined by patient's immune status, comorbidities, methicillin resistant staphylococcus aureus (MRSA) history or risk factors, degree of purulence, systemic involvement, and rapidity of spread.

Mild, uncomplicated infections in otherwise healthy patients can be managed as an outpatient with oral antibiotic therapy and close follow-up. Surgical consultation and/or imaging studies should be considered in severe cases. Empiric antibiotic therapy should be administered based on antimicrobial resistance patterns in patient's local community and MRSA risk factors. The leading edge of the erythema should be marked and the patient's response should be re-assessed every 4–6 h. Escalation of therapy is warranted if unresponsive after 24–48 h of therapy.

Condition

Tinea corporis, "Ringworm"

ICD-10

B35.4

Physical Exam Findings

Classically seen annular scaly erythematous patches or thin plaques with central clearing. Areas of involvement are typically larger in diabetic or immunocompromised patients. May also see maceration in intertriginous areas.

Pathophysiology/Symptoms

Superficial skin infection by a dermatophytic species of fungus, commonly Trichophyton, Microsporum, or Epidermophyton. May be pruritic and result in secondary lichenification over time. Can also be asymptomatic or minimally pruritic.

Differential Diagnosis

Allergic or irritant contact dermatitis, atopic dermatitis, nummular eczema, granuloma annulare, erythema annulare centrifugatum, seborrheic dermatitis, scabies, fixed drug eruption, tinea versicolor, psoriasis, lichen planus, erythrasma, intertrigo.

Diagnostic Tests

Can be difficult to distinguish from eczema/dermatitis. Scraping and KOH preparation of lesions may help identify fungal hyphae in cases where diagnosis is equivocal. Fungal

culture may be used to determine speciation but takes several weeks and is not routinely performed. Certain species will fluoresce under Wood's lamp examination.

Management
Localized involvement in healthy individuals can be managed with topical antifungals twice daily for 1–6 weeks, and topicals should be applied at least 2 cm beyond the border of active areas. Nystatin is not effective. Extensive involvement will require oral antifungals, which requires liver enzyme monitoring and is contraindicated in patients with liver disease. Terbinafine 250 mg PO daily for 2–4 weeks is commonly prescribed. Lifestyle modification including avoiding occlusive clothing, avoiding re-inoculation/autoinoculation, and wearing cotton clothing, should be advised.

Condition
Epidermoid cyst, Epidermal inclusion cyst (EIC)

ICD-10
L72.0

Physical Exam Findings
A mobile, skin-colored, dome-shaped papule or nodule more commonly located on the face, head and neck/scalp, but can be found on the trunk as well. May also have a dark punctum and express a cheesy, viscous material.

Pathophysiology/Symptoms
Several etiologies have been implicated but are thought to arise from disruption of the follicular structures or traumatically implanted or ectopic epithelium. Generally asymptomatic lesions but can be painful or tender if traumatically ruptured or if they become secondarily infected.

Differential Diagnosis
Abscess, dermoid cyst, non-melanoma skin cancer, lipoma, pilar cyst, pilomatricoma, calcinosis cutis, xanthoma, steatocystoma, rheumatoid nodule, adnexal related malignancies.

Diagnostic Tests
The diagnosis is generally clinical. However, histopathological examination is used to confirm the diagnosis upon excision of the lesion.

Management
Small, asymptomatic lesions do not require treatment and can be observed. Rapidly growing or symptomatic cysts should be excised. Infected cysts without systemic symptoms may be managed with either incision and drainage with or without antibiotics or a trial of systemic antibiotics alone, depending on the clinician's best judgement, but either approach may only provide temporary relief. It is reasonable to advise patients to have a previously infected cyst excised due to risk of recurrent infections. In cases of actively infected cysts, excision should be delayed until infection resolves. If elective excision is desired, excision can be performed, with care to ensure the entire wall/cavity is removed. Incomplete removal of the cyst wall can result in recurrence.

Condition
Urticaria unspecified, "Hives"

ICD-10
L50.9

Physical Exam Findings
Transient well-defined annular or serpiginous erythematous, edematous papules or plaques of variable size often with central pallor. Individual lesions resolve within 24 h, rapid resolution and transience are key characteristics. May be seen in association with angioedema.

Pathophysiology/Symptoms
Lesions are caused by both the allergic and non-allergic release of histamine and other vasoactive molecules from mast cells. Most cases are idiopathic, followed by upper respiratory infection (URI) and medication-induced, and, lastly, food related. Acute urticaria refers to an episode lasting less

than 6 weeks' duration. Chronic urticaria implies that the condition lasts longer than 6 weeks.

Differential Diagnosis
Urticarial vasculitis, dermatographism, contact dermatitis, erythema multiforme, urticaria multiforme, angioedema, serum sickness, papular urticaria.

Diagnostic Tests
Acute urticaria generally does not require further diagnostic testing. Individual lesions that persist beyond 24 h should be biopsied to evaluate for urticarial vasculitis. Evidence of vasculitis should prompt laboratory evaluation that may include complete blood count (CBC), comprehensive metabolic panel (CMP), erythrocyte sedimentation rate (ESR), urinalysis, C3, C4, CH50, hepatitis serologies, antinuclear antibodies (ANA), cryoglobulins, immunoglobulins, serum and urine protein electrophoresis (SPEP/UPEP). In cases of chronic urticaria, allergy testing, Helicobacter pylori testing, thyroid stimulating hormone (TSH), CBC with differential, and ESR may be helpful.

Management
Non-sedating H1 antagonists such as cetirizine, loratidine, or fexofenadine are the mainstays of pharmacologic management. First generation antihistamines can be administered at night time. Antihistamines can also be co-administered with leukotriene inhibitors. In general, patients should be counseled regarding avoidance of known triggers such as aspirin, alcohol, food additives, and excessive heat. In severe cases, a brief course of oral prednisone 0.5–1 mg/kg daily can be administered in the first 5 days. Most cases of acute urticaria resolve within 6 weeks.

Condition
Viral warts

ICD-10
B07.8

Physical Exam Findings
Rough, hyperkeratotic skin-colored papules or plaques of variable size with irregular surface/verrucous texture. Can occur on any bodypart at any age, but more commonly seen on digits, distal extremities, and knees of school-aged children. Close inspection may reveal tiny black/red dots, which are thrombosed capillaries.

Pathophysiology/Symptoms
Skin proliferations resulting from infection of keratinocytes by the human papillomavirus. They are generally transmitted by direct contact and patients frequently autoinoculate themselves.

Differential Diagnosis
Squamous cell carcinoma, verrucous carcinoma, actinic keratosis, hypertrophic actinic keratosis, clavus/corn, seborrheic keratosis, molluscum contagiosum, keratoacanthoma, prurigo nodularis, cutaneous horn.

Diagnostic Tests
The diagnosis is generally clinical. Atypical lesions, lesions that are highly recalcitrant to therapy, or rapidly growing and painful lesions should be biopsied to assess for malignancy.

Management
Over a prolonged period of time, warts may spontaneously involute without treatment. Observation alone is reasonable in some cases. Intervention is typically implemented for cosmesis and to prevent spread. Numerous modalities exist and surgical excision is rarely warranted, but lesions frequently persist or recur despite treatment. Females with genital lesions should be appropriately screened as determined by their gynecologist. Lesions may be pared down prior to therapy to improve efficacy/penetration. Over the counter (OTC) salicylic acid treatments can be employed under occlusion with adhesive tape. Cryotherapy and intralesional immunotherapy are commonly employed in office. Topical treatments with 5-fluorouracil, imiquimod, or tretinoin may also be pre-

scribed although response rate is variable. Patients should be instructed to take appropriate measures to prevent spread to others as well as to prevent autoinoculation.

Condition

Basal cell carcinoma of skin, unspecified

ICD-10

C44.91

Physical Exam Findings

Most commonly seen on the head and neck, a smooth or shiny well-defined pink to red papule or plaque with telangiectasias. May also see ulceration and "arborizing" blood vessels on closer inspection.

Pathophysiology/Symptoms

The most common cutaneous malignancy. This entity is a malignant proliferation of basal keratinocytes most commonly due to disruption of sonic-hedgehog signaling pathway from both environmental (UV light exposure) and genetic factors. Variable symptoms ranging from asymptomatic to painful, and it often presents as a non-healing lesion in sun-exposed areas. Very low metastatic potential but can cause significant local destruction.

Differential Diagnosis

Squamous cell carcinoma, actinic keratosis, amelanotic melanoma, extramammary Paget disease, atopic dermatitis, tinea corporis, psoriasis, lichenoid keratosis.

Diagnostic Tests

The diagnosis is made on histopathological examination. As such, skin biopsy is generally required to confirm the diagnosis.

Management

Numerous modalities exist including electrodessication and curettage (ED&C), excision, cryotherapy, oral and topical agents, radiation, and Mohs surgery. In general, Mohs surgery is

preferred for lesions on high risk areas but should be employed in accordance with appropriate use criteria [1, 2]. Generally speaking, excisional modalities tend to have lower recurrence rates [2]. However, the choice of treatment will depend on several factors including anatomic location, histologic subtype, cosmetic considerations, lesion size, patient comorbidities, patient preference, and other considerations. All patients should be educated regarding sun protective and proper avoidance measures and should have scheduled full skin examinations after their first diagnosis, as they are at increased risk for developing additional cutaneous malignancies.

Condition

Squamous cell carcinoma of skin, unspecified

ICD-10

C44.92

Physical Exam Findings

One should see background actinic damage with neighboring/adjacent actinic keratoses and/or lentigines in photodistributed areas. May also arise in skin with chronic ulcers, previously irradiated sites, chronic lymphedema, or burn scars. SCC generally presents as an erythematous or skin-colored papule or plaque with overlying hyperkeratosis. The lesions may erode or ulcerate and exhibit incomplete healing with hemorrhagic crust.

Pathophysiology/Symptoms

Malignant proliferation of keratinocytes generally from cumulative UV exposure. Entity generally appears on chronically sun-damaged areas, but in immunocompromised patients, can occur anywhere on the body. Can have highly variable presentation. May present as erythematous hyperkeratotic papule, plaque, or nodule. Can be painful but are more commonly asymptomatic. Lesions arising within scars or chronic ulcers should prompt clinical/histopathological evaluation for SCC.

Differential Diagnosis
Verruca vulgaris, keratoacanthoma, amelanotic melanoma, actinic keratosis, merkel cell carcinoma, prurigo nodularis, irritated seborrheic keratosis, eccrine poroma, basal cell carcinoma.

Diagnostic Tests
The diagnosis is made on histopathological examination. As such, skin biopsy is generally required to confirm the diagnosis.

Management
For primary cutaneous disease, numerous modalities exist including ED&C, excision, cryotherapy, oral and topical agents, radiation, and Mohs surgery. In general, Mohs surgery is preferred for lesions on high risk areas but should be employed in accordance with appropriate use criteria [1, 2]. Generally speaking, excisional modalities tend to have lower recurrence rates [2]. However, the choice of treatment will depend on several factors including anatomic location, histologic subtype, cosmetic considerations, lesion size, patient comorbidities, patient preference, and other considerations. All patients should be educated regarding sun protective and proper avoidance measures and should have scheduled full skin examinations after their first diagnosis, as they are at increased risk for developing additional cutaneous malignancies. Immunocompromised patients have a tendency to have much more histologically aggressive subtypes.

Condition
Malignant melanoma of skin, unspecified

ICD-10
C43.9

Physical Exam Findings
Morphology and degree of pigmentation can be variable and can range from amelanotic to deeply pigmented. The ABCDE

mnemonic/features of melanoma and the "ugly duckling" sign can be useful physical examination considerations when evaluating individual pigmented lesions. Additionally, dermoscopy, also known as epiluminescence microscopy (ELM), is a helpful non-invasive adjunct. Concerning features include an irregular/atypical pigment network or blue-white veil.

Pathophysiology/Symptoms
Malignant proliferation of melanocytes. Risk increases with family history, being fair-skinned, tanning bed use, and cumulative UV light exposure.

Differential Diagnosis
Solar lentigo, ink spot lentigo, atypical nevus, blue nevus, pigmented basal cell carcinoma, seborrheic keratosis, angiokeratoma, dermatofibroma, recurrent melanocytic nevus.

Diagnostic Tests
The diagnosis is made on histopathological examination. As such, skin biopsy is generally required to confirm the diagnosis. Punch or excisional biopsy is generally preferred as to ascertain depth of the lesion as well as to determine appropriate margins, followed by surgical excision.

Management
Early identification and intervention are critical in lower mortality/morbidity. Surgical excision ± sentinel lymph node (SLN) biopsy, depending on staging, as outlined by the American Joint Committee on Cancer (AJCC) for primary melanoma tumor staging (2018) [3]. Appropriate additional intervention should be determined based on stage and corresponding National Comprehensive Cancer Network (NCCN) guideline recommendations [4]. The role of lymph node dissection is unclear and controversial, but more recent data suggests that it does not appear to increase melanoma-specific surival [5]. Treatment of metastatic disease and or locally advanced disease should include a discussion from a multidisciplinary team consisting of dermatologists, pathologists, oncologists, and surgical oncologists.

Condition
Acne vulgaris

ICD-10
L70.0

Physical Exam Findings
Most commonly in peripubertal adolescents, with a predilection for the face, upper chest and upper back. Erythematous papules and pustules as well as open and closed comedones (blackheads and whiteheads, respectively) can also be observed. Nodules and cysts are seen in more severe forms, which can lead to scarring as well as post-inflammatory hyperpigmentation and hypopigmentation.

Pathophysiology/Symptoms
Inflammatory response involving the pilosebaceous unit in response to increased sebum production (due to puberty/androgens), hyperkeratinization, and Propionibacterium acnes proliferation. Generally asymptomatic in milder cases. Can bleed or drain with excoriation. Nodulocystic form can be painful/tender to palpation. Female patients with hormonally-driven acne will notice flaring around menses.

Differential Diagnosis
Cosmetic-induced acne, pomade acne, medication-induced/drug-induced acne, steroid acne, perioral dermatitis, folliculitis, pseudofolliculitis barbae, Pityrosporum folliculitis, rosacea, sebaceous hyperplasia, gram negative folliculitis.

Diagnostic Tests
The diagnosis is generally clinical. In the setting of other clinical findings such as hirsutism or a history of irregular menses, laboratory evaluation of sex hormone levels is warranted to assess for hormonal derangements or polycystic ovarian syndrome. Consider nasal swabs to assess for gram-negative folliculitis if unresponsive to therapy.

Management
Choice of therapy will depend on patient's severity and presence/absence of comedones. Patients should be instructed to avoid comedogenic product use on the affected areas. For mild to moderate cases, benzoyl peroxide washes in conjunction with topical antibiotics and topical retinoids are the foundations of therapy. Topical antibiotics such as clindamycin 1% lotion should always be co-administered with benzoyl peroxide to prevent antibiotic resistance. It is advised to start with the lowest concentration of retinoid such as tretinoin 0.025% and use it just 2–3 times per week initially. The patients can be instructed to advance to nightly as tolerated over the course of several weeks to prevent excessive redness and irritation. In cases of moderate to severe acne, a 3–4 month course of oral antibiotics with a tetracycline such as doxycycline or minocycline is warranted. Severe cases with significant scarring warrant consideration with oral isotretinoin. Female patients with perimenstrual exacerbations may respond more favorably to oral contraceptives and spironolactone.

Condition
Herpes zoster (shingles)

ICD-10
B02.9

Physical Exam Findings
Dermatomally-distributed unilaterally clustered vesicles or small bullae on an erythematous base. Classically does not cross the midline. Can affect any nerve root, but T3 through L2 are generally the most commonly affected dermatomes. Trigeminal dermatomes can also be affected.

Pathophysiology/Symptoms
Reactivation of dormant varicella-zoster virus in dorsal root ganglion after remote history of primary infection (chickenpox). Typically triggered by immunosuppression, medications,

or physical/emotional stress. Typically begins with a prodromal burning in the affected dermatome followed by cutaneous eruption 24–72 h later. The lesions will crust over and resolve generally within 7–14 days. Often leaves scarring, post-inflammatory hyperpigmentation, and possible postherpetic neuralgia (PHN) which can persist weeks to months following resolution of skin eruption.

Differential Diagnosis
Herpes simplex, cellulitis, contact dermatitis, bullous drug eruption, eczema herpeticum, primary or disseminated varicella infection.

Diagnostic Tests
The diagnosis is generally clinical. If involvement of ophthalmic branch of trigeminal nerve is suspected, emergent ophthalmic referral is warranted. A Tzanck smear can be prepared from cell scrapings gathered near the base of a vesicle. PCR and immunohistochemistry may also be performed in atypical cases.

Management
Antiviral therapy administered within 72 h of onset can decrease length of disease, lessen the severity of the episode, and reduce risk of postherpetic neuralgia (PHN). Corticosteroids may reduce acute pain associated with the episode but do not appear to prevent PHN. Coadministration of valacyclovir and gabapentin during the acute phase may reduce incidence of PHN [6]. Commonly employed antiviral regimens include acyclovir 800 mg Q4 hours for 7–10 days. Alternatively, famciclovir 500 mg and valacyclovir 1000 mg can be given Q8 hours for 7 days. Foscarnet is generally reserved for acyclovir-resistant cases. Gabapentin, pregabalin, tricyclic antidepressants, and topical capsaicin cream can be implemented for PHN, although treatment success is highly variable. If involvement of ophthalmic branch of trigeminal nerve is suspected, emergent ophthalmic referral is warranted to assess for ocular complications.

Condition
Actinic keratosis (Solar keratosis)

ICD-10
L57.0

Physical Exam Findings
Scaly, "gritty" erythematous macules, papules, or plaques with ill-defined borders in fair-skinned individuals on sun-exposed areas of skin. Commonly observed on the dorsal hands, forearms, ears, scalp, and face. Can be difficult to observe clinically but have a rough, "gritty" sensation/texture on palpation, and hence, the diagnosis is more properly made with tactile examination as opposed to observation alone.

Pathophysiology/Symptoms
Neoplastic, precancerous epithelial lesions found on sun-exposed skin of fair-skinned individuals. These lesions are the result of accumulated sun-exposure over the course of one's lifetime. The frequency increases with age, degree and duration of immunosuppression, and cumulative sun exposure. Lesions are usually asymptomatic but can be pruritic.

Differential Diagnosis
Squamous cell carcinoma, verruca vulgaris, seborrheic keratosis, seborrheic dermatitis, psoriasis.

Diagnostic Tests
The diagnosis is generally clinical. For atypical appearing, rapidly-growing, painful, large, indurated, or recurrent lesions, biopsy is warranted to assess for underlying squamous cell carcinoma. Threshold for biopsy should be lower in immunocompromised or immunosuppressed patients.

Management
Few, scattered isolated lesions can be managed effectively with cryotherapy. For innumerable lesions and larger areas of involvement in the setting of extensive actinic damage, will likely require field therapy. Possible field modalities include

photodynamic therapy (PDT), 5-fluorouracil (5-FU) 5% cream BID for 2–3 weeks, topical imiquimod 5% 2–3 times weekly for 12 weeks, or ingenol mebutate 0.015% gel daily for 3 consecutive days on face and scalp or ingenol mebutate 0.05% gel for 2 consecutive days on the trunk and extremities. Patients should be counseled/educated regarding proper sun protective and avoidance measures and instructed to use broad spectrum (UVA and UVB) sunscreen with a minimum of SPF 30. Patients with this condition are at increased risk of non-melanoma skin cancer and should be screened annually for the development of skin cancer.

Condition
Psoriasis

ICD-10
L40.0

Physical Exam Findings
Sharply demarcated pink or erythematous plaques with thick, adherent, silvery ("micaceous") scale classically of the scalp, extensor elbows and knees, although any anatomic location may be involved. May also classically see nail pitting ("oil spots") or onycholysis in association with the condition.

Pathophysiology/Symptoms
Aberrant T-cell function/activation and hyperactive keratinocyte responses are believed to be major culprits in the pathogenesis of psoriasis.

Differential Diagnosis
Atopic dermatitis, lichen simplex chronicus, seborrheic dermatitis, drug eruption, sarcoidosis, scabies, secondary syphilis, subacute cutaneous lupus erythematosus (SCLE), CTCL.

Diagnostic Tests
The diagnosis is generally clinical. Biopsy is reserved for atypical cases or if there is overlap with other conditions.

Management
The medical management of the psoriasis patient can be complex and cannot be comprehensively summarized here. Nevertheless, the appropriate treatment of psoriasis should be tailored to the individual patient depending on several factors including body surface area involvement and/or anatomic location as well as presence of joint involvement. Patients should be routinely screened and prompted through review of systems for development of psoriatic arthritis/joint symptoms and followed by their PCP due to the increased association with metabolic and cardiovascular disease. Lesions that are thin and isolated can be managed topically with combinations of mid-high potency topical steroids in conjunction with Vitamin D analogs and/or topical retinoids. Lesions that encompass a large body surface area (BSA) or patients with psoriatic arthritis, however, may be candidates for systemic therapy, in which case oral agents, immunosuppressive therapies, biologics, and/or UV light therapy may be considered. In general, systemic/oral corticosteroids should be avoided in these patients, as this can trigger pustular psoriasis upon discontinuation. Treatment should be evaluated on a case-by-case basis; systemic treatments often require monitoring and carry a potential risk of systemic side effects. Referral to rheumatologic colleagues should be considered if joint involvement is suspected.

Condition
Seborrheic dermatitis, unspecified

ICD-10
L21.9

Physical Exam Findings
Ill-defined pink/erythematous patches or thin plaques with greasy yellow or white loose scale affecting the sebum-rich areas of the body including the nasolabial folds, eyebrows, scalp, neck, upper chest, and back.

Pathophysiology/Symptoms
Unknown, possibly an aberrant inflammatory response to Pityrosporum (Malassezia) yeast, a common skin commensal organism. Immunocompromised patients and patients with Parkinsons disease or stroke can have severe and refractory disease.

Differential Diagnosis
Atopic dermatitis, psoriasis of the scalp, rosacea, perioral dermatitis.

Diagnostic Tests
The diagnosis is generally clinical. Biopsy is reserved for atypical cases or if there is overlap with other conditions.

Management
Shampoos containing salicylic acid, selenium sulfide, pyrithione zinc, or ketoconazole can be used as monotherapy or in combination with topical corticosteroid preparations depending on severity. A single shampoo may be used 3 times per week or more and alternating shampoos can improve efficacy. For non-scalp locations, the shampoos can be used as cleansers or, alternatively, zinc pyrithione bar soap can also be used. Antifungal creams can be applied to the face BID until clear.

Condition
Seborrheic Keratosis

ICD-10
L82.1

Physical Exam Findings
Well-demarcated, waxy, classically "stuck on" appearing verrucuous or papillomatous papules or plaques that can have large variance in color, including skin-colored, tan, light brown, and/or black.

Pathophysiology/Symptoms
Common benign neoplasm of skin. Etiology is unknown. There does appear to be some familial inheritance patterns and lesions are typically associated with increasing age.

Differential Diagnosis
Verruca vulgaris, melanoma, pigmented basal cell carcinoma, lentigo, melanocytic nevus, acrochordon, nevus sebaceous, epidermal nevus.

Diagnostic Tests
This diagnosis is generally clinical. Dermoscopy may differentiate between seborrheic keratoses, melanocytic nevi, and melanoma. Biopsy is reserved for unclear cases.

Management
In most cases, removal is performed for cosmetic reasons, as these lesions are benign. Symptomatic or irritated lesions can be treated with destructive modalities such as cryotherapy (most common) whereas larger lesions can be removed via shave technique and/or ED&C. Recently approved newer therapies such as topical 40% hydrogen peroxide can also be offered.

Condition
Rosacea

ICD-10
L71.9

Physical Exam Findings
Ill-defined erythema with or without papules and pustules predominantly the cheeks and nose that typically spares the nasolabial folds. Absence of comedones may favor rosacea over acne. Commonly see concurrent seborrheic dermatitis.

Pathophysiology/Symptoms
Chronic benign inflammation limited to the skin. Tends to be otherwise asymptomatic, but patients may complain of burn-

ing, tenderness, and increased warmth. Etiology is uncertain, but vascular alterations, UV light exposure, microbial infestation, and lighter skin types all may play a role. There also tends to be a familial predilection.

Differential Diagnosis
Acne vulgaris, perioral dermatitis, folliculitis, sarcoidosis, lupus miliaris disseminatus faciei, seborrheic dermatitis, polymorphous light eruption, systemic lupus erythematosus, cutaneous flushing.

Diagnostic Tests
The diagnosis is generally clinical. Biopsy is reserved for atypical cases or if there is overlap with other conditions.

Management
All patients should be counseled regarding avoidance of common triggers, including sunlight, hot or spicy foods, alcohol, and temperature extremes. Patients should then be stratified based on severity as well as subtype (either papulopustular vs. erythematotelangiectatic), as this will guide their management and likelihood of response to certain therapies. Treatment is nuanced and cannot be comprehensively summarized here as multiple new topicals and advancements in laser technology are now being utilized to treat this disorder. Topical metronidazole 0.75% may be applied BID. Oral tetracyclines can be used in high- and low-dose formulations as well if topicals do not provide satisfactory relief. Cosmetic laser treatment may be considered in patients with predominantly erythematotelangiectactic subtype. Patients should be screened for concurrent ocular involvement, specifically asking about dry/gritty sensations as well as prolonged redness and/or ocular pruritus. Patients with suspected ophthalmic involvement should be referred for examination by an ophthalmologist.

Condition
Scarring alopecia

ICD-10
Multiple, depending on subtype

Physical Exam Findings
Early scarring alopecias can be extremely difficult to discern on physical examination alone, which is where biopsy can be useful. ELM can be a useful tool to identify the loss of ostiae, which is a key characteristic of these disorders. Additional features such as perifollicular scale are commonly seen in central centrifugal cicatricial alopecia (CCCA) and lichen planopilaris (LPP). Distribution of hair loss is also important and can influence the differential diagnosis.

Pathophysiology/Symptoms
Immunologically mediated destruction of the pilosebaceous unit. Can be lymphocytic driven process in cases such as LPP and CCCA, or neutrophilic in the cases of dissecting cellulitis and folliculitis decalvans.

Differential Diagnosis
Frontal fibrosing alopecia, CCCA, LPP, folliculitis decalvans, dissecting cellulitis, acne keloidalis

Diagnostic Tests
A horizontally transected punch biopsy specimen should be performed if the etiology is unclear.

Management
Treatment of these conditions is highly nuanced and cannot be comprehensively summarized here. Patients should be counseled regarding the nature of their condition as well as expectations of therapy. Patients should be informed that loss of hair follicles is irreversible and that treatment is largely aimed at preserving remaining hairs. Treatment is aimed at addressing/mitigating the underlying inflammation to prevent further loss of hair follicles but will depend on the underlying diagnosis.

Condition
Alopecia – non-scarring

ICD-10
Multiple, depending on subtype.

Physical Exam Findings
Distribution and history can be the most important feature in distinguishing the specific type of non-scarring hair loss. Presence of miniaturized follicles in symmetric distribution, with sparing of the occipital scalp, is suggestive of androgenetic alopecia (AGA). Discrete patches of hair loss that are asymptomatic and followed by spontaneous periods of regrowth is suggestive of alopecia areata. Diffuse increased hair shedding is suggestive of telogen effluvium. Presence of pustules and hair loss in children with lymphadenopathy suggest tinea capitis.

Pathophysiology/Symptoms
Hair loss in non-scarring alopecias has a tendency to be asymptomatic. Family history is typically observed in AGA, but pathophysiology is thought to be due to innate sensitivity of hair follicle to circulating androgens resulting in miniaturization of follicles. Family history of auto-immune conditions are typically seen in alopecia areata, which is thought to be due to loss of immune privilege. Telogen effluvium is believed to be triggered by significant physical or mental stressor resulting in widespread truncation of the anagen phase and entry into the telogen phase manifesting 2–3 months after major stressor.

Differential Diagnosis
Alopecia areata, telogen effluvium, androgenetic alopecia, tinea capitis (pediatric patients).

Diagnostic Tests
For non-scarring alopecias, typically the diagnosis is made clinically. A horizontally transected punch biopsy specimen should be utilized if the etiology is unclear. Potassium hydroxide (KOH) preparation can be performed in children with suspected tinea capitis.

Management

Telogen effluvium is typically self-limited and patient reassurance is all that is required. Patients should be advised that it can take several months before their hair length returns to normal. In alopecia areata, ophiasis pattern hair loss can be associated with a poor prognosis, but mild-moderate forms of alopecia areata can be managed with topical steroids and intralesional kenalog injections in the affected areas. AGA is typically treated with topical minoxidil or oral finasteride in men, and topical minoxidil/spironolactone in affected female patients. Children with tinea capitis should be treated with appropriate antifungal, typically oral terbinafine or griseofulvin, based on suspected organism.

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Chapter 7
Guidelines from the Academy

Jacqueline Watchmaker and Neelam A. Vashi

Table 7.1 Guideline treatment algorithm for the management of acne vulgaris in adolescents and young adults

	Mild	Moderate	Severe
1st line treatment	Benzoyl peroxide – or – topical retinoid – or – Combination therapy (choose one): Benzoyl peroxide + topical antibiotic Benzoyl peroxide + topical retinoid	Combination therapy (choose one): Benzoyl peroxide + topical antibiotic Benzoyl peroxide + topical retinoid Benzoyl peroxide + topical antibiotic + topical retinoid – or – Oral antibiotic + topical retinoid + benzoyl peroxide – or –	Oral antibiotic + topical combination therapy (choose one): Benzoyl peroxide + topical antibiotic Benzoyl peroxide + topical retinoid Benzoyl peroxide + topical antibiotic + topical retinoid

(continued)

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Table 7.1 (continued)

	Mild	Moderate	Severe
	Benzoyl peroxide + topical antibiotic + topical retinoid		– or – oral isotretinoin
Alternative Treatment	Add topical retinoid or benzoyl peroxide (if not already on) – or – consider alternate/ different strength topical retinoid – or – consider topical dapsone	Consider alternate combination therapy – or – consider change in oral antibiotic – or – add combined oral contraceptive or oral spironolactone (females) – or – consider oral isotretinoin	Consider change in oral antibiotic – or – add combined oral contraceptive or oral spironolactone (females) – or – consider oral isotretinoin

Information adapted from Zaenglein et al. [1] and Thiboutot et al. [2]

TABLE 7.2 Guideline recommendations for topical therapy in the treatment of acne vulgaris

	Mechanism	Dosing, available forms and strengths	Side effects	Pregnancy category	Comments
Benzoyl peroxide (BP)	Antibacterial + mildly comedolytic	Dosing: topically qd to BID Strengths range from 2.5% to 10%. Available in topical washes, foams, creams or gels. Can be used as leave-on or wash-off agent.	Irritation, can bleach hair/fabric, contact allergy (uncommon)	C	• Addition of BP to regimens of topical antibiotic therapy may reduce resistance. • For patients with sensitive skin, recommend lower concentrations (2.5–5%), water-based and wash-off agents • Can be used as maintenance therapy • Available over the counter
Clindamycin	Anti-inflammatory and antibacterial (ideal for inflammatory acne)	Dosing: topically qd to BID Available in 1% solution or 1% gel	Dermatitis, photosensitivity, rare reports of diarrhea or clostridium difficile related colitis	B	• Topical antibiotic of choice; do not use as monotherapy (can cause resistance); do not use as maintenance therapy alone • Use in combination with BP to prevent resistance • Prescription only

(continued)

TABLE 7.2 (continued)

	Mechanism	Dosing, available forms and strengths	Side effects	Pregnancy category	Comments
Retinoids	Comedolytic (ideal for comedonal acne)	Dosing: topically qHS • Tretinoin (0.025–0.1% in cream, gel or microsphere gel vehicles) • Adapalene (0.1% gel, 0.3% cream or 0.1% lotion) • Tazarotene (0.05%, 0.1% cream, gel or foam)	Dryness, peeling, erythema, irritation, photosensitivity	Tretinoin = C Adapalene = C Tazarotene = X	• Some formulations of tretinoin are not photostable. Adapalene is photostable. • Tretinoin may be oxidized and inactivated by BP • Can be used as maintenance therapy • Adapalene 0.1% gel is available over the counter. • Tretinoin and tazarotene are by prescription only.
Azelaic acid	Comedolytic, antibacterial and anti-inflammatory	Dosing: topically BID Available in 4–20% cream or serum	Pruritus, burning, erythema, dryness dermatitis	B	• Can help treat postinflammatory hyperpigmentation • Over the counter strengths range from 4–15%. • Prescription strengths range from 15–20%.

Dapsone	Anti-inflammatory	Dosing: topically BID Available in 5% and 7.5% gel	Oiliness, peeling, dryness, orange-brown discoloration when used with BP	C	• Do not need to test for G6PD prior to starting • Not available over the counter
Salicylic acid	Comedolytic	Dosing: topically qd-TID Strengths range from 0.5% to 2%. Both wash-off and leave-on formulations. Available in cream, lotion, wash and gel	Hypersensitivity reactions, salicylate toxicity, erythema, scaling	C	Clinical trials demonstrating the efficacy of salicylic acid in acne are limited. Available over the counter

Table 7.3 Guideline recommendations for systemic therapy in the treatment of acne vulgaris

	Mechanism	Dosing	Side effects	Pregnancy category	Comments
Doxycycline	Antibacterial and anti-inflammatory	100 mg qd to 100 mg BID Also available in extended release tablets (brand name Doryx ®)	GI upset (esophagitis, nausea, abdominal pain), photosensitivity, esophagitis, pseudotumor cerebri	D	• More frequently associated with GI upset than minocycline • Systemic antibiotics should not be used as monotherapy • Limit duration of therapy to 3–4 months
Minocycline	Antibacterial and anti-inflammatory	Adults: 50 mg-100 mg qd to BID Also available in extended release tablets (brand names Solodyn ® and Ximino ®); dosing based on weight, 45 mg–135 mg daily	Dizziness, vertigo, pseudotumor cerebri, hyperpigmentation of skin/nails/teeth/mucous membranes, serum sickness-like reactions, drug induced Sweet's syndrome, autoimmune hepatitis, allergic reaction (DRESS), lupus-like syndrome	D	• Minocycline is not superior to doxycycline for the treatment of acne • Photosensitivity is less severe with minocycline than with doxycycline • Limit duration of therapy to 3–4 months

Isotretinoin	Vitamin A derivative	Starting dose: 0.5 mg/kg/day for the first month then increase to 1.0 mg/kg/day as tolerated (can be divided into BID dosing) Duration of therapy: until full clearance of acne	Transaminitis, hyperlipidemia, decreased night vision, depression, xerosis/chelitis, hyperostosis, myalgias, pseudotumor cerebri, teratogen	X	• Initial lab screening: Pregnancy test, lipid panel, LFTS • Lab monitoring • Q month: pregnancy test (females) • Month 2: lipid panel and LFTs • Screen for history of IBD and depression • Can be used first line for very severe, cystic acne • Previously goal cumulative dose was (120–150 mg/kg) but recent guidelines state isotretinoin should be continued until full clearance of acne

(continued)

Table 7.3 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Comments
Spironolactone	Aldosterone receptor antagonist	50–200 mg qd (can be divided into BID dosing).	Diuresis, menstrual irregularities, hyperkalemia, breast tenderness, breast enlargement, fatigue, headache, dizziness	C	• Useful in hormonal acne (flares with menstruation) • Only for use in females • Checking potassium in young, healthy women is unnecessary. • Check potassium level only if patient is on ACE-I, ARBs, NSAIDs, digoxin or other medication that alters potassium level

Oral contraceptive pills	Inhibit gonadotropin-releasing hormone	Varies depending on type	DVT, small increased risk of breast cancer	X	• OCPs approved by the FDA of the treatment of acne: drospirenone/ethinyl estradiol (YAZ ®), ethinyl estradiol/norgestimate (Ortho Tri-Cyclen®) and norethindrone acetate and ethinyl estradiol • (Estrostep Fe®) • Patients can be on both OCPs and oral antibiotics concurrently (except griseofulvin and rifampin) • May not see results for 3+ months • As effective as oral antibiotics at 6 months

(continued)

Table 7.3 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Comments
Tetracycline	Antibacterial and anti-inflammatory	Adults: 1 gram/day given in divided doses; when improvement occurs decrease to maintenance dose of 125–500 mg qd	GI upset, rash, photosensitivity, pseudotumor cerebri	D	Doxycycline and minocycline are more effective than tetracycline (tetracycline rarely used now).
Cephalexin	Antibacterial	Adults: 500 mg BID	Gastrointestinal upset, rash, eosinophilia, hepatic disturbances	B	Useful option in pregnant patients or in patients with allergies to other classes of antibiotics
Amoxicillin	Antibacterial	Adults 250 mg BID, up to 500 mg TID	Rash, GI upset	B	Useful option in children and during pregnancy. Safe with nursing.

Information adapted from Zaenglein et al. [1] and Thiboutot et al. [2]

Table 7.4 Guideline recommendations for anesthetics

	Use	Dosing	Onset	Duration	Use in pregnancy	Comments
Topical anesthesia	Nonablative laser treatments, injections, skin biopsies, curettage, dermal lacerations in children	Topical lidocaine 4% or 5% (L.M.X.4/5): maximum recommended adult daily dose is 17 to 20 g Lidocaine 2.5% with prilocaine 2.5% (EMLA): maximum recommended adult daily dose is 60 g	Topical lidocaine (L.M.X.4/5): 30 min Topical lidocaine 2.5% with prilocaine 2.5% (EMLA): 60 min	Topical lidocaine: about 30 min Topical Lidocaine/ prilocaine (EMLA): 60–120 min	Topical lidocaine (pregnancy category B) is safe for use on pregnant or nursing women but there is insufficient evidence to recommend use of other topical anesthetics	Topical lidocaine is the anesthetic of choice in pregnant women Only use EMLA on intact skin given risk of methemoglobinemia

(continued)

TABLE 7.4 (continued)

	Use	Dosing	Onset	Duration	Use in pregnancy	Comments
Local infiltration anesthesia	Biopsy, excision, wound closure, skin grafting, cauterization, nonablative and ablative skin resurfacing	Adults: maximum of 4.5 mg/kg of lidocaine without epi and 7.0 mg/kg of lidocaine with epi Children: maximum of 2 mg/kg of lidocaine without epi and 4.5 mg/kg of lidocaine with epi For multistage procedures, no more than 50 mL of 1% lidocaine over several hours	Lidocaine (xylocaine) onset within 1 min	Duration without epi: 30–120 min Duration with epi: 60–400 min	Lidocaine is pregnancy category B Epinephrine is pregnancy category C	For patients with true allergies to lidocaine use ester-type local anesthetic, bacteriostatic normal saline or 1% diphenhydramine. Toxicity: circumoral numbness, slurred speech, hypertension, tachycardia, metallic taste, seizure, CNS depression

Tumescent local anesthesia	Office-based liposuction	10-fold dilution of standard 1% lidocaine (0.1% lidocaine with 1:1,000,000 epi) maximum dose is 55 mg/kg for patient's weighing 43.6–81.8 kg	Lidocaine (xylocaine) onset within 1 min	Duration with epi: 60–400 min	Lidocaine is pregnancy category C Epinephrine is pregnancy category C	Advantages of tumescent anesthesia: decreased bleeding, avoids complications associated with general surgery

Information adapted from Kouba et al. [3]

Table 7.5 Guideline recommendations for additives to local infiltrate anesthesia

	Use	Dosing	Pregnancy	Comments
Epinephrine	Prolongs duration, reduces peak blood levels, provides hemostasis	1:200,000 equally as effective with decreased toxicity as 1:100,000	Pregnancy category C	Full vasoconstrictive effects in 7–15 min Extensive research has advocated for the addition of epi to local anesthesia on the ear, nose and digits. Ok to use on penis as well.
Hyaluronidase	Enhances diffusion of the anesthetic solution and decreases tissue distortion from fluid infiltration	1–15 IU/mL	Pregnancy category C	Cross-reactivity between bee venom and hyaluronidase; don't use in patients with a history of bee sting allergy
Sodium bicarbonate	Decreases patient pain during drug delivery	Mix 8.4% sodium bicarbonate with lidocaine with epinephrine in a 1:10 ratio	Pregnancy category C	Buffered solutions of 1% lidocaine with epinephrine may be prepared up to 1 week in advance (rise in pH will cause precipitation of epinephrine)

Information adapted from Kouba et al. [3]

Table 7.6 Guideline recommendations for the treatment of atopic dermatitis

	Mechanism	Dosing	Side effects	Pregnancy category	Monitoring	Comments
Topical corticosteroids	Act on a variety of immune cells and suppresses the release of pro-inflammatory cytokines	Dosing: daily to BID for flares followed by 1–2×/week as maintenance	Purpura, telangiectasia, striae, acneiform eruptions, atrophy, allergic contact dermatitis	C	Monitor for skin changes associated with prolonged/ inappropriate use	• Can apply under wet wraps/ occlusion for increased efficacy • Caution with use in sensitive skin areas (ie groin, face, axillae)

(continued)

Table 7.6 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Monitoring	Comments
Topical calcineurin inhibitors (TCIs)	Steroid sparing agent; inhibits calcineurin-dependent T-cell activation	Dosing: BID Topical tacrolimus ointment (0.03% and 0.1% strengths) and 1% pimecrolimus cream	Stinging, burning (more frequent than seen with topical steroids) Black box warning due to potential development of malignancies but no definite causal relationship has been established	C	No specific monitoring recommended	• Useful in sensitive skin areas given less side effects than topical steroids • Tacrolimus 0.03% ointment + 1% pimecrolimus cream are approved for patients >2 years of age. Tacrolimus 0.1% is approved for patients > than 15 years of age.

Phototherapy	Apoptosis of T cells	According to patient Fitzpatrick skin type	Actinic damage, local erythema, tenderness, pruritus burning, stinging, increased NMSC, HSV reactivation	Phototherapy with nbUVB is safe in pregnancy	Monitor and adjust based on erythema and patient discomfort	• Second line treatment after failure of emollients, topical steroids and topical calcineurin inhibitors • Numerous studies document the efficacy of phototherapy for AD

(continued)

Table 7.6 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Monitoring	Comments
Cyclosporine	Immunosuppressant of T cells and IL-2	5 mg/kg/day, standardly 150–300 mg/day in adults. Start lower and increase based on response. Pediatric: 5 mg/kg/day	Nephrotoxicity, gingival hyperplasia, hypertrichosis, increase K, increase uric acid, decreased Mg, hyperlipidemia, increased risk of skin cancer and lymphoma	C	Screening: CBC, CMP, hepatitis panel fasting lipid panel, Mg, uric acid, tuberculin test, UA, blood pressure ×2, pregnancy test Month 1: CBC, CMP, lipid panel, UA, blood pressure, Mg Month 2: repeat month 1 Q3 months: CBC, CMP, lipid panel, Mg, uric acid, UA, BP	• Maximum usage 1 year • If Cr increases > 25% above baseline, reduce dose by 1 mg/kg/day for 2–4 weeks then recheck; stop CSA if Cr remains >25% above baseline, hold at lower dose if level is within 25% of baseline • If Cr increased >50% above baseline, discontinue until levels return to baseline. • Cyclosporine is effective for refractory AD

Azathioprine	Purine analog that inhibits DNA production	1–3 mg/kg/day (~50–150 mg qd) Pediatric: 1–4 mg/kg/day	GI upset, bone marrow suppression, new onset malignancy, hypersensitivity syndrome	D	Screening: TMPT, CBC, CMP, UA, pregnancy test, tuberculin test Month 1: CBC with diff, CMP Month 2: CBC with diff, CMP Q3 months: CBC with diff, CMP	• Dosing may be guided by TMPT enzyme activity • AZA is recommended for the treatment of refractory AD

(continued)

Table 7.6 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Monitoring	Comments
Methotrexate	Antifolate metabolite that blocks the synthesis of DNA, RNA and purines and negatively affects T cell function	7.5–25 mg/week	Pancytopenia (risk increases with renal disease), idiosyncratic pulmonary fibrosis, hepatotoxicity, teratogen	X (males and females must wait 3 months after discontinuation prior to attempting to conceive)	Screening: CBC, CMP, tuberculin test, hepatitis panel, pregnancy test Week 2: CBC Week 4: CBC, CMP Month 2: CBC, CMP Q3 months: CBC, CMP Liver biopsy may be considered at 3.5–4.0 g of cumulative MTX in adults	• Liver enzymes transiently increase after MTX dosing; optimal to obtain lab results 5–7 days after last dose • MTX is recommended for the treatment of refractory AD • Patients should take between 1–5 mg/day of folate while on methotrexate.

Mycophenolate mofetil (MMF)	Immunosuppressant that blocks the purine biosynthesis pathway of cells via inhibition of inosine monophosphate dehydrogenase	1.0–1.5 g BID Pediatric: 30–50 mg/kg/day	GI upset (dose dependent), bone marrow suppression, No renal or hepatic toxicity	D	Screening: CBC, CMP, Hepatitis B, Hepatitis C, tuberculin test, pregnancy test Month 1: CMP, CBC with diff Month 2: CMP, CBC with diff Q3 months: CMP, CBC with diff	Aggregate data on MMF for AD is highly variable and efficacy is inconsistent.

(continued)

Table 7.6 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Monitoring	Comments
Systemic steroids	Immunosuppressant	0.5–1.0 mg/kg/day followed by a taper	Hypertension, glucose intolerance, gastritis, weight gain, decreased bone density, adrenal suppression	C	Long term use may require blood pressure monitoring, Vitamin D and calcium supplementation, ophthalmologic examination, HPA axis suppression testing, infection precautions, bone density evaluation (adults) and growth-velocity measurement (children)	Systemic steroids should be avoided if possible for the treatment of AD. Their use should be exclusively reserved for acute, severe exacerbations and as short-term bridge to other systemic, steroid-sparing therapy

Dupilumab (Dupixent®)[a]	Monoclonal antibody against IL-4 and IL-13	Initial dose of two injections (600 mg) followed by one injection (300 mg) every other wk	Injection site reactions, hypersensitivity, conjunctivitis and keratitis, blepharitis, HSV	Not assigned (not recommended for use during pregnancy)	None	Can cause transient eosinophilia

Information adapted from Eichenfield et al. [4], Eichenfield et al. [5], Sidbury et al. [6], Sidbury et al. [7]
[a]Denotes information not found in guidelines but added for completeness

Table 7.7 Guideline recommendations for topical treatment of psoriasis

	Mechanism	Dosing	Side effects	Pregnancy category	Comments
Topical steroids	Anti-inflammatory, anti-proliferative, immunosuppressive, vasoconstrictive	1–2× daily	Skin atrophy, telangiectasia, striae, contact dermatitis	C	Mainstay of topical therapies for psoriasis
Calcipotriene	Vitamin D analogue which inhibits keratinocyte proliferation and the enhancement of keratinocyte differentiation	Twice daily	Irritation, reversible elevation of serum calcium (>100 g/week)	C	Use in combination with topical steroids; gives added benefit About equal in efficacy to mid-potency steroid Inactivated by UVA but no contraindications to combining with UVB

Tazarotene	Vitamin A analog that normalized abnormal keratinocyte differentiation and diminishes expression of inflammatory markers	Once daily	Irritation, photosensitizing	X	Best used in combination with topical steroids
Calcineurin inhibitors (tacrolimus and pimecrolimus)	Block synthesis of inflammatory cytokines	Twice daily	Burning, pruritus (more significant with tacrolimus)	C	Best for intertriginous and facial psoriasis Avoid use in patients also receiving phototherapy

(continued)

Table 7.7 (continued)

	Mechanism	Dosing	Side effects	Pregnancy category	Comments
Salicylic acid	Keratolytic agent	Once daily	Systemic absorption	C	Use in combination with topical steroids; or calcineurin inhibitors Avoid use in patients also receiving phototherapy
Coal tar	Not well understood	Differs pending on formulation	Staining of clothes, tar odor, irritant contact dermatitis, folliculitis, photosensitivity	Contraindicated due to lack of available data	Many formulations exist and standardization of these products is not always ideal

Information adapted from Menter et al. [12]

Table 7.8 Guideline recommendations for systemic treatment of psoriasis.

	Mechanism	Dosing	Lab screening/ monitoring	Pregnancy category	Main side effects	Comments
Methotrexate	Inhibits dihydrofolate reductase	Available in oral pill or injectable form Test dose of 2.5 or 5 mg followed by weekly PO dosage of 7.5–25 mg 0.1 mL of a 25 mg/mL multidose vial is equivalent to 2.5 mg oral tablet	Screening: CBC with diff, CMP, tuberculin test, hepatitis panel, pregnancy test, ± HIV Week 2: CBC Week 4: CBC, CMP Q3 months: CBC, CMP, consider liver biopsy 3.5–4.0 g cumulative dose	X (males and females must wait 3 months after discontinuation prior to attempting to conceive)	Nausea, stomatitis, fatigue, myelosuppression, hepatotoxicity, pulmonary fibrosis	After increase in dose, it may take up to 4 weeks for a clinical response to occur Patients should take between 1–5 mg/day folate while on methotrexate Use of Bactrim is contraindicated Limit alcohol intake and NSAID usage.

(continued)

Table 7.8 (continued)

	Mechanism	Dosing	Lab screening/ monitoring	Pregnancy category	Main side effects	Comments
Cyclosporine	Inhibits T-cell activation	Dosing based on ideal body weight: can start with 2.5–3 mg/kg/day in two divided doses. After 4 weeks can increase by 0.5 mg/kg/day until disease control achieved (do not exceed 5 mg/kg/day)	Screening: CBC with diff, CMP, hepatitis panel, fasting lipid panel, Mg, uric acid, tuberculin test, UA, blood pressure, preg test Month 1: CBC, CMP, lipid panel, UA, blood pressure, Mg Month 2: repeat month 1 Q3 month: CBC, CMP, lipid panel, Mg, uric acid, UA, BP	C	Renal impairment, hypertension, malignancies, hypertrichosis, gingival hyperplasia, GI upset, hyperTG, hypomagnesemia, hyperkalemia, hyperbilirubinemia	Maximum use: 1 year Useful in crisis management and as a bridge to other therapies for severe disease

Acitretin	Modulate epidermal proliferation and differentiation and has anti-inflammatory activity	10–50 mg daily	Screening: CBC, CMP, lipid panel pregnancy test Month 1: CBC, CMP Q3 month: CBC, CMP, lipid panel, pregnancy test if applicable	X	Chelitis, alopecia, xerosis, joint pain, hypertriglyceridemia, abnormal LFTs, headache	Enhanced clinical response when used in combination with phototherapy Woman should not attempt to conceive until 3 years after discontinuation of acitretin; therefore do not give to women of childbearing age

(continued)

Table 7.8 (continued)

	Mechanism	Dosing	Lab screening/ monitoring	Pregnancy category	Main side effects	Comments
Adalimumab (Humira ®)	Fully human anti-TNF-alpha monoclonal antibody	SQ: 80 mg day 1, 40 mg day 8, then 40 mg q2weeks	Screening: CBC with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC, CMP Q1year: tuberculin test	B	Injection site reactions, rare reports of serious infections and malignancies, MS, exacerbation of and new onset of CHF, cytopenia, rare reports of drug induced lupus	Formation of antibodies against adalimumab is reported to occur in 6–50% of patients and may reduce response to therapy

Etanercept (Enbrel®)	Recombinant human TNF alpha receptor protein fused with the Fc portion of IgG1	SQ: 50 mg twice weekly for 12 weeks followed by 50 mg weekly	Screening: CBC with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC with diff, CMP Q1year: tuberculin test	B	Injection site reactions, rare reports of serious infections and malignancies, MS, exacerbation of and new onset of CHF, cytopenias, rare reports of drug induced lupus	Approved for patients age four years or older

(continued)

Table 7.8 (continued)

	Mechanism	Dosing	Lab screening/ monitoring	Pregnancy category	Main side effects	Comments
Infliximab (Remicade®)	Chimeric antibody constructed from murine and human DNA sequences comprising a mouse variable region and human IgG1-alpha constant region	IV: 5 mg/kg dose infusion over 2–3 h at week 0, 2, and 6 and then every 6–8 weeks; dose and interval may be adjusted as needed	Screening: CBC with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC with diff, CMP Q1year: tuberculin test	B	Infusion reactions and serum sickness, rare cases of serious infections and malignancies, drug induced lupus, cytopenia, MS and exacerbation of and new onset CHF	Onset of action is faster than other biologics

Ustekinumab (Stelara®)[a]	Human monoclonal antibody that targets IL-12 and IL-23	Adults ≤100 kg: 45 mg given at weeks 0,4 and every 12 weeks thereafter Adults ≥100 kg: 90 mg dose with same schedule as above	Screening: CBC, with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC with diff, CMP Q1year: tuberculin test	B	Headache, upper respiratory infections (most common) hypersensitivity reactions, malignancy, re-activation of TB, neurotoxicity (reversible posterior leukoencephalopathy)	No dose-related/cumulative toxicity was observed with increasing duration of ustekinumab exposure for up to 5 years Rates of adverse effects are generally comparable with those reported for other biologics approved for the treatment of psoriasis

(continued)

Table 7.8 (continued)

	Mechanism	Dosing	Lab screening/ monitoring	Pregnancy category	Main side effects	Comments
Secukinumab (Cosentyx®)[a]	Anti-IL-17A monoclonal antibody	300 mg given subq once weekly at weeks 0, 1, 2, 3 and 4 and followed by 300 mg every four weeks Doses of 150 mg are sufficient for some patients Auto-injectors and pre-filled syringes come in 150 mg/mL and 300 mg/mL sizes	Screening: CBC with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC with diff, CMP Q1year: tuberculin test	B	Infection, hypersensitivity, GI upset, exacerbations and new onset of IBD	Secukinumab has demonstrated greater efficacy for moderate to severe plaque psoriasis than ustekinumab with a similar degree of safety

Ixekizumab (Taltz®)[a]	Anti-IL-17A monoclonal antibody	160 mg at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12 then 80 mg every 4 weeks	Screening: CBC with diff, CMP, hepatitis panel, tuberculin test Monitoring: Q6 months: CBC with diff, CMP Q1year: tuberculin test	C	Neutropenia, upper respiratory infection (most common), injection site reaction	Similar side effect profile to TNF-alpha inhibitors but no increased risk of lymphoma, heart failure, or neuromuscular disorders Studies have shown IL-17 inhibitor class to be more effective than etanercept and ustekinumab

Information adapted from: Menter et al. [8], Gottlieb et al. [9], Sidbury et al. [6], Menter et al. [10], Menter et al. [11]
[a]Denotes information not found in guidelines but added for completeness

Table 7.9 Guideline recommendations for the management of basal cell carcinoma

1. **Suspect basal cell carcinoma**
2. **Perform a biopsy.** There is no single optimal biopsy technique. Recommended biopsy techniques for BCC are punch, shave and excision biopsy. The biopsy technique will depend on the characteristics of the suspected malignancy (morphology, location etc.), patient specific factors and the judgement of the patient and physician.
3. **Send biopsy to pathology.** Important information to provide to the pathologist includes patient age, sex, anatomic location, if lesion is recurrent, size of lesion, if patient is immunosuppressed and other medical history (ie history of burn or organ transplant)
4. **Receive pathology report.** If BCC is detected, pathology report should include histologic subtype, if lesion invades beyond reticular dermis and if there is perineural involvement.
5. **Determine if BCC is high risk or low risk (see chart below)**

Parameters	**Low risk**	**High risk**
Location/size	Area L[a] < 20 mm or Area M[a] < 10 mm	Area L[a] ≥ 20 mm Area M[a] ≥ 10 mm Area H[a]
Borders	Well defined	Poorly defined
Primary vs recurrent	Primary	Recurrent
Site of prior radiation therapy	No	Yes
Growth pattern (pathologic)	Nodular, superficial	Aggressive[b]
Perineural involvement	No	yes

6. **Determine appropriate treatment option based on risk stratification, patient preference and physician judgement.**
   (a) **Low risk BCC treatment options**

Table 7.9 (continued)

(i) Surgical excision with 4 mm clinical margins and histologic margin assessment

- Recurrence rate of 2–4% after 3–5 years

(ii) Currettage and electrodessication (C&E)

- May be considered for low risk-tumors in non-terminal hair-bearing locations

(iii) Cryosurgery may be considered when more effective therapies are contraindicated or impractical

- Recurrence rate of 6.3% at 1 year to 39% at 2 years

(iv) If surgery is not feasible, topical therapy (imiquimod or 5-FU), ALA/MAL-PDT and radiation therapy can be considered with the understanding that cure rates may be lower

- RCT have shown that imiquimod is superior and topical 5-FU is comparable to MAL-PDT for superficial BCCs. The likelihoods of tumor-free status at 3 years were 80%, 68% and 58% for imiquimod, 5-FU and MAL-PDT respectively
- Imiquimoid: many dosing approaches have been used but once-a-day treatment 5 times a week for 6 weeks or longer is a common regimen.
- 5-FU: many dosing approaching have been used but twice daily application for 3–6 weeks is a common regimen

(b) **High risk BCC treatment options**

(i) Mohs micrographic surgery

- Recurrence rate of 1% at 5 years for primary BCCs

(ii) Standard excision with 4mm margins or 6mm maargins may be considered for select high-risk tumors

(continued)

Table 7.9 (continued)

(c) **Locally advanced or metastatic BCC**

(i) Multidisciplinary consultation and smoothened inhibitors; if treatment of metastatic BCC with smoothened inhibitors is not feasible, platinum-based chemotherapy or best supportive care is recommended.

7. **Follow-up after treatment for BCC:** full body skin exam every 6–12 months for life, along with counseling regarding the need for sun protection.

(a) The use of topical retinoids, oral retinoids and beta-carotene is not recommended to reduce the incidence of future keratinocyte cancers in those with a history of BCC

(b) There is insufficient evidence to make a recommendation on the use of oral nicotinamide in the chemoprevention of BCC

Information adapted from: Kim et al. [13]

[a]Area L consists of trunk and extremities; area M consists of cheeks, forehead, scalp, neck and pretibial; area H consists of central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, preauricular and postauricular skin/sulci, temples, ear, genitalia, hands and feet

[b]Aggressive growth pattern includes morpheaform, basosquamous, sclerosing, mixed infiltrative, micronodular

Table 7.10 Guideline recommendations for the management of squamous cell carcinoma

1. **Suspect squamous cell carcinoma**

2. **Perform a biopsy.** There is no single optimal biopsy technique. Recommended biopsy techniques for SCC are punch, shave and excision biopsy. The biopsy technique will depend on the characteristics of the suspected malignancy (morphology, location etc.), patient specific factors and the judgement of the patient and physician.

3. **Send biopsy to pathology.** Important information to provide to the pathologist includes patient age, sex, anatomic location, if lesion is recurrent, size of lesion, if patient is immunosuppressed and other medical history (ie history of burn or organ transplant)

4. **Receive pathology report.** If SCC is detected, pathology report may include the degree of differentiation and when possible and appropriate, any features that would classify the lesion as high risk.

5. **Determine if SCC is high risk or low risk (see chart below)**

Parameters	**Low risk**	**High risk**
Location/size	Area L[a] <20mm or Area M[a] <10mm	Area L[a] ≥20mm Area M[a] ≥10mm Area H[a]
Borders	Well defined	Poorly defined
Primary vs recurrent	Primary	Recurrent
Immunosuppression	No	Yes
Site of prior radiation therapy or chronic inflammatory process	No	Yes
Rapidly growing tumor	No	Yes
Neurologic symptoms	No	Yes

(continued)

Table 7.10 (continued)

Degree of differentiation (pathologic)	Well to moderately differentiated	Poorly differentiated
High-risk histology subtype (pathologic)[b]	No	Yes
Depth (thickness or Clark level)	<2.0mm, or I, II, III	≥2.0mm or IV, V
Perineural, lymphatic, or vascular involvement	No	Yes

6. **Determine appropriate treatment option based on risk stratification, patient preference and physician judgement.**

   (a) **Low risk SCC treatment options**

      (i) Surgical excision with 4–6mm clinical margins and histologic margin assessment

      (ii) Currettage and electrodessication (C&E)

         May be considered for low risk-tumors in non-terminal hair-bearing locations

      (iii) If surgical therapy is not feasible or preferred, radiation therapy can be considered with the understanding that the cure rate may be lower

      (iv) Cryosurgery can be considered when more effective therapies are contraindicated or impractical

      (v) Topical therapies (imiquimod or 5-FU) and PDT are NOT recommended for the treatment of SCC on the basis of available data. (Can consider topical therapies for SCCIS[a])

   (b) **High risk SCC treatment options**

      (i) Mohs micrographic surgery

      (ii) Standard excision may be considered for select high-risk tumors

Table 7.10 (continued)

(c) **Locally advanced or metastatic SCC**

(i) Multidisciplinary consultation and management

(ii) Surgical resection, with or without adjuvant radiation therapy and possible systemic therapy are recommended for regional lymph node metastases

7. **Follow-up after treatment for SCC:** full body skin exam every 6–12 months for life, along with counseling regarding the need for sun protection.

(a) The use of topical retinoids, oral retinoids and beta-carotene is not recommended to reduce the incidence of future keratinocyte cancers in those with a history of BCC

(b) There is insufficient evidence to make a recommendation on the use of oral nicotinamide in the chemoprevention of BCC

Information adapted from: Kim et al. [14]

[a]Area L consists of trunk and extremities; area M consists of cheeks, forehead, scalp, neck and pretibial; area H consists of central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, preauricular and postauricular skin/sulci, temples, ear, genitalia, hands and feet

[b]Adenoid (acantholytic), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes

Table 7.11 Guideline recommendations for the treatment of cutaneous melanoma

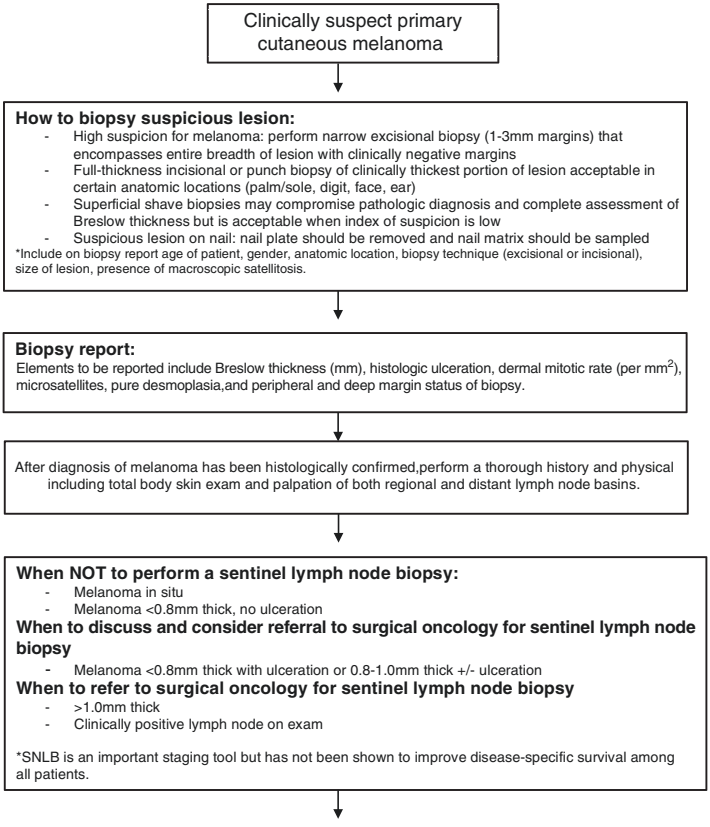
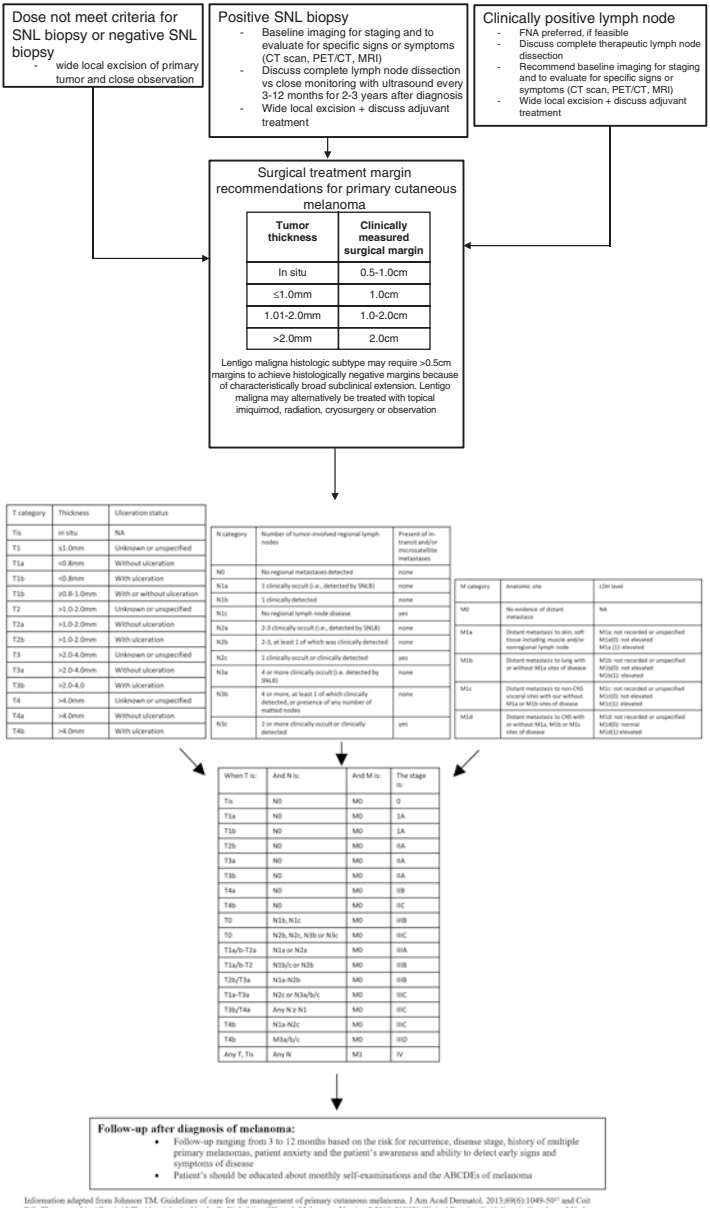


TABLE 7.11 (continued)



Information adapted from Johnson TM. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2013;69(6):1049-50[2] and Coit DG, Thompson JA, Albertini MR, Algazi A, Andtbacka R, Bichakjian CK et al. Melanoma, Version 2.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2018[3]

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Chapter 8
Commonly Used Drugs and Medication Guidelines

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Corticosteroids

A. **Topical Steroids** [1, 2] (Tables 8.1 and 8.2)

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Table 8.1 Indications for topical steroids [3]

Category	Conditions
Dermatitis	Atopic dermatitis Lichen simplex chronicus Seborrheic dermatitis Contact dermatitis Prurigo nodularis
Papulosquamous	Psoriasis Lichen planus
Vesiculobullous	Bullous pemphigoid Pemphigus foliaceous Cicatricial pemphigoid
Pigmentary	Vitiligo
Autoimmune	Cutaneous lupus Dermatomyositis Morphea
Others	Early stage CTCL

Table 8.2 Classes and formulations of topical steroids

Generic name	Trade name	Formulation(s)	Available sizes
Class I (Super High Potency)			
Betamethasone Dipropionate	Diprolene	0.05% gel and ointment	15, 50 g
Clobetasol propionate	Clobex	0.05% lotion	1, 2 oz
Clobetasol propionate	Olux	0.05% foam	50, 100 g
Clobetasol propionate	Temovate	0.05% cream, ointment, gel	15, 30, 45, 60 g
Clobetasol propionate	Temovate E	0.05% cream	15, 30, 60 g
Diflorasone diacetate	Psorcon	0.05% ointment	60 g

Table 8.2 (continued)

Generic name	Trade name	Formulation(s)	Available sizes
Halobetasol propionate	Ultravate	0.05% cream and ointment	15, 50 g
Class II (High)			
Amcinonide	Cyclocort	0.1% ointment	15, 30, 60 g
Betamethasone Dipropionate	Diprolene AF	0.05% cream	15, 50 g
Mometasone furoate	Elocon	0.1% ointment	15, 45 g
Fluocinonide	Lidex	0.05% cream, gel, ointment	15, 30, 60 g
Clobetasol propionate	Temovate	0.05% solution	50 ml
Desoximetasone	Topicort	0.25% cream and ointment, 0.05% gel	15, 60 g
Class III (Medium-High)			
Fluticasone propionate	Cutivate	0.005% ointment	15, 30, 60 g
Amcinonide	Cyclocort	0.1% cream and lotion	15, 30, 60 g; 20, 60 ml
Fluocinonide	Lidex-E	0.05% cream	15, 30, 60 g
Triamcinolone acetonide	Kenalog	0.5% cream, ointment	15 g
Class IV			
Clocortolone Pivalate	Cloderm	0.1% cream	45 g
Mometasone furoate	Elocon	0.1% cream	15, 45 g
Fluocinolone acetonide	Synalar	0.025% ointment	15, 60 g

(continued)

Table 8.2 (continued)

Generic name	Trade name	Formulation(s)	Available sizes
Triamcinolone acetonide	Kenalog	0.1% ointment	15, 30, 80, 454 g
Desoximetasone	Topicort LP	0.05% cream	15, 60 g
Hydrocortisone valerate	Westcort	0.2% ointment	15, 45, 60 g
Class V			
Fluticasone propionate	Cutivate	0.05% cream	15, 30, 60 g
Prednicarbate	Dermatop	0.1% cream	15, 60 g
Hydrocortisone butyrate	Locoid	0.1% cream	15, 45 g
Triamcinolone acetonide	Kenalog	0.1% cream	15, 30, 80, 454 g
Betamethasone valerate	Luxiq	0.12% foam	50, 100 g
Hydrocortisone valerate	Westcort	0.2% cream	15, 45, 60 g
Class VI			
Aclometasone dipropionate	Aclovate	0.05% cream	15, 45, 60 g
Fluocinolone acetonide	Synalar	0.025% cream 0.01% solution	15, 60 g 20, 60 ml
Class VII			
Hydrocortisone	Hytone	2.5% cream, lotion, ointment 1% cream, lotion, ointment	20, 30, 120 g 20, 30, 120 g

Most Common Adverse Effects of Topical Steroids (Table 8.3)
- Atrophic changes (easy bruising, purpura, striae, telangiectasias)
- Infection (e.g. tinea incognito)
- Contact dermatitis
- Acneiform eruption
- Delayed wound healing
- Perirorificial dermatitis
- Systemic effects rare

Topical Steroids in Pregnancy (pregnancy category c)
- Appear to be safe in pregnancy, though some studies suggest increased risk of fetal growth restriction with potent/super potent topical corticosteroids
- Mild- to moderate-potency topical corticosteroids preferred over higher potency
- Avoid high- and super-potency topical corticosteroids if possible

B. **Oral Corticosteroids**

Clinical Indications
- Eczema/dermatitis
- Vesiculobullous disorders
- Cutaneous lupus
- Sarcoidosis
- Vasculitis

General Guidelines for Steroid Treatment
- Generally, higher dose prescribed initially (0.5–1 .5 mg/kg) with decrease after 2–4 weeks
- Risk of adverse effects increases with longer length of use and higher dosage
- Best if taken as single dose in AM to reduce suppression of HPA axis
- Short-term steroid treatment
  - Generally safe for acute dermatitis
  - No need for tapering if used for <1–2 weeks

Table 8.3 Adverse effects of long-term use of oral corticosteroids

Cutaneous	Infections (bacterial, fungal, viral) Atrophic changes (striae, purpura, skin fragility) Acne Hypertrichosis
Ocular	Glaucoma Posterior subcapsular cataracts
Cardiovascular	Hypertension Hyperlipidemia
Gastrointestinal	Peptic ulcer disease Fatty liver
Reproductive	Hirsutism Irregular menstruation
Musculoskeletal	Bone fracture Osteoporosis Avascular necrosis of the femur Myopathy
Neuropsychological	Mood changes Psychosis Insomnia
Metabolic	Hyperglycemia Cushing syndrome

- Long-term steroid treatment (See Table 8.3 for Adverse Effects of Oral Steroids)
  - Monitor blood pressure, weight and blood sugar
  - Consider bone density scan to evaluate for osteoporosis and/or bisphosphonate therapy
  - Taper slowly to avoid risk of acute adrenal insufficiency
  - Consider stress dose steroids if illness, trauma or surgical procedure

Oral Steroids in Pregnancy/Lactation (pregnancy category c)
- Not preferred for initial therapy
- Avoid in first trimester
- Use at lowest effective dose in second and third trimester

- Present in breastmilk
- Generally acceptable in usual doses, however monitoring of infant should be performed

Antibiotics

1. **Topical Antibiotics (**Table 8.4**)**

Clinical Indications
- Acne vulgaris
- Treatment/prophylaxis of wound infections
- Impetigo
- MRSA nasal carriers

Table 8.4 Commonly used topical antibiotics

Medication	Indication	Comments	Pregnancy category
Clindamycin	Mild to moderate Acne Vulgaris	Bacteriostatic against P. acnes Use with Benzoyl Peroxide for reduced resistance	B
Erythromycin	Acne Vulgaris	Bacteriostatic against P. acnes Effectiveness decreases over time	B
Bacitracin ointment	Wound infections	Bacteriostatic against gram-positive and gram-negative organisms Increasing contact allergy	B

(continued)

Table 8.4 (continued)

Medication	Indication	Comments	Pregnancy category
Mupirocin 2% cream/ ointment	Wound infections Impetigo MRSA nasal carriage	Bactericidal MRSA-resistance increasing Not for use in children <2 months	B
Gentamicin 0.1% cream/ ointment	Minor skin infections (folliculitis, furunculosis, impetigo)	Bactericidal activity against gram-positive and gram-negative organisms	D

2. **Oral Antibiotics**

Clinical Indications

- Acne Vulgaris (Table 8.5) [4, 5–7]
  - Moderate-severe inflammatory acne, resistant to topical treatments
  - Limit use to 3 months and re-evaluate
  - Avoid monotherapy – use with topical products including benzoyl peroxide and retinoid during and after antibiotic therapy
- Skin and Soft Tissue Infections [8] (Table 8.6)
  - Includes impetigo, ecthyma, erysipelas and mild cellulitis
  - Recommend culture and gram stain if possible
  - If no culture performed, treat with Dicloxacillin 500 mg QID PO for presumed MSSA unless MRSA suspected

Table 8.5 Commonly used antibiotics for acne vulgaris

Antibiotic	Dosing (adult)	Contraindications	Adverse effects	Comments
Doxycycline (hyclate and monohydrate)	50–100 mg daily to BID Also available in extended release tablets (brand name Doryx ®)	Children <8 Pregnancy (2nd/3rd trimester) Breastfeeding	GI upset, photosensitivity, esophagitis, ulceration	First line treatment, less photo-sensitizing than Minocycline Limit use to 3–4 months
Minocycline	50–100 mg daily or BID Also available in extended release tablets (brand names Solodyn ® and Ximino ®); dosing based on weight, 45–135 mg daily	Children <8 Pregnancy (2nd/3rd trimester) Breastfeeding	Vestibular symptoms (i.e. dizziness, tinnitus, vertigo), tissue hyperpigmentation, less commonly photo-sensitivity	First line treatment; rarely may cause autoimmune phenomena, DRESS, hepatotoxicity Limit use to 3–4 months

(continued)

Table 8.5 (continued)

Antibiotic	Dosing (adult)	Contraindications	Adverse effects	Comments
Erythromycin	250–500 mg daily or BID	Caution in patients with hepatic disease, altered cardiac conduction, myasthenia gravis	GI upset	Increasing bacterial resistance, use for short-term only
Azithromycin	Multiple pulse-dosing regimens (e.g. 500 mg daily × 4 days per month × 3 months)	Caution in patients with hepatic disease, altered cardiac conduction, myasthenia gravis	GI upset	
Trimethoprim	100 mg TID or 300 mg daily	Caution in patients with hepatic or renal disease	Drug eruptions, hematologic abnormalities, GI upset	May also use in combination with Sulfamethoxazole

Table 8.6 Commonly used topical/oral antibiotics for skin and soft tissue infection (SSTI)

Infection/organism	Treatment (generally seven-day course)
Limited impetigo	Retapamulin or Mupirocin topical ointment BID
Streptococci Alone	Penicillin VK 250–500 mg q6H PO Cephalexin 500 mg q6H PO
Methicillin-Sensitive Staph Aureus	Dicloxacillin 500 mg QID PO Clindamycin 300–450 mg QID PO
Methicillin-Resistant Staph Aureus	Linezolid 600 mg BID PO Clindamycin 300–450 mg QID PO Doxycycline/Minocycline 100 mg BID PO Trimethoprim-Sulfamethoxazole 1–2 DS tablets BID PO

Antivirals [9] (Table 8.7)

Table 8.7 Commonly used antiviral medications

Drug	Indication/dose	Monitoring	Adverse reactions	Comments
Acyclovir	**Primary/recurrent HSV-1 or HSV-2:** 200 mg 5× daily for 10 days **HSV PPx:** 200–400 mg daily for up to 12 months **Primary VZV infections:** 800 mg 4× daily for 5 days **Shingles:** 800 mg 5× daily for 7–10 days	In select patients, can check creatinine at baseline for dosing purposes	GI, reversible nephropathy, weakness, headache, tremors, seizures	Pregnancy category B Minimal risk when used while breastfeeding Recommend starting within the first 72 h

Valacyclovir	**Oral HSV:** 2 g BID × 1 day **Genital HSV:** 1 g BID × 10 days **Recurrent HSV:** 500 mg BID × 3 days **HSV PPx:** 500–1000 mg daily **VZV:** 20 mg/kg TID × 5 days **Shingles:** 1 g TID × 7 days	In select patients, monitor creatinine	GI, headache, fatigue, depression, dizziness, LFT elevation, nasopharyngitis	Pregnancy Category B Minimal risk when used while breastfeeding Caution with prolonged courses in elderly or patients with renal disease Recommend starting within the first 72 h
Famciclovir (Prodrug of penciclovir)	**Oral HSV:** 1500 mg × 1 dose **Genital HSV:** 1000 mg BID × 1 day **Shingles:** 500 mg TID × 7 days **Prevent recurrent genital HSV:** 250 mg BID for up to 1 year	Creatinine at baseline and on therapy as clinically indicated. CBC if given long-term	Headache, nausea, diarrhea Rare: Leukocytoclastic vasculitis	Pregnancy category B No adequate studies in breastfeeding women

(continued)

TABLE 8.7 (continued)

Drug	Indication/dose	Monitoring	Adverse reactions	Comments
Foscarnet	**Acyclovir resistant HSV:** 40 mg/kg TID or 60 mg/kg BID for 14–21 days	Baseline: electrolytes, 24-h creatinine clearance, ECG CBC and electrolytes once a week	Renal impairment, seizures, headache, hypokalemia, hypocalcemia, GI, anemia, granulocytopenia, fever	Pregnancy Category C No adequate studies in breastfeeding women
Cidofovir	**Acyclovir-Resistant HSV:** 1% gel topically daily × 5 days; 5 mg/kg IV daily × 3 weeks, then q2 weeks × 3 doses	Creatinine and urine protein levels at baseline and after each dose CBC with differential before every dose	GI, renal dysfunction, Rare: Fanconi-type syndrome	Pregnancy category C No adequate studies in breastfeeding women

Antifungals (Tables 8.8 and 8.9)

Table 8.8 Commonly used oral anti-fungal medications

Name	Indications/dosing (adults)	Adverse effects	Contra-indications	Comments
Griseofulvin	**Tinea capitis:** 500–1000 mg daily (microsize) for 4–6 weeks **Tinea corporis:** 500–1000 mg daily (microsize) for 2–4 weeks **Tinea pedis:** 500–1000 mg daily (microsize) for 4–8 weeks	GI, excessive thirst, hypersensitivity, headache Rare: photosensitivity, drug-induced SLE, TEN, serum sickness-like reaction, hepatotoxicity	Pregnancy category X Porphyria Liver failure	Prolonged Use: Check BUN/Cr, LFTs, CBC Poor efficacy for onychomycosis, candida, tinea versicolor or deep mycoses Better efficacy for M. Canis

(continued)

Table 8.8 (continued)

Name	Indications/dosing (adults)	Adverse effects	Contra-indications	Comments
Terbinafine	**Onychomycosis:** 250 mg daily × 6–12 weeks **Tinea capitis** (>35 kg): 250 mg daily × 6 weeks **Systemic mycoses:** 500 mg BID, treat for 2–4 weeks after resolution	GI, taste disturbance, headache, rash, pruritus, elevated LFTs Rare: SCLE/SLE, hepatotoxicity, EM, SJS/TEN, AGEP, alopecia, cytopenias	Pregnancy category B Caution in liver disease, renal impairment, SLE	Check baseline CMP/CBC, recheck after 6–8 weeks Severe liver disease can develop within 4–6 weeks, discontinue drug immediately Better efficacy for T. Tonsurans
Itraconazole	**Onychomycosis (toenail):** 200 mg daily for 12 weeks or 200 mg BID for 1week/month × 12 weeks **Tinea versicolor:** 200 mg daily × 5–7 days	GI, rash, headache, elevated LFTs, cystitis Rare: anaphylaxis, SJS, peripheral neuropathy, QT prolongation, liver disease, neutropenia, CHF	Pregnancy category C CHF, ventricular dysfunction Caution in renal disease, liver disease	Check baseline LFTs, repeat after 1 month Azoles may increase serum levels/toxicity of drugs that are CYP3A4 substrates

Fluconazole	**Cutaneous candidiasis:** 50 mg daily or 150 mg weekly for 2–4 weeks **Tinea versicolor:** 150–300 mg/week for 2 weeks **Candidal onychomycosis:** 50 mg daily/300 mg weekly for 6 weeks (finger nails) or 3 months (toe nails)	GI, headache, rash Rare: SJS/TEN, parasthesias, QT prolongation, cytopenias, agranulocytosis, elevated cholesterol	Pregnancy category D Severe liver disease Caution in renal disease, liver disease, dysrhythmias	Check periodic LFTs, Cr, K+ if long-term use Caution with CYP3A4 inhibitors/inducers (e.g. warfarin)
Ketoconazole	**Systemic fungal infections (second line):** 200–400 mg daily until clear	GI, pruritus Rare: severe hepatotoxicity	Pregnancy category C Severe hepatoxicity	LFTs at baseline and weekly, discontinue if elevated Caution with CYP3A4 inhibitors/inducers (e.g. warfarin) Use only when other effective antifungal therapy is not available or tolerated due to possibility of serious adverse events

(continued)

Table 8.8 (continued)

Name	Indications/dosing (adults)	Adverse effects	Contra-indications	Comments
Voriconazole	**Cutaneous candidiasis:** <40 kg 100 mg BID, >40 kg 200 mg BID	Skin photosensitivity, vision disturbances, hallucination, hepatotoxicity	Teratogenic and embryotoxic Caution in arrhythmias, liver disease	Baseline CMP, weekly × 4 weeks and then monthly Severe photosensitivity associated with increased risk of cutaneous malignancy
Nystatin (suspension)	**Oral candidiasis:** 400,000–600,000u QID (swish and swallow)	GI	Pregnancy category C	

Table 8.9 Commonly used topical antifungal medications

Generic name	Trade name(s)	Formulation(s)	Available sizes
Imidazoles			
Clotrimazole	Clotrimazole	1% cream, solution	Cream: 15 g, 30 g, 45 g Solution: 10 ml, 30 ml
	Lotrimin AF	1% cream, lotion, solution	Cream: 12 g, 24 g Lotion: 10 ml
Econazole	Econazole	1% cream	15 g, 30 g, 85 g
Ketoconazole	Ketoconazole	2% cream, shampoo	Cream: 15 g, 30 g, 60 g Shampoo: 120 ml
	Extina	2% foam	100 g
	Nizoral	2% shampoo	120 ml
	Xolegel	2% gel	45 g
Oxiconazole	Oxistat	1% cream, lotion	Cream: 15 g, 30 g, 60 g Lotion: 30 ml
Sertaconazole	Ertaczo	2% cream	30 g
Sulconazole	Exelderm	1% cream, solution	Cream: 15 g, 30 g, 60 g Solution: 30 ml

(continued)

Table 8.9 (continued)

Generic name	Trade name(s)	Formulation(s)	Available sizes
Allylamine			
Naftifine	Naftin	1% cream, gel	Cream: 30 g, 60 g, 90 g Gel: 40 g, 60 g, 90 g
Benzylamine			
Butenafine	Mentax	1% cream	15 g, 30 g
Polyenes			
Nystatin	Nystatin	100,000 units/g cream, ointment, powder	Cream: 15 g Powder: 15 g Ointment: 15 g
	Mycostatin	100,000 units/g cream, ointment, powder	Cream: 15 g Powder: 15 g Ointment: 15 g
	Nyamyc	100,000 units/g powder	15 g, 30 g, 60 g
	Pedi-Dri	100,000 units/g powder	56.7 g
Others			
Ciclopirox	Ciclopirox	0.77% cream, gel, suspension; 8% solution	Cream: 15 g, 30 g, 90 g Suspension: 30 ml, 60 ml
	Loprox	0.77% cream, gel, suspension; 1% shampoo	Cream: 30 g, 90 g Gel: 30 g, 45 g, 100 g Shampoo: 120 ml
	Penlac nail Laquer	8% solution	6.6 ml

Antihistamines [10] (Table 8.10)

TABLE 8.10 Commonly used anti-histamines

Drug	Indication	Typical dose	Adverse reactions	Comments
First Generation H1 Blockers				
Diphenhydramine *(Benadryl)*	Allergic rhinitis or conjunctivitis Anaphylaxis Urticaria Chronic idiopathic urticaria	Oral form: 25–50 mg q 4–8 h Injection form: 10–50 mg	*CNS* Sedation Dizziness Tinnitus Blurry vision Impaired concentration Headache *GI* Nausea, vomiting, diarrhea *Anticholinergic effects* Dry mucous membranes Constipation Urinary retention Postural hypotension Tachycardia, palpitations	Pregnancy category B Not recommended for insomnia in adults
Dimenhydrinate *(Dramamine)*	Atopic dermatitis or contact dermatitis	Oral: 50–100 mg q 4–6 h Injection form: 50 mg q 4 h		Pregnancy category B
Chlorpheniramine *(Chlor-Trimeton)*	Pruritus secondary to another condition Angioedema	Short-acting oral form: 4 mg q 4–6 h Long-acting oral form: 12 mg twice daily		Pregnancy Category B
Hydroxyzine *(Atarax)*	Insomnia [11] Motion sickness and nausea [a]Caution in patients 65 yrs. and older [15]	Pruritus: 25 mg 3–4× daily Nausea: 25–100 mg/dose Anxiety: 50–100 mg 4× daily Renal dosing: CrCl >50 mL/min: no adjustment CrCl ≤50 mL/min: 50% dosage reduction recommended		Pregnancy Category C

(continued)

Table 8.10 (continued)

Drug	Indication	Typical dose	Adverse reactions	Comments
Second Generation H1 Blockers				
Loratadine *(Claritin)*	Allergic rhinitis or conjunctivitis	10 mg once daily or 5 mg twice daily	[a]Same as above but cause fewer CNS effects such as sedation due to less penetration of the blood-brain barrier	Pregnancy Category B
Fexofenadine *(Allegra)*	Anaphylaxis Urticaria	60 mg twice daily or 180 mg once daily		Pregnancy Category C
Cetirizine *(Zyrtec)*	Chronic idiopathic urticaria Atopic dermatitis or contact dermatitis Pruritus secondary to another condition Angioedema Insomnia [11] Motion sickness and nausea	5–10 mg once daily		Pregnancy Category B

[a]With close monitoring of these medications, clinicians may choose to up-titrate the dosages to 2–4 times above dosing as necessary.

Acne Medications [12] (Table 8.11)

Table 8.11 Commonly used acne medications

Drug	Formulations/Typical dosage	Adverse reactions	Comments
Topical Medications			
Salicylic acid	Cream: 6% Foam: 2%, 6% Gel: 2%, 3%, 5%, 6%, 17%, Lotion: 5% or 6% Shampoo: 2%, 3%, 5%, 6%	Nausea, vomiting, dizziness, headache, burning or irritation at site of application, desquamation, tinnitus, hyperapnea	Mild to moderate acne Pregnancy Category C Lack of consensus on breast-feeding Limit usage in children less than 12 yrs Salicylic acid 6% is contraindicated in children <2 years

(continued)

Table 8.11 (continued)

Drug	Formulations/Typical dosage	Adverse reactions	Comments
Benzoyl peroxide	Benzaclin gel (5% BP, 1% clinda) Benzamycin gel (5% BP, 3% erythro) Duac gel (5% BP, 1% clinda) Epiduo (2.5% BP, 0.1% adapalene) Acanya gel (2.5% BP, 1.2% clinda)	Contact dermatitis, erythema, desquamation, xeroderma	Mild acne (monotherapy) Moderate-Severe Acne (in combination) Prevents bacterial resistance for patients on topical or systemic antibiotics Preadolescent acne in children Pregnancy Category C
Clindamycin	Topical (generic) 1%, gel, lot, sol Evoclin 1% foam Benzaclin gel (5% BP, 1% clinda) Duac gel (5% BP, 1% clinda) Acanya gel (2.5% BP, 1.2% clinda)	Xeroderma, erythema, burning, exfoliation, oiliness	Mild-moderate acne Use with benzoyl peroxide for decreased resistance Pregnancy Category B Caution in breast-feeding

Azelaic Acid	Azelex (20% cream) Finacea (15% gel)		Pruritus, reythema, skin burning, tingling, stinging, contact dermatitis, desquamation, xeroderma Rare: hypopigmentation	Pregnancy Category B
Retinoids	Adapalene (Differin)	gel 0.1%, 0.3%; cream 0.1%	*Adapalene*: Dry skin, pruritus, skin irritation, desquamation, sunburn *Tazarotene*: Dry skin, pruritus, erythema, desquamation, burning of skin *Tretinoin:* Painful skin, skin irritation, pruritus, erythema, pharyngitis	Pregnancy Category Adapalene: C Tazarotene: X Tretinoin: C Lack of consensus on breast-feeding Tazarotene: contraindicated in pregnancy or in women who may become pregnant
	Tretinoin (Retin-A)	micro 0.04%, 0.1% cream 0.025%, 0.05%, 0.1% gel 0.01%, 0.025%		
	Tazarotene (Tazorac)	micro 0.04%, 0.1% cream 0.025%, 0.05%, 0.1% gel 0.05%, 0.1%		

(continued)

Table 8.11 (continued)

Drug	Formulations/Typical dosage	Adverse reactions	Comments
Oral Medications			
Spironolactone	**Hormonal acne, Hirsutism** [13] **(females):** 50–200 mg daily *(Aldactone)*	Hyperkalemia, gynecomastia, GI upset (nausea, vomiting, diarrhea, abdominal cramps), irregular menses, dizziness, hypotension	If normal kidney function, no need for monitoring of potassium levels during therapy Pregnancy category C Do not use with eplerenone Do not give to men
Erythromycin	250–500 mg BID, then 250–500 mg daily	GI (nausea, vomiting, diarrhea), prolonged QT or ventricular arrhythmias, hepatitis, cholestatic jaundice, abnormal LFTs, fungal/bacterial superinfection	Pregnancy Category B Highest rate of resistance

Doxycycline	50–200 mg daily to BID	GI (nausea, vomiting, epigastric pain, esophagitis), pseudotumor cerebri, photosensitivity, hyperpigmentation	Pregnancy Category D Avoid long-term usage while breastfeeding given effects on tooth development and bone growth Do not use tetracyclines in children <8 yrs. of age Doxycycline: Take with food, do not take 30 min before lying down. Only tetracycline that can be given in renal failure, as excreted by GI tract
Minocycline [14]	50–200 mg daily to BID	Pseudotumor cerebri, vertigo, dizziness, autoimmune conditions (hepatitis, lupus-like syndrome, serum sickness), hyperpigmentation	

(continued)

Table 8.11 (continued)

Drug	Formulations/Typical dosage	Adverse reactions	Comments
Isotretinoin	**Severe recalcitrant acne:** 0.5 -2 mg/kg/day, start low then increase as tolerated Goal total dose: 120–150 mg/kg *(Accutane)*	Dry eyes and lips, myalgias, headaches, vision changes, diarrhea, hepatitis, transaminitis, mood changes Rare: SJS/TEN, acute pancreatitis due to elevated triglycerides, worsening depression/suicidality Teratogenic	Requires consent and monitoring through the IPledge program due to teratogenicity Screen: Negative pregnancy test x2, CBC, CMP, lipids Monitoring: pregnancy test monthly, LFTs/Lipids at baseline and after 2 months and/or with dosage changes Pregnancy category X Women must be on 2 forms of contraception

Combination products (topical): Duac®: benzoyl peroxide and clindamycin; Epiduo®: benzoyl peroxide and adapalene; Acanya®: benzoyl peroxide and clindamycin; Benzaclin®: benzoyl peroxide and clindamycin; Ziana®: clindamycin and tretinoin

Biologic Therapy (Table 8.12)

Table 8.12 Commonly used biologic medications

Medication	Indication/dose	Adverse reactions	Monitoring	Comments
TNF Inhibitors				
Etanercept (Enbrel®) *SC injection*	**Psoriasis/PsA:** 50 mg 2×/week × 12 weeks, then 50 mg/week	Injection site reactions, CHF exacerbation, infections/ reactivation of TB, CNS demyelination, lupus-like syndrome	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC/CMP q6 months, quant gold yearly	Pregnancy category B Avoid live vaccines
Adalimumab (Humira®) *SC injection*	**Psoriasis:** 80 mg day 1, 40 mg day 8, 40 mg q2 weeks **Hidradenitis Suppuritiva:** 160 mg day 1, 80 mg day 14, 40 mg weekly	Injection site reactions, CHF exacerbation, infections/ reactivation of TB, CNS demyelination, lupus-like syndrome	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC/CMP q6 months, quant gold yearly	Pregnancy category B Avoid live vaccines

(continued)

Table 8.12 (continued)

Medication	Indication/dose	Adverse reactions	Monitoring	Comments
Infliximab (Remicade®) *IV infusion*	**Psoriasis/PsA:** 5 mg/kg at 0, 2, and 6 weeks, then q6 weeks	Injection site reactions, CHF exacerbation, infections/ reactivation of TB, CNS demyelination, lupus-like syndrome Rare: acute liver failure, lymphoma	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: LFTs q2 months, CBC/BMP q3-mos, yearly quantiferon gold	Pregnancy category B Avoid live vaccines Pre-mediate with Tylenol/benadryl
T-Cell Inhibitors				
Ustekinumab (Stelara®) *SC injection*	**Psoriasis:** ≤100 kg: 45 mg at week 0 and 4; then 45 mg q 12 weeks ≥100 kg: 90 mg at week 0, 4; 90 mg q 12 weeks	Infection, URI, nasopharyngitis, headache, malignancy (including nonmelanoma skin cancer), antibody formation, reversible posterior leukoencephalopathy	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC, CMP, q6 months, yearly quantiferon gold	Limited human data available in pregnant women, no observed toxicity in animal reproductive studies Avoid live vaccines

Ixekizumab (Taltz®) *SC injection*	**Psoriasis:** 160 mg × 1 dose, 80 mg at week 2, 4, 6, 8, 10, 12, then 80 mg q 4 weeks	Neutropenia, antibody development, infection, injection site reaction, upper respiratory infection, onset/exacerbation of IBD	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC, CMP, q3-6 months, yearly quantiferon gold	Increased risk of neonatal deaths observed in animal reproductive studies Avoid live vaccines
Secukinumab (Cosentyx®) *SC injection*	**Psoriasis:** 300 mg at weeks 0, 1, 2, 3, 4, then 300 mg every 4 weeks; 150 mg may be sufficient in some patients	Infection, nasopharyngitis, URI, diarrhea, IBD	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC, CMP, q3–6 months, yearly quantiferon gold	Limited human data available in pregnant women, no observed toxicity in animal reproductive studies Avoid live vaccines

(continued)

Table 8.12 (continued)

Medication	Indication/dose	Adverse reactions	Monitoring	Comments
Brodalumab (Siliq®) *SC injection*	**Psoriasis:** 210 mg at weeks 0, 1, and 2, then 210 mg every 2 weeks	Infection, nasopharyngitis, URI, diarrhea, IBD, suicidal ideation/behavior associated in clinical trials	Screen: CBC, CMP, hepatitis B/C serologies, quantiferon gold Monitoring: CBC, CMP, q3–6 months, yearly quantiferon gold	Limited human data available in pregnant women, no observed toxicity in animal reproductive studies Avoid live vaccines Boxed warning about suicidal ideation and behavior; available only through Risk Evaluation and Mitigation Strategy (REMS) Program Contraindicated in patients with IBD
Dupilumab (Dupixent®)	**Atopic Dermatitis:** 600 mg × 1 dose, then 300 mg q 2 weeks	Injection site reaction, conjunctivitis/keratitis, oral herpes	No labs required; consider CBC, hepatic panel, pregnancy test	Limited human data available in pregnant women, no observed toxicity in animal reproductive studies Avoid live vaccines

Miscellaneous medications (Table 8.13)

Table 8.13 Commonly used miscellaneous medications

Medication	Indication/dose	Adverse reaction	Monitoring	Comments
Methotrexate	**Psoriasis/Sezary Syndrome:** 5–25 mg PO once weekly; concomitant 1 mg folic acid supplementation daily (except day of MTX) reduces side effects *many additional off-label uses	Diarrhea, nausea/vomiting, alopecia, cytopenias, skin toxicity, pneumonitis, infections, acute LFT elevations, hepatotoxicity after prolonged use, lymphoma	Screen: HCG, CBC, LFTs, Hepatitis panel, BUN/Cr, HIV, quantiferon gold Monitoring: CBC & LFTs q 2 weeks × 1 month (and 2 weeks after each dose increase), then q 3–4 months	Pregnancy category X Some recommend liver biopsy after cumulative dose of 3.5 grams Minimize alcohol use Avoid co-administration of Bactrim/NSAIDS

(continued)

Table 8.13 (continued)

Medication	Indication/dose	Adverse reaction	Monitoring	Comments
Azathioprine (Imuran®)	**Atopic Dermatitis, Aphthous Stomatitis (off-label): s**tart at 0.5mg/kg/day; if no cytopenias by 6–8 weeks, increase by 0.5mg/kg/day q 4 weeks; goal dose of 2–3 mg/kg/day	Nausea, vomiting, cytopenias, infection, hepatotoxicity, severe myelosuppression if TPMT deficient	Screen: HCG, CBC, CMP, quantiferon gold, TMPT level (dose according to level) Monitoring: CBC weekly × 4 weeks, then q2 weeks for 8 weeks, then monthly or with dosage changes; CMP q3 months	Pregnancy Category D Reduce dose if on Allopurinol
Mycophenolate Mofetil (Cellcept®)	**Psoriasis, atopic dermatitis, bullous diseases, urticaria, connective tissue diseases (off-label):** 500–1000 mg BID; titrate up to 3–5 gram/day	GI, weakness, fatigue, insomnia, HA, tremor, infection, urinary urgency/frequency, dysuria	Screen: CBC, CMP Monitoring: CBC q2 weeks × 2–3 months then q1 month × 1 year; CMP at 1 month then q3 months	Pregnancy category D Take on empty stomach Antacids decrease absorption Discontinue therapy if WBC < 3.5–4.0

Cyclosporine (Sandimmune®/ Neoral®)	**Psoriasis/off-label: severe Atopic Dermatitis, Pyoderma Gangrenosum:** 2.5 mg/kg/day, increase by 0.5mg/kg/day if insufficient response after 4 weeks (max 4 mg/kg/day)	Hypertension, hyperlipidemia, nephrotoxicity, hypertrichosis, gingival hyperplasia, nausea, headache, tremor, electrolyte abnormalities, malignancy (including skin cancer)	Screen: Blood pressure, U/A, CBC, CMP, fasting lipids, Mg, random spot urine protein to creatinine ratio, quantiferon gold Monitoring: BP, CMP, Mg, fasting lipids, CBC, q 2 weeks for 2 months, then monthly; random urine protein: creatinine q3 months, annual quantiferon gold	Pregnancy category C Significant drug interactions; caution with nephrotoxic medications Avoid grapefruit juice as this increases concentration If Cr increases to >30% baseline, repeat Cr in 2 weeks and decrease by 1 mg/kg x1 month if increase sustained, if decreases to <30% baseline OK to continue, otherwise discontinue until Cr normalizes

(continued)

Table 8.13 (continued)

Medication	Indication/dose	Adverse reaction	Monitoring	Comments
Dapsone	**Dermatitis Herpetiformis:** Start at 50 mg daily and increase to 300 mg daily as needed **Leprosy:** Tuberculoid: 100 mg daily with rifampin for 12 months Lepromatous: 100 mg daily with rifampin and clofazimine for 24 months *Off label: Pemphigus Vulgaris, apthous stomatitis	Hemolytic anemia, methemoglobinemia, hepatotoxicity, neuropathy Rare: blood dyscrasias, severe dermatologic reactions	Screen: G6PD, CBC, CMP, U/A Monitoring: CBC q1 week × 1mo; q2 weeks × 2 mos; then q3 mos; CMP, retic count q3 months; MetHgb levels if symptomatic	Pregnancy category C Use with caution in patients with G6PD deficiency Many drug interactions, metabolized by CYP3A4 Sulfa derivative (caution in sulfa allergic)

Hydroxychloroquine (Plaquenil®)	**Lupus, DLE:** 200–400 mg daily; do not exceed 5 mg/kg/day or 400 mg *Off label: PMLE, PCT, dermatomyositis, sarcoidosis	GI, premaculopathy and retinopathy, blue-grey hyperpigmentation, headache, hemolysis with G6PD deficiency	Screen: ophtho exam; CBC, G6PD, CMP Monitoring: ophtho exam annually; CBC, CMP monthly × 3 months, then q 4 months.	No evidence of increased fetal ocular toxicity with maternal use
Acitretin (Soriatane®)	**Psoriasis (pustular):** 10–50 mg daily (with largest meal) **Darier's disease, icthyoses:** 25–35 g daily × 4 weeks, then adjust to maintenance of 10–50 mg daily	Dry mucous membranes, hair loss, elevated triglycerides, transaminitis, myopathy, IBD flares, leukopenia	Screen: 2 negative pregnancy tests, CBC, LFTs, BUN/Cr, lipids Monitoring: Lipid profile q2 weeks for 8 weeks, then, LFTs q2 weeks until stable, pregnancy tests monthly	Pregnancy category X Patients advised not to get pregnant × 3 years following discontinuation

(continued)

Table 8.13 (continued)

Medication	Indication/dose	Adverse reaction	Monitoring	Comments
Rituximab (Rituxan®)	**Bullous disorders:** 1 g q2 weeks × 2 doses or 375 mg/m^2 weekly × 4 doses **Primary cutaneous B Cell Lymphoma:** 375 mg/m^2 IV weekly × 4 doses	Opportunistic infections, HBV reactivation, infusion reactions, cytopenias mucocutaneous reactions (SJS, TEN), renal toxicity	Baseline: Hep B/C serologies, CBC, CMP, quantiferon gold Monitoring: CBC weekly to monthly	Pregnancy category C Pretreatment with acetaminophen and antihistamine recommended
Gabapentin (Neurontin®)	**Pruritus, neuropathic pain:** 300 mg* TID, up-titrate to up to 1800 mg daily Dose adjustment for renal impairment *immediate-release	Dizziness, drowsiness	Baseline: renal function Monitoring: periodic renal function	Pregnancy category C

Doxepin (Sinequan®/ Silenor®)	**Chronic urticaria:** 10 mg TID or 10–30 mg QHS	Sedation, hypertension, nausea, gastroenteritis, mania/hypomania in patients with bipolar disorder	Evaluate mental status at initiation and with dosage changes	Pregnancy category C Use with caution in elderly patients
Amitriptyline (Elavil®)	**Neuropathic pain:** 10–25 mg QHS or divided, up-titrate up to 200 mg/day	Anticholinergic effects, sedation, bone marrow suppression, mania/hypomania in patients with bipolar disorder	Evaluate mental status at initiation and with dosage changes	Pregnancy category C Use with caution in elderly patients
Apremilast (Otezla®)	**Psoriasis:** 10 mg on day 1, increase by 10 mg day 2–5, then 30 mg BID CrCl<30: 30 mg daily	Diarrhea, nausea, URI, headache, weight loss, depression	Monitor: weight, mood changes	Pregnancy category C

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Chapter 9
Pediatric Dermatology Practical Approaches and Prescribing Tips

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General Pediatric Dermatology Prescribing Tips

- Children develop at very different rates depending on both nature and nurture, including at what age they can take pills instead of liquid suspensions! Always ask to confirm for children 8 years and up, even for teens, whether a liquid suspension or pill is preferred.
- Remember to inform families when meds must be taken with food and what types of food/drink to avoid or select (e.g. give griseofulvin with fat-containing foods, generic isotretinoin with fatty food, doxycycline generally better-tolerated with food and does NOT have to be 2–3 h before/after eating as is recommended for tetracycline).

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- Once or twice a day dosing is MUCH easier than TID or QID for parents/caregivers. Usually letters are required for daycare or school nurses/staff to administer meds when the child is not at home.
- Children often split time at two or more homes (divorced parents, grandparents providing daytime care). Ask whether two tubes/bottles of a prescription are needed, especially if it is critical that doses are not missed.
- Always try to have proof you require oral therapy, e.g. KOH or culture for griseofulvin for tinea capitis, and make sure the parent/patient is clearly counseled on the most common and the most concerning risks/benefits/expectations of medications. Remember that patients do experience life-threatening drug reactions from oral antimicrobials prescribed for extremely benign conditions like acne and pityrosporum versicolor.
- Head off noncompliance due to anxiety about black box warnings, e.g. for calcineurin inhibitors pimecrolimus and tacrolimus, by counseling parents/guardians about the safety record that has now been established for these topicals, even in patients under 2 years of age, at the time you first prescribe.
- Suspensions are listed as mg/5 ml by convention and because 5 ml = 1 teaspoon. Make sure families know this is a specific amount to be administered with a syringe, not just any teaspoon! It is safest to prescribe in terms of milliliters, not teaspoons.
  - Try to prescribe amounts that are easy to administer. For example, calculate based on weight, then round to an easy volume to measure. CHECK YOUR MATH (e.g. by calculating in the other direction) and make it easier for the pharmacist to confirm your calculation by showing your calculation or at least by providing the patient's weight somewhere in the prescription. Ex: hydroxyzine for a 30 lbs child
    - 30 lb. ÷2.2 lb/kg = 13.6 kg
    - Hydroxyzine 2 mg/kg/day × 13.6 kg = 27.2 mg/day divided TID = 9 mg/dose for TID dosing
    - OR for evening/bedtime dosing just for itch causing sleep disturbance, approx. 0.6 mg/kg/dose × 1 = 8 mg/dose

- Hydroxyzine comes as 10 mg/5 ml suspension (2 mg/ml) so 8 mg/dose ÷ 2 mg/ml = 4 ml/dose.
- In note to pharmacist and your clinic note show your math:
  - "4 ml/dose = 8 mg/dose = 0.6 mg/kg/dose for 13.6 kg child"

Antifungals

Antifungal Prescribing Tips (Table 9.1)

- Griseofulvin has a long safety and usage history, and since it is so affordable, it is easiest to prescribe for all insurance carriers. Note that in the early days of treatment a patient may develop an id-like reaction to fungal antigen on the head/face that is not a drug reaction; of course, do stop the medication if significant rash generalizes or if there are other signs of a serious drug reaction.
- Sensitivity testing for griseofulvin is often not available or difficult to obtain. Resistance to griseofulvin is not common, so consider inappropriate dosing (e.g. not taken with fat-containing foods), reinfection or the need for longer therapy before you worry about resistance (especially if family members are not treated at the same time with antifungal shampoo). Kerion sometimes requires months of therapy, especially if you treated with oral prednisone for severe inflammation. Resistance is most likely if a patient has been treated for several months and signs of infection are worsening and you obtain proof of active infection, as opposed to an inflammatory disorder such as seborrheic dermatitis.
- Itraconazole should be the last choice based on safety profiles.
- Not all parents will want to put their child on oral antifungal therapy for one or two infected nails. Sometimes a trial of topical antifungal cream and excellent tinea foot care practices, including cutting down infected nail as often as possible, can lead to resolution of partial onychomycosis.

Table 9.1 Antifungal prescribing tips

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Griseofulvin-Microsize	Grifulvin-V	20–25[a] mg/kg/day QD or divided BID Max 1 gram/day	25 mg/ml	250 or 500 mg	6–8 weeks for tinea capitis, longer for M. canis or kerion. Take with fat-containing foods (a meal or pudding, not juice). Not treatment of choice for onychomycosis. Superior to terbinafine for M canis tinea capitis [1].
Griseofulvin-Ultramicrosize	Gris-PEG	15–20 mg/kg/day[a] QD or divided BID Max 750 mg/day	NA	125 or 250 mg	6–8 weeks for tinea capitis, longer for M. canis or kerion.
Fluconozole	Diflucan	6 mg/kg/day QD	10 mg/ml 40 mg/ml	50,100,200 mg	Alternative to griseofulvin: 6 mg/kg/day × 6 weeks for tinea capitis [2]. 12–16 weeks for fingernail onychomycosis, 18–26 weeks for toenails onychomycosis.

Itraconozole	Sporonox	5 mg/kg/day divided BID	10 mg/ml	100 mg	Better to give on empty stomach. Solubilized by hydroxypropyl-β-cyclodextrin (400 mg/mL) which causes diarrhea & caused pancreatic adenocarcinoma in rats but not mice[b]. Consider monthly pulsing 1 week × 3 months for onychomycosis [3]. 5 mg/kg/d daily × 1 week or weekly dosing. OR For weight 10–15 kg: 100 mg every other day 16–20 kg: 100 mg QD 21–40 kg: 100 mg BID >40 kg, 200 mg BID [3].
Terbinafine	Lamisil	<20 kg: 62.5 mg 21–40 kg: 125 mg >40 kg: 250 mg QD	N/A	250 mg	Lamisil granules DISCONTINUED. 250 mg tabs can be cut. 6 weeks for fingernails, 12 weeks for toenails.

[a]2003 Red Book: Report of the Committee on Infectious Diseases, 26th edition. American Academy of Pediatrics, 2003. Note this is higher than listed by UpToDate or FDA, and paediatricians have often already tried the lower published dosing before referral. Dosing is otherwise as per FDA prescribing info

[b]FDA prescribing info

- Sample calculation for griseofulvin
  - Ex: griseofulvin for a 20 kg child
    - Griseofulvin microsize comes as 125 mg/5 ml (25 mg/ml) which makes dosing easy if you use 25 mg/kg because the milliliters/day = kg of the child.
    - 25 mg × 20 kg = 500 mg/day divided by 25 mg/ml = 20 ml/day
    - Divide 20 ml/day into two 10 ml doses (eg with breakfast and dinner)
    - In note to pharmacist and your clinic note show your math:
      - "20 ml/day = 500 mg/day = 25 mg/kg/day for 20 kg child"

Antivirals

Antiviral Prescribing Tips (Table 9.2)

- Doses provided aim to reduce the number of daily doses required. There are many options for dosing acyclovir that are not listed, since the range of therapeutic effect is broad and it is a relatively safe medication.
- Suppressive dosing for herpes simplex is indicated if a patient not only has 5 or more episodes per year, but also if he/she experiences erythema multiforme or Stevens-Johnson episodes due to HSV, even after the second episode in a few months.
- Herpes gladiatorum is a common problem that may require suppressive dosing throughout wrestling season and beyond if the patient participates in wrestling camps off-season.

Table 9.2 Antiviral prescribing tips

Generic	Brand	Total Daily Dose (oral, for immunocompetent only)	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Acyclovir	Zovirax	**HSV:2-11 yrs (first episode)** 40-80 mg/kg/day div q6–8h × 5–10 days Max 1000 mg/day **HSV: ≥12 yrs (first episode)** 1200 mg/day PO div Q8hrs × 7–10 days **HSV:≥12 yrs(recurrence)** 1600 mg/day PO div Q12hrs × 5 days OR 2400 mg/day PO div q8h × 2 days **Suppression 2-11yo** 30 mg/kg/day PO div q8h × 6–12 mos Max 1000 mg/day **Suppression:≥12 yrs** 800 mg/day PO div q12h 6–12 mos **VZV (2yo and up):** 80 mg/kg/day PO divided q6h for 5 days VZV Max: 3200 mg/day	40 mg/ml	200,400,800 mg	Note: there are other dosing options for 5×/day which is harder for patient to comply with. American Academy of Pediatrics does not recommend oral antiviral therapy for healthy children <12yo with varicella. Supportive therapy is sufficient.
valacyclovir	Valtrex	Herpes labialis: 2000 mg q12hr × 1 day Suppression: 500–1000 mg/day	NA	500, 1000 mg	

Antihistamines

Antihistamine Prescribing Tips (Table 9.3)

- Although atopic dermatitis itch is not mediated primarily through histamine pathways, if a patient has true allergies, antihistamine therapy can be helpful to limit or prevent dermatitis flares.
- Some patients have a paradoxical hyperactivity reaction to Benadryl and hydroxyzine. If a parent reports that their child is not sedated at all, consider this paradoxical reaction or the possibility that he/she needs a higher dose. Higher doses of hydroxyzine are needed for a central anxiolytic effect.
- It is often helpful to administer a nonsedating antihistamine in the morning and a sedating antihistamine at night.
- Warn the family about excessive sedation with first-generation antihistamines (diphenhydramine, hydroxyzine) that prevents alertness at school. First-time administration can be tested on a Friday or Saturday night just in case. Excessive drowsiness can be addressed by giving the medication a bit earlier in the evening or by reducing the dose. The longer a patient has been on the same daily dose, the more likely it is that dose escalation will be required.
- Patients can still experience fatigue or sleepiness with second-generation antihistamines. Different second-generation antihistamines have differing therapeutic effectiveness and sedation, so try exchanging one for another depending on patient experience.
- For patients with many food allergies, or give before bedtime that day in order to accurately monitor for anaphylaxis symptoms.

TABLE 9.3 Antihistamine prescribing tips

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Cetirizine	Zyrtec	>6mo<2yr = 2.5mg 2–5 yr = 2.5–5 mg >6 yr = 5–10 mg QD (but higher doses are often required for chronic therapy)	1 mg/ml	5 mg or 10 mg tab/chewable	Can Rx cetirizine in AM for nonsedating Tx and a sedating antihistamine for itch disturbing sleep.
Fexofenadine	Allegra	30 mg QD or BID	6 mg/ml	30 tab/ODT, 60, 180 mg tab	

(continued)

Table 9.3 (continued)

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Diphenydramine	Benadryl	5 mg/kg/day divided q6-8h Max 300 mg/day Or 2 mg/kg/dose for anaphylaxis	2.5 mg/ml	25 mg, 50 mg Chewable 12.5 mg tab	1.25 mg/kg/dose QHS for itch disturbing sleep or up to QID. Some children have a paradoxical hyperactivity reaction, so consider giving for first time under adult observation (eg nap time) so the family is not awake all night. Generally not needed or recommended off-label for infants, but over 6mos of age can trial 1 mg/kg at bedtime (max 6.25 mg initial dose)[a] for severe atopic dermatitis flare disturbing sleep (generally not needed if topical care is adequate, best for concomitant allergen exposure flaring the eczema under allergist advice). Cream formulations irritate eczematous skin and are not as effective as oral administration and other skin care strategies.

Hydroxyzine	Atarax	2 mg/kg/day divided TID or QID OR 0.6 mg/kg per dose QID	2 mg/ml	10 mg or 25 mg	Can trial 0.6 mg/kg QHS for itch disturbing sleep (sometimes higher doses required but start low in case of severe drowsiness, especially on school nights). Sedative effect tends to wear off after a few days, so if used for atopic dermatitis flares disturbing sleep, use in beginning of flare therapy. Has a CNS anxiolytic effect especially at higher doses. May have a paradoxical hyperactivity reaction, although mainly seen with diphenhydramine. Additionally has bronchodilator activity and analgesic effects.
Loratidine	Claritin	2–5 yr = 5 mg >= 6 yr = 10 mg QD	1 mg/ml	10 mg tab/ODT	
Cyproheptadine	Periactin	0.25 mg/kg/day, then 2 mg/kg/day divided bid/tid, Max 12 mg/day	0.4 mg/ml	4 mg	

(continued)

Table 9.3 (continued)

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Doxepin		Variable, QHS to TID	10 mg/ml	10, 25, 50 mg	Literature supports starting at 10 mg/day for adults with pruritus unresponsive to other Rx. There is very little data on use of doxepin for dermatologic conditions [4] in children and it seems to be highly sedating. Due to increased risk of suicidality in children/adolescents started on antidepressants, strongly recommend administration by or with pediatric psychiatry especially if you consider this medication for depression in your patient related to or concomitant with chronic itch or atopic dermatitis. As stated elsewhere, if the eczema is well-controlled by topical or other means, oral doxepin should not be necessary. Doxepin cream is not recommended in children due to systemic absorption leading to toxicity, as well as the irritant/allergen concerns about creams in general.

[a]PDR.net

Antibiotics

Antibiotic Prescribing Tips (Table 9.4)

- Diarrhea or other GI upset is a very common side effect and the most common reason parents self-discontinue treatment other than lack of palatability and refusal to take the medication. You can almost always have them administer the medication with breakfast and dinner (or pudding vs apple sauce for bad taste, though this does not always work).
- If you are not treating an acute bacterial infection, you often can prescribe a BID regimen (with breakfast and dinner); compliance is much higher.

Table 9.4 Antibiotic prescribing tips

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Cephalexin	Keflex	25–50 mg/kg/day divided BID, TID or QID Max 4gm/day	25 mg/ml 50 mg/ml	250, 500 mg	BID is much easier for family because midday dosing requires school nurse.
Cefadroxil	Duricef	30 mg/kg/day QD or divided BID Max 2 g/day	25 mg/ml 50 mg/ml 10 mg/ml	500 mg	
Dicloxacillin	Dynapen	**Infants, Children, and Adolescents weighing <40 kg:**[a] 12.5–25 mg/kg/day PO q6h for mild to moderate infections, 25–50 mg/kg/day PO q6h for severe infections. Maximum dose: 500 mg/dose **Adolescents and Children weighing >= 40 kg:**[a] 125–250 mg PO q6 hours for mild to moderate infections. 250–500 mg PO q6 hours for severe infections. Adolescents Max 4 g/day PO	NA	250, 500 mg	On empty stomach.

Doxycycline	Oracea, Monodox, Doryx etc	2 mg/kg/day divided BID Adult dosing if >45 kg Max 100 mg/dose	5 mg/ml	20, 50, 75, 100 mg	Lower doses often given QD or 100 mg if difficult to remember or tolerate an AM dose. Not recommended for children younger than 8yo EXCEPT when treating Rocky Mountain Spotted Fever this is still drug of choice.
Erythromycin	EES	30–50 mg/kg/day divided BID, TID or QID 60–100 mg/kg/day for severe infections Max 2 gm/day	40 mg/ml 80 mg/ml	200 mg chew 400 mg	Give with food; has a prokinetic effect & can cause GI upset. An alternative to doxycycline for younger children with perioral dermatitis.
Clarithromycin	Biaxin	7.5–15 mg/kg/day divided BID Max 1000 mg/day	25 mg/ml 50 mg/ml	250, 500 mg	

(continued)

Table 9.4 (continued)

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Azithromycin	Zithromax	5–10 mg/kg/day QD Max 500 mg/day	20 mg/ml 40 mg/ml	250 mg, 500 mg	Can trial 10 mg/kg/day when erythromycin and doxycycline are contraindicated or not tolerated.
Cefuroxime	Ceftin	30 mg/kg/day divided BID 100 mg/kg/day divided BID for severe infections Max 1 gm/day	25 mg/ml 50 mg/ml	125,250, or 500 mg	

Additional dosing info from FDA prescribing info and/or Antibiotic Dosing for Children: Draft expert Recommendations for the 2017 Essential Medicines List for Children (EMLc)

[a]PDR.net

Miscellaneous Prescribing Tips (Table 9.5)

- For oral steroid tapers for acute inflammatory conditions, start with BID dosing and then go to qAM dosing as the taper progresses.
- Cimetidine for warts and molluscum seems to work better for younger children. Try calculating 30–40 mg/kg/day and dividing into BID doses. Continue therapy for 1–2 months before stopping, unless you are concerned about side effects.
- Most people prescribe 1 mg/day folate on the days not giving methotrexate dose, but some give folate every day, and others 7 mg folate just the day after methotrexate.
- Methotrexate has a long history of safe and effective use in children for severe dermatoses; however, because it can take 3–6 months to see an effect with methotrexate, many people use an oral steroid or cyclosporine as a bridge to longterm therapy with methotrexate.

Table 9.5 Miscellaneous prescribing tips

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Isotretinoin	Claravis Amnesteem Myorisan Zenatane Absorica (others)	Variable, usually QD or BID Usually max dose is 1 mg/kg/day	NA	10,20,30,40	Take with high fat meal. Risk of paradoxical acne fulminans-like reaction is higher in severe teen acne, or reportedly if macrocomedones. Start with prednisone × 2 weeks with 40 mg/day or higher, or low dose isotretinoin eg 10 mg/day and ramp up slowly.
Prednisone		Variable	1 mg/ml syrup; Conc soln: 25 mg (5 mg/ml; 30% alcohol)	1,2.5,5,10,20,50 mg	More physiologic to give in AM but for severe inflammation and higher doses divide BID.

Prednisolone	Prelone/ Orapred	Variable	3 mg/ml	5 mg	More physiologic to give in AM but for severe inflammation and higher doses divide BID. Orapred reportedly tastes better.
	Pediapred		1 mg/ml		
Timolol	Timoptic	Variable (as few drops per day as possible), usually BID	0.5% regular vs gel-forming solution, currently available only as ophthalmic drops	NA	Topical therapy can buy time until comfortable with propranolol based on infant size, other health concerns, or possibility that propranolol is not needed. Systemic levels and side effects reported, especially for larger doses and deeper hemangiomas. The copay of gel-forming solution can be very high, so warn families or just use regular timolol maleate.

(continued)

Table 9.5 (continued)

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Propranolol	Inderal Hemangeol	1–3 mg/kg/day	4 mg/ml generic, 4.28 mg/ml Hemangeol	Infantile hemangioma patients needing oral treatment are never old enough for pills	Usually BID although sometimes TID. MUST BE FEEDING q8h or more. Advise to skip doses even for days for reduced/poor PO intake or wheezing, to decrease risk of systemic side effects.
Cimetidine	Tagamet	20–40 mg/kg/day divided BID Max:1600 mg or 2400 mg for ≥12yo	60 mg/ml	100,200,300,400, or 800 mg	Most often used 30–40 mg/kg/day for recalcitrant warts in younger children who are not good candidates for cryotherapy or injections; when it works well it can have an obvious effect within 1–2 months.
Mycophenolate mofetil	Cellcept	30–50 mg/kg/day divided BID Max:2000 mg	200 mg/ml	250, 500 mg	

Cyclosporine	Neoral Sandimmune	3-5 mg/kg/day divided BID (up to 6 mg/kg/day by some) [5]	100 mg/ml	25,100 mg	Common first-line for severe atopic dermatitis inadequately controlled with topical approach alone due to most rapid onset of noticeable effect, i.e. within 2–4 weeks (except for dupilumab – see below). Consider full dosing × 2–6 months (some use up to 7 mg/kg/day) until good control of atopic dermatitis, taper by 1 mg/kg/day each month until back on only topicals or supplemental weekend maintenance dosing [6].

(continued)

Table 9.5 (continued)

Generic	Brand	Total Daily Dose	Oral Suspension Formulation	Oral tab/cap Formulation	Prescriber tips & Examples
Methotrexate		0.3–0.5 mg/kg/week [5] or 5–15 mg/m^2/week Max 25 mg/week		2.5 mg	Once weekly. Always give with folic acid (prescribers differ whether to give on the methotrexate day). Onset takes 6–8 weeks. Better for longer-term therapy than cyclosporine or if cyclosporine is not tolerated or contraindicated.
Etanercept	Enbrel	0.8 mg/kg SC Max: 50 mg/week			Once weekly.
Dupilumab	Dupixent	< 60 kg: 400 mg SQ loading dose, then 200 mg SQ every other week ≥60 kg: 600 mg SQ loading dose, then 200 mg SQ every other week	NA	NA	Approved March 2019 for 12yo and up. Noticeable improvement in itch reported by patients within days of loading dose. Main barrier to use is pediatric fear of needles and cost/insurance coverage.

Topical Corticosteroid Prescribing Tips

- The choice of a topical steroid should take into account that children have thinner skin and a higher surface area to volume ratio than adults. Sometimes you will use this to your advantage, because you can avoid systemic steroids while targeting the affected organ since skin is on the outside.
- Higher potency steroids and shorter follow-up plans work better for itchy rashes and pediatric patients (arguably all patients), despite the above concerns about thinner skin and surface area to volume ratios.
- Try to limit prescribed steroids to 1–2 different potencies, and educate the patient/family clearly on effective vs safe usage. Many clinicians prescribe a lower potency steroid for face and folds, a stronger one for the body, and then further increase potency during atopic dermatitis flares. Over just a few months a family can acquire a collection of 3–5 different topical steroids this way, then not know which ones to use for the next flare. They may wait for an urgent clinic appointment, but even if that visit is just a day or two later the child has scratched so much that the flare is even worse; it only takes a few minutes to go from clear skin to red, bleeding skin during an acute flare.
- You must get comfortable with the amounts needed to accomplish the treatment course you intend. Restrict the number of refills as appropriate but do not over-restrict the amount you intend to be used for the next month. The number of grams you prescribe is assumed by insurance to be a monthly supply, and the patient/guardian will not be able to get a refill until 26 days later.
- Knowing how many grams or tubes of topical steroid a family has used will help you gauge how compliant vs steroid-phobic the patient/family is. Ask how many tubes and how much of a current tube/jar is left to help you understand whether the steroid is being overused vs underused.

- Contact allergy to topical steroids do occur, but when your prescribed regimen has failed first rule out other factors including insufficient potency, parental steroid phobia causing inadequate adherence to your prescribed regimen, inadequate barrier compensation teaching and compliance, contact allergens and irritants in skin care products, and behavioral factors like continued scratching. Even crusted excoriations can be itchy in an atopic patient. Never, ever just blame the patient for scratching; teach behavioral replacement strategies.

Topical Timolol Prescribing Tips

- Topical timolol should only be considered if the size and thickness of the infantile hemangioma (IH) is small enough and thin enough (eg ideally 2 mm thick or less). Topical therapy will not adequately treat most thick and/or rapidly-proliferating and deep IH.
- If you need several drops a day to cover the lesion or if there is ulceration, risk of systemic absorption increases and you should consider oral propranolol. If you are knowingly using topical timolol in larger amounts because parents/guardians insist on avoiding oral propranolol, you must still counsel regarding same side effects as oral propranolol.
- A trial of topical therapy is reasonable for many young infants, but the larger the IH at time of presentation, the more rapidly you think the IH is growing, the younger the infant in general, and the more critical the location of the IH, the shorter your follow-up time should be so that you do not miss a window to convert to oral propranolol.

Oral Propranolol Prescribing Tips

- Most prescribers are comfortable initiating propranolol in an outpatient setting. There must be a plan for monitoring

the patient's vitals for a couple of hours after the first dose administration. This can be in an outpatient clinic (eg periodically check the patient who is mostly in the waiting area) or an outpatient infusion center. If the patient is very young, low weight, or has other comorbitidies, propranolol should be started as an inpatient.

- Hemangeol official dosing recommendations: Start with 0.15 mL/kg (0.6 mg/kg)BID, taken at least 9 h apart. After 1 week, increase the daily dose to 0.3 mL/kg (1.1 mg/kg) twice daily.
- Because of the risk of hypoglycemia, advise parents/guardians to give a feeding just before propranolol is given, to ensure that the patient is taking good PO. If PO decreases or stops due to illness, propranolol should be held even if it is for several days. It can be restarted at the usual dose (no tapering or ramping up).
- Most prescribers adjust the dose monthly to maintain the same dose by weight for several months, since infants grow and gain weight quickly over the first year of life.
- While most patients do very well on 2 mg/kg/day, some patients with aggressive IH might do better on 3 mg/kg/day. Parents/guardians should be counseled on signs that the 2 mg/kg/day dose is inadequate (obvious growth of the IH despite taking and tolerating the medication, ulceration starting/progressing/not healing).
- The clinical course of IH is modified by propranolol, so the typical expectations for clinical behavior no longer apply (several months of a growth or growth then plateau phase, and several years of involution). Deep IH tend to rebound in growth if propranolol is stopped too soon, often even at one year of life. For this reason, infants with larger deep IH should be kept on propranolol for over a year.
- The weight-based dosing can be tapered by patient growth toward the end of propranolol therapy. For example, after 9 months (except for a large, deep IH), you might stop adjusting the dose for weight. Toward the end of therapy the dose can be tapered more rapidly.

Isotretinoin Prescribing Tips

- Adolescents who have larger, painful lesions and who develop scarring are candidates for isotretinoin even if they have not tried many other oral therapies. The younger a patient is when they present with acne scars, the sooner you should consider isotretinoin because there is a high chance the inflammation and scarring will continue and even worsen for several years otherwise. These younger patients with severe inflammatory acne and scarring are at high risk for negative psychosocial and mental health outcomes.
- Some providers use a standard ramp-up schedule: 0.5 mg/kg/day for the first month, then 1 mg/kg/day for subsequent months if there are no side effects or laboratory concerns.
- Another way to dose isotretinoin is to be attentive to clinical response and side effects such as xerosis and retinoid dermatitis, which can occur in some patients during the winter on as low as 20 mg/day. Many patients do extremely well and feel well continuing their whole course on 20 mg or 40 mg/day; the only down-side is the course may take longer to achieve 120–150 mg/kg cumulative goal dosing. However, not all patients need to reach this amount and some patients need more; hence, best management is individualized to patient response and the severity of their acne when they start therapy.
- Isotretinoin is lipophilic and much more bioavailable when taken with fatty food. Absorica reduces need to take with fatty food but some still recommend that it be taken with some fat. Others promote BID dosing as more effective, but most patients will be more compliant with once daily dosing with dinner (usually the largest meal of the day) because many patients skip breakfast and it is difficult to remember to take medication to school/work for a lunchtime dose.
- The American Academy of Dermatology guidelines for laboratory monitoring are currently to limit exhaustive testing and just check AST, ALT and triglycerides. Also go

by patient history, review of systems and polypharmacy (if any). If lab abnormalities are going to occur, it is usually seen in the first month or so of therapy, so check labs before and after a dose increase, but coasting on the same dose for several months does not require monthly lab testing except for pregnancy testing in females of childbearing potential *as long as the patient continues to feel well and has started no other medications.*

- Counsel the patient regarding common transient worsening of inflammatory acne vs a severe paradoxical acne fulminans-like reaction to isotretinoin (aka pseudo-acne fulminans lacking systemic findings such as fever) so that he/she presents promptly for evaluation and possible prednisone therapy. Consider starting male teens who are 14 or 15 yo with severe acne and any patient with macrocomedones on a preventive 2-week short taper of prednisone and at least 40 mg/day of isotretinoin.
- Never assume an underage patient will not succumb to peer pressure to drink alcohol at a party. Patients should be taught that the kind of party binge-drinking done by teens and college-age patients is the worst for the liver, and being on isotretinoin magnifies the risk. Teach the "red cup trick": walking around a party with a plastic party cup containing soda or water might be enough to stave off peer pressure to drink. No one has to know there is no alcohol in the cup, and one does not necessarily even need to lie that there is.
- Many teens and college students are very active athletes. Isotretinoin increases the natural risk of exertional rhabdomyolysis. Patients need not be discouraged from participating in sports, but they should be counseled to be mindful about sudden increases in physical effort, to always hydrate well with water, and to inform an MD for unusual muscle swelling or weakness.
- Brand-name Accutane has not been on the market since 2006. Prescribers can acknowledge that patients call it Accutane, but why continue to promote this name? There are several generics, some of which have also been discontinued. It's safest to call it isotretinoin.

Prescribing Tips for Medicaid and Other Forms of Free Care

- Brand-name medications and more elegant formulations tend to cost more and are difficult to obtain on Medicaid/free care. For example, timolol gel-forming solution may not be covered but timolol regular ophthalmic solution can be prescribed for infantile hemangiomas. Some medications, such as isotretinoin, are expensive as generics, so prior authorizations may be required regardless.

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Chapter 10
Dermatologic Surgery

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Surgical Anatomy (Figs. 10.1, 10.2, and 10.3)

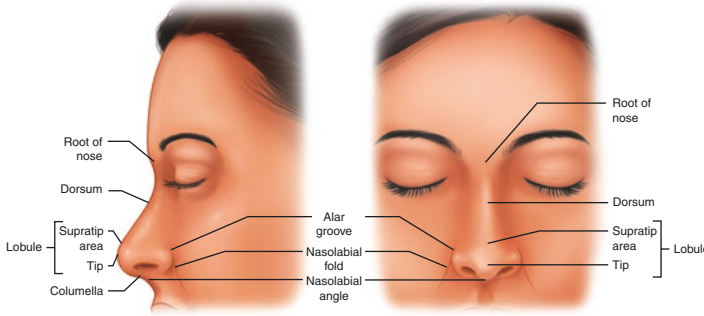

Figure 10.1 Anatomy of the nose

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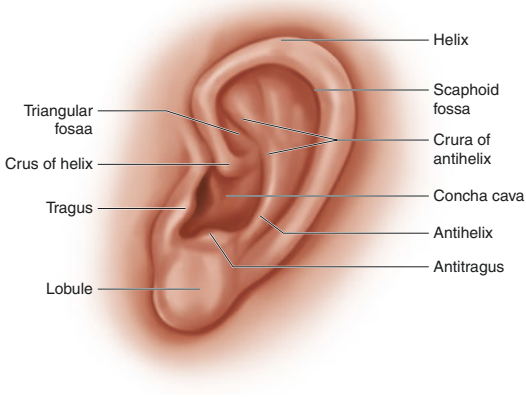

FIGURE 10.2 Anatomy of the ear

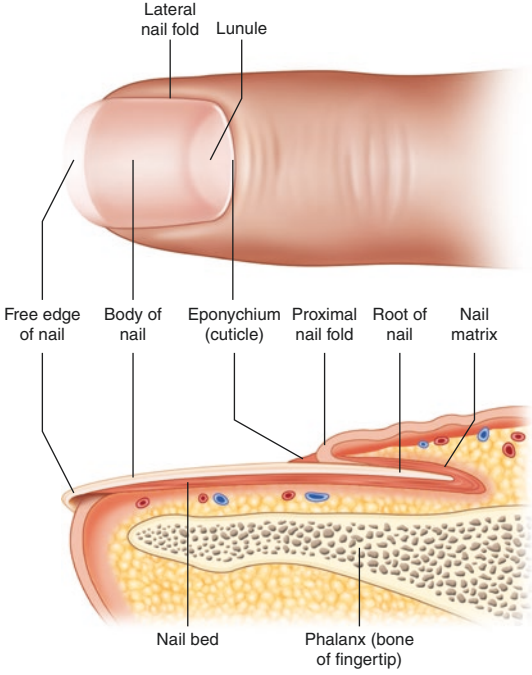

FIGURE 10.3 Anatomy of the fingernail

Preoperative Preparation

- Review allergies
  - Including allergies to medications, latex and adhesives
- Review the past medical history, with an important focus on:
  - Cardiac history, including:
    - Any indication for prophylaxis for the prevention of endocarditis
    - History of an implanted cardiac device
  - History of blood borne diseases
  - Impaired immune system
  - History of a prosthetic joint
- Review medications
  - With an emphasis on anticoagulant and antiplatelet medications
- Review the relevant pathology report
- Correctly identify and mark the operative site and have the patient confirm
  - Wrong site surgery is among the most common reason for claims against dermatologic surgeons
- Administer preoperative antibiotics if indicated (more below)
- Check vital signs
- Perform a time out

Special Considerations for Implanted Cardiac Devices (ICD)

- Implanted cardiac devices include pacemakers, defibrillators and cardiac resynchronization devices
- Although complications involving electrosurgery and ICDs are rare, in general it is preferred to limit or avoid electrosurgery in patients with such devices

- While there is a lack of evidence and no consensus on the use of electrosurgery in patients with ICDs, if they do need to be used, true thermal cautery (electrocautery) or bipolar forceps are safer options

Antibiotic Prophylaxis (Table 10.1)

- There are three main instances when antibiotics are used perioperatively
  - Preoperative antibiotics given to patients at risk for infective endocarditis
  - Preoperative antibiotics given to patients at risk for septic arthritis
  - Pre- or postoperative antibiotics given to patients at risk for postop wound infection
- There is scant hard data to guide decisions about prophylaxis, but the following guidelines should be considered:
- Standard prophylaxis regimens
  - Non-oral surgical site: Cephalexin 2 grams PO, or if PCN allergic consider clindamycin 600 mg PO or azithromycin 500 mg PO
  - Oral surgical site: Amoxicillin 2 grams PO, or if PCN allergic clindamycin 600 mg PO or azithromycin 500 mg PO

Anticoagulants and Antiplatelet Management

- Complications of moderate to severe bleeding include hematoma formation, dehiscence and flap or graft necrosis
  - However, the rate of post-op bleeding or hematoma is <1%
- Nearly half of patients undergoing cutaneous surgery are on at least 1 anticoagulant or antiplatelet agent, so it is important to be comfortable managing them

Table 10.1 Guidelines for antibiotic prophylaxis [21]

Patients at high risk for infective endocarditis with procedure involving oral mucosa or infected skin	**Patients at high risk for hematogenous total joint infection**	**Patients at high risk for surgical site infection**
Prosthetic cardiac valve	First 2 years following joint placement	Lower extremity
Previous infective Endocarditis	Previous prosthetic joint infection	Groin
Congenital heart disease[a]	Immunocompromised/ immunosuppressed patients, including those with HIV	Wedge excision of the lip or ear
Cardiac transplant recipients who develop cardiac valvulopathy	Type 1 diabetes	Skin grafting
	Malignancy, malnourishment or hemophilia	Extensive inflammatory disease

[a]Congenital heart disease including unrepaired cyanotic CHD, including palliative shunts and conduits; completely repaired congenital heart defects with prosthetic material or device, whether placed by a surgery or a catheter intervention (during the first 6 months after the procedure); Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

- General guidelines for managing anticoagulant and antiplatelet medications preoperatively include:
  - If a patient is taking any antiplatelet or anticoagulant medication because of a history of a heart attack, angina, transient ischemic attack or stroke, the patient should continue it
    - Any increased risk of bleeding does not outweigh the much more serious risk of a thrombotic event

    - Furthermore, systematic studies have shown that rates of bleeding when continuing warfarin are not significantly increased
    - For patients that remain on these, special consideration should be made to ensure adequate intraoperative hemostasis, including electrocautery or hemostatic agents

- How to handle specific medications:
  - Warfarin
    - A recent INR should be obtained to make sure it is within therapeutic range (2–3.5). For an INR > 3.5, the risk of hemorrhage should be weighed against the benefit of surgery
  - Although there is little data to guide management of novel oral anticoagulants (i.e. dabigatran, rivaroxaban and apixaban) based on experience with warfarin, there are no additional testing or management guidelines [4]
    - It has been shown that there is no difference in the rate of bleeding complications with patients on any of these novel oral anticoagulants compared with all other patients who underwent Mohs micrographic surgery [2]
    - However, it is important to remember that unlike warfarin, which can be reversed with fresh frozen plasma or vitamin K in the event of hemorrhage, these new oral anticoagulants lack a mechanism to be reversed [17]
  - Aspirin/NSAIDS
    - If the patient has NO history of stroke or heart attack and is only taking the medication for primary prevention, they may discontinue aspirin (10 days before the procedure) or NSAIDs (3 days) and resume 3 days after the procedure
  - Clopidogrel, prasugrel and ticagrelor have no additional testing or management guidelines

Basics of Excision and Closure

- The basics of excising a lesion are broken down into four main steps: excising the tissue, undermining, hemostasis and repair. Each of these steps can be broken down further as below
- Excising the tissue
  - Incision: aimed to achieve uniform release along the entire skin edge
    - In a standard excision, the edges should be perpendicular and smooth (not beveled as in Mohs surgery)
    - The depth of the incision varies based on the location and nature of the lesion being excised
      - Trunk and extremities: the junction of subcutaneous fat and deep fascia
      - Lateral aspect of the face and neck: the junction of the subcutaneous fat and the superficial musculoaponeurotic system (SMAS)
      - Central third of face: Deep to the muscles of the SMAS (or for smaller lesions, the junction of subcutaneous fat and SMAS)
      - Scalp: Deep to the galea aponeurotica
    - It is not necessary to use significant downward force on the scalpel, as too much downward force creates a jagged wound edge. It is fine to use more than 1 pass of the scalpel to achieve the desired depth
    - The nondominant hand should stabilize the skin with *downward* pressure as opposed to lateral traction, which can create a jagged edge
    - Trim any subcutaneous fat to the level of the epidermis and dermis which will make approximation of the wound easier
  - Excision: remove the skin in a uniform anatomic plane
    - The anatomic plane used to cut below the tissue being removed should ideally be at the level of the

initial incision, and varies based on location of the body (above)
    - Avoid collateral damage to important anatomic structures
    - The use of scissors can help the surgeon maintain a uniform anatomic plane by providing more tactile feedback relative to a scalpel
    - Ultimately the tissue being excised should be of uniform thickness

- Undermining
  - Undermining aids in advancing the wound edges when suturing the wound closed, particularly in sites where the fascia is adherent to the overlying dermis
    - The plane in which one undermines is typically identical to the anatomic plane used for excision
    - To determine the extent of undermining necessary, use a skin hook to pull the wound edge to its desired location
    - Be careful when undermining a flap, as it could threaten the flap's blood supply

- Hemostasis
  - Prior to suturing the wound closed, it is important to achieve effective hemostasis
  - The surgeon must strike a balance between hemostasis and ensuring adequate blood flow to the surrounding tissue [11, 12]
  - Topical hemostatic agents include:
    - Mechanical agents that create a physical blockade (pressure, ostene)
    - Synthetic agents such as cyanoacrylates that polymerize to form an adhesive
    - Chemical agents that cause destruction of tissue leading to thrombus and occlusion (Zinc paste, Monsel's solution, silver nitrate and aluminum chloride)

    - Physical agents that create a 3D meshwork on which platelets can clot (Gellatin, cellulose, microfibrillar collagen, hydrophylic polymers)
    - Physiologic agents such as epinephrine
  - Electrosurgery is commonly used for hemostasis, with special attention for patients with implanted cardiac devices (as above)
- Repair (Figs. 10.4, 10.5, and 10.6)
  - Repair is performed with a series of superficial and deep sutures [15]
  - Deep sutures
    - Deep sutures have three primary goals: reapproximate the tissue, reduce and redistribute tension and create tissue eversion
    - The workhorse of most cutaneous procedures is the buried vertical mattress suture, which has a heart shape creating maximal eversion

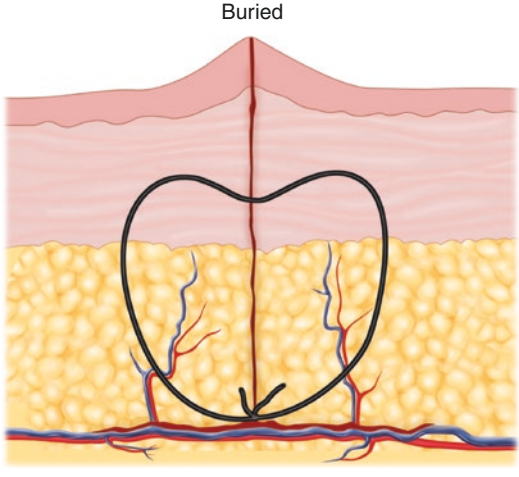

Figure 10.4 The buried vertical mattress suture, demonstrating the desired heart shape which facilitates eversion

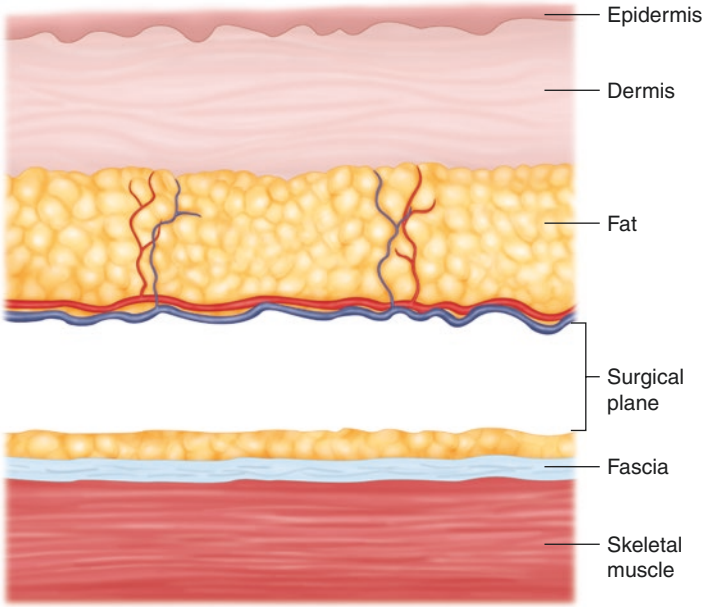

Figure 10.5 The surgical plane on the trunk and extremities is between the subcutaneous fat and deep fascia [14]

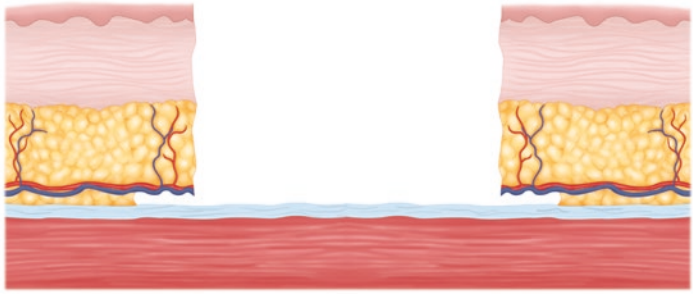

Figure 10.6 The proper appearance after excising a lesion and undermining the defect, demonstrating clean vertical wound edges of uniform thickness which allows it to be reapproximated easily [14]

    - It is important to ensure that the needle path is mirrored on both sides of the wound to prevent any discrepancy in height
    - Using forceps or a skin hook to evert the skin edge while throwing the suture allows for accurate placement and maximizes eversion
  - Superficial sutures
    - If the deep sutures are properly placed, the superficial sutures should not bear any tension
    - The primary goal of superficial sutures is to correct any minor height discrepancies
    - Skin with a thinner dermis (such as the face) requires sutures placed closer together to avoid leaving track marks
    - Height discrepancies can be corrected by taking a shallow, narrow bite on the high side followed by matching the lower side with a deeper, wider bite
    - Superficial sutures should be removed as early as possible to avoid track marks as followed:
      - Eyelid – 3–5 days
      - Face, neck and ears – 7 days
      - Scalp – 7–10 days
      - Trunk and extremities – 10–14 days

Sutures

Use the smallest caliber suture possible

- Suture size is inversely related to its number, so a 3-0 suture is larger than a 6-0
- The appropriate size depends on the location, and a rough guideline is as follows but is variable based on the patient including their activity level and the amount of tension at the site
  - Scalp
    - Superficial nonabsorbable sutures: 4-0 or 5-0
    - Deep sutures: 3-0 or 4-0

  - Face
    - Superficial: 6-0
    - Deep: 5-0
  - Trunk and extremities
    - Superficial: 4-0 or 5-0
    - Deep: 3-0 or 4-0
  - Hand
    - Superficial: 5-0
    - Deep: 5-0
- Sutures are characterized by many different properties including their composition (natural or synthetic), configuration (monofilament or multifilament), surface (smooth or barbed), coating (which can be coated to decrease the coefficient of friction or with an antibiotic), absorption and color.
  - Although it is important to understand these, in practice most surgeons have a few types of sutures which they use for the majority of their procedures and the biggest variation is the size
  - An abbreviated table listing some of these qualities is below (Table 10.2)
- Suture needles are categorized based on their length, point type and curvature

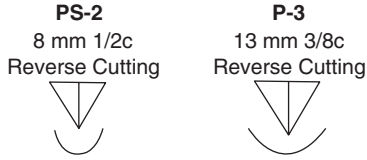

Table 10.2 Properties of commonly used sutures in dermatology [19]

Suture	Tensile strength	Complete absorption time	Tissue reactivity	Comment
Absorbable Sutures				
Fast absorbing surgical cut	Poor	24–42 days	High	Often used as superficial sutures for patients that do not want to come back to have them removed
Polyglactin 910 (Vicryl)	High	56–70 days	Low to intermediate	The most commonly used absorbable suture
Poliglecaprone 25 (Monocryl)	Quite high	91–119 days	Very low	
Polydioxanone (PDS)	High	183–238	Low	Good for areas with high tension such as the back
Polyglycolic acid (Dexon)	Intermediate	60–90 days	Low to intermediate	
Nonabsorbable Sutures				
Silk	Low	N/A	High	Preferred for mucosal sites
Nylon	High	N/A	Low	
Polypropylene	Moderate	N/A	Low	

Table 10.3 Properties of commonly used anesthetics in dermatology

Amide	Onset	Duration	Adult max dosing without Epi	Adult max dosing with Epi	
Lidocaine	<1 min	0.5–2 h	4.5 mg/kg	<7 mg/kg	Anesthetic of choice for pregnant women (pregnancy category B). It is also considered to be compatible with breast feeding
Bupivacaine	5–8 min	2–4 h	2 mg/kg	Max 225 mg	Useful for its long duration of action
Mepivacaine	5–20 min	0.5–2 h	Max 300 mg	Max 500 mg	
Prilocaine	5–6 min	0.6–2 h	5.7–8.5 mg	Max 600 mg	Used topically
Ester					
Tetracaine	15–45 min	4–6 h			Used topically

Adapted from: Park and Sharon [16]

Anesthetics

- There are two main classes of anesthetics: amides and esters (Table 10.3)
  - Amides include lidocaine, mepivacaine, prilocaine and bupivacaine
  - Esters include procaine (used mainly in dentistry) and tetracaine
- The addition of epinephrine to anesthetics causes vasoconstriction which localizes the anesthetic, thereby increasing its safety and duration
  - Vasoconstriction also decreases bleeding
  - Epinephrine is pregnancy category C
- Buffering lidocaine
  - Lidocaine with epinephrine is approximately 1000 times more acidic than subcutaneous tissue
  - Sodium bicarbonate is commonly buffered with lidocaine, which acts to decrease its acidity and thereby decrease the pain of injection
  - The proper volume ratio of 8.4% sodium bicarbonate to 1% lidocaine with 1:100,000 epinephrine is approximately 1 mL:10 mL [8]
- Lidocaine toxicity
  - Mild: tinnitus, lightheadedness, circumoral numbness, metallic taste and double vision
  - Moderate: nystagmus, speech slurring, muscle twitching and fine tremors
  - Severe: seizure activity, respiratory depression, coma and cardiopulmonary arrest

Electrodessication and Curettage (ED&C)

- Indications
  - Low risk tumors on the trunk or extremities, including superficial and nodular BCCs, SCCiS and keratoacanthomas
    - Recurrence rate for appropriately selected low risk tumors has been reported to be 4.9%, but increases up to 27% for aggressive histologic subtypes of BCC [3, 6]

  - Benign superficial epidermal growths such as seborrheic keratoses and pyogenic granulomas
- Surgical technique
  - Sharply curette the area of tumor, which debulks it as well as gives the provider a sense of its diameter based on the friability of the tumor relative to normal skin. Scrape the base in several different directions for complete clearance
  - Subsequently treat the area with electrodesiccation or electrofulguration
  - Repeat this process for a total of three treatments for malignant lesions, while benign lesions only require one treatment
- Benefits
  - Quick
  - Cost effective
  - Limited patient downtime
- Limitations
  - Does not allow histologic confirmation of tumor removal
  - Operator dependent
  - Healing process can take 4–6 weeks

Wide Local Excision (Table 10.4)

- Indications
  - Small NMSC (<10 mm tumors on noncritical areas of the face and < 20 mm tumors on trunk or extremities)
  - Recurrence rates for the treatment of non-morpheaform BCCs with 5-, 4-, 3-, and 2-mm surgical margins were found to be 0.39%, 1.62%, 2.56%, and 3.96%, respectively [9]
  - Well defined, small SCCs without high risk features can be treated with a 4-mm margin to give a 95% cure rate
  - SCCs on the trunk or extremities greater than 2 cm WITHOUT any other high-risk features should be excised with 6- to 10 mm margins [20]
- Benefits
  - Well tolerated, high cure rate
  - Allows for histologic assessment of the specimen's margins
  - Better cosmetic outcome than ED&C

Table 10.4 Recommended margins of tumors treated by wide local excision

Surgical margins	
Angiosarcoma	At least 2 cm
Basal cell carcinoma (low risk primary)	4 mm
Dermatofibrosarcoma protuberans	2–3 cm or more (and down to and including the fascia) (but Mohs is treatment of choice)
Squamous cell carcinoma (low risk primary)	4–6 mm
Melanoma: in situ	0.5–1.0 cm
: ≤1.0 mm	1 cm
: 1.01–2.0 mm	1–2 cm
: >2.0 mm	2 cm
Merkel cell carcinoma	1–2 cm
Squamous cell carcinoma (low risk primary)	4–6 mm

- Limitations
  - Not tissue sparing
  - Bread loafing only allows for the examination of a small portion of the margins

Mohs Micrographic Surgery (MMS)

- Indications
  - MMS is most commonly used for high risk BCCs and SCCs. High risk features are outlined below. The American Academy of Dermatology developed detailed criteria for 270 clinical scenarios for the appropriate use of MMS
    - For more detailed information see paper by Connolly et al. in Ref. [7]
  - Other tumors that are commonly treated with MMS include lentigo melanoma, melanoma, dermatofibrosar-

coma protuberans (DFSP), microcystic adnexal carcinoma, sebaceous carcinoma, Merkel cell carcinoma and atypical fibroxanthoma
    - Tumors with non-contiguous growth patterns, such as angiosarcoma are not routinely treated with MMS
- Surgical technique
  - The tumor is often debulked with a curette to help delineate its margins
  - The tumor is excised with a narrow (1–2 mm margin) at a beveled (oblique) angle (roughly 45 degrees from the skin surface) which facilitates tissue processing
  - Reference nicks are placed onto the tissue and wound edge to maintain anatomic orientation, and the tissue is mapped on a diagram and sent to the lab for frozen tissue processing
    - MMS is most commonly stained with hematoxylin and eosin, although some surgeons prefer to use toluidine blue.
    - Immunostaining is also employed including melan-A (MART-1) for melanoma, cytokeratins for SCC and CD34 for DFSP
  - The tissue is the examined under a microscope by the surgeon to ensure the tumor was removed in its entirety. If tumor is still present, the surgeon demarcates on the Mohs map precisely where the tumors remains and takes a second stage only in the area(s) the tumor is present
  - The process is repeated until the tumor is cleared, and then the wound is closed in the most appropriate fashion
- Benefits
  - Allows 100% of the peripheral and deep margins to be evaluated
  - Maximizes preservation of normal tissue, which is particularly important in cosmetically sensitive areas
  - Has the highest cure rate of any treatment for NMSC as well as the other rarer forms of skin cancer listed above
- Limitations
  - More resource intensive than WLE, although has been shown to be cost-effective compared to WLE for appropriately selected tumors

Criteria for treating NMSC with MMS

Anatomic location (anywhere tissue preservation is essential)

Central face, nose, lips, eyelids, eyebrows, periorbital skin, chin, mandible, temples
Cheeks, forehead, scalp and neck (for tumors that are greater than or equal to 10 mm)
Hands/feet
Genitalia

Tumor characteristics

Tumors >2 cm

Recurrent tumors or incompletely excised tumors

Poorly defined clinical borders

Aggressive histologic features including:

Morpheaform, micronodular, infiltrative BCC

Basosquamous

Poorly differentiated or deeply infiltrative SCC

Perinerual invasion

Chronic scar (Marjolin's ulcer)

Patient characteristics

Immunosuppressed

Irradiated skin

Genetic syndrome such as xeroderma pigmentosum, Gorlin or basal cell nevus syndrome

Complications and Management of Dermatologic Surgery

- Dermatologic surgery is generally considered safe, with a low rate of complications [1, 10]
  - The overall complication rate of MMS is roughly 2.6% [13]

  - When complications do occur, they are almost always considered minor
- Complications include:
  - Bleeding
    - Active bleeding
      - Active bleeding is the most commonly reported complication of MMS [5]
      - Patients should pre-emptively be told that if any bleeding occurs, they should apply direct pressure for 10–15 min
        - If bleeding continues they should hold pressure for an additional 15–20 min
        - If bleeding continues after holding pressure for a total of 3 cycles, then the patient should alert their surgeon or go to the emergency department
        - Patients may be tempted to look at the surgical site prior to holding pressure for the full period of time, but it is important to stress that they should not do this
    - Hematomas
      - Hematomas, although rare, can lead to more serious complications such as infection, dehiscence and necrosis
      - Hematomas should be treated by either partially or completely opening the surgical wound, suturing or ligating the bleeding vessel(s), and then either re-suturing the wound or making the decision that it is better left to heal by secondary intention
  - Infection [18]
    - Wound infection is the second most commonly reported complication of MMS, and happens in approximately 1% of cases
    - Signs and symptoms of wound infection typically present 4–6 days after surgery
    - Sites most prone to infection include the scalp and legs
    - Flaps and grafts are more prone to infection than primary closures or secondary intention

- If there is any concern for abscess than the area should be drained, otherwise the patient can be treated with oral antibiotics such as cephalexin if MRSA is not suspected or trimethoprim-sulfamethoxazole or a tetracycline antibiotic if MRSA is suspected

– Dehiscence
  - Wound dehiscence can be secondary to overactivity by the patient, or can occur secondary to bleeding, infection or tissue necrosis
  - If wound dehiscence occurs it is important to take a culture to rule out infection
  - The tissue can be re-sutured if the wound is clean and the edges are healthy, or it can be allowed to heal in secondarily
– Necrosis of a flap or graft
  - Grafts which become necrotic are frequently left in place to act as a biologic dressing
  - There are no pharmacological interventions available to treat necrotic flaps that have been shown to achieve consistent results
  - The surgeon should not debride the wound but rather continue proper wound care until the flap is fully healed, as debridement of a superficial necrotic flap can result in a full thickness injury

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Chapter 11
Cosmetic Pearls

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Overview

This chapter offers a succinct overview of common cosmetic procedures performed by dermatologists. Neuromodulation, soft-tissue augmentation, resurfacing procedures, lasers, sclerotherapy, and platelet-rich-plasma therapy are reviewed. Understanding general principles, risks, indications, and con-

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traindications of a procedure are discussed to ensure the safe and efficacious treatment of patients. This concise chapter contains both FDA and non-FDA approved treatments and should not be used as a comprehensive review. All procedures should be performed with or by those fully adept and trained in cosmetic dermatology.

Neuromodulator Botulinum Toxin Serotype A

- OnabotulinumtoxinA – **Botox®**
- IncobotulinumtoxinA– **Xeomin®**
- AbobotulinumtoxinA – **Dysport®**

Mechanism of action:
Blocks the synaptic fusion complex subunit SNAP-25, blocking the release of acetylcholine vesicles at the neuromuscular junction [1].

Reconstitution
(Tables 11.1, 11.2, 11.3, and 11.4):

Absolute Contraindications:
1. Neuromuscular diseases (ALS, myasthenia gravis, Lambert- Eaton syndrome) [6]
2. Hypersensitivity to any botulinum toxin product or excipients
3. Allergy to cow's milk protein
4. Infection at the proposed injection site(s)
5. Pregnancy or nursing

Table 11.1 Dilution instructions for BOTOX cosmetic vials (100 Units and 50 Units) as per prescribing information

Dilution with preservative-free 0.9% sodium chloride injection	Resulting dose units per 0.1 mL in 50 vial	Resulting dose units per 0.1 mL in 100 vial
1.25 ml	4	
2.5 ml	2	4

Adapted from Botox® prescribing information [2]

Table 11.2 Dilution instructions for XEOMIN cosmetic vials (200 units, 100 units and 50 units) as per prescribing information

Dilution with preservative-free 0.9% Sodium chloride injection (ml)	Resulting dose units per 0.1 mL in 50 vial	Resulting dose units per 0.1 mL in 100 vial	Resulting dose units per 0.1 mL in 200 vial
0.25	20		
0.5	10	20	40
1	5	10	20
1.25	4	8	16
2	2.5	5	10
2.5	2	4	8
4	1.25	2.5	5
5	1	2	4

Adapted from Xeomin® prescribing information [3]

Table 11.3 Dilution instructions for DYSPORT cosmetic vials (300 units and 500 units) as per prescribing information

Dilution with preservative-free 0.9% sodium chloride injection (ml)	Resulting dose units per 0.1 mL in 300 vial	Resulting dose units per 0.1 mL in 500 vial
0.6	50	
1		50
1.5	20	
2.5	12	20
3	10	
5		10

Adapted from Dysport® prescribing information [4]

Table 11.4 Comparison table between different neurotoxins

Neuromodulator	OnabotulinumtoxinA	IncobotulinumtoxinA	AbobotulinumtoxinA
Vials	50, 100	50, 100, 200	300, 500
Activity relative to Botox	1	1:1	~1:3
Storage once reconstitution	2–8 °C	2–8 °C	2–8 °C
Life span once reconstituted	24 h[a]	24 h	24 h
Onset of action	4–7 days	4–7 days	2–4 days

[a]If kept properly stored, studies have shown that it can last up to 4 weeks [5]

Relative Contraindications:
6. Recent antibiotic intake, particularly aminoglycosides [6]

Adverse Reactions:
1. Injection site reactions: pain, hematoma and infection
2. Eyelid ptosis
3. Facial asymmetry
4. Headache

Injection sites over facial muscles (Fig. 11.1):

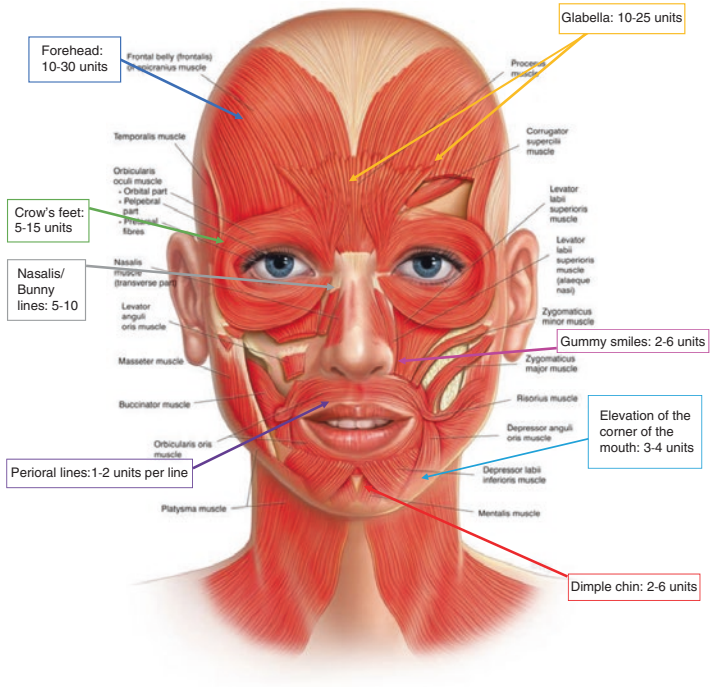

FIGURE 11.1 Facial muscles and the average amount of botulinum-toxin A units needed per facial area

Treatment of severe axillary hyperhidrosis:
- OnabotulinumtoxinA (Botox®) is FDA approved for axillary hyperhidrosis that is inadequately managed by topical agents in adult patients.
- The recommended dose is 50 Units per axilla.
- The recommended dilution is 100 Units/4 mL with preservative-free 0.9% Sodium Chloride Injection, USP.
- Using a sterile 30 gauge needle, 50 Units (2 mL) is injected intradermally in 0.1–0.2 mL aliquots to each axilla in multiple, evenly distributed sites [10–15] approximately 1–2 cm apart.

Sclerotherapy

Mechanism of action:
Involves the injection of a liquid or foam into veins, usually of the lower extremities (but also can be used for venous malformations). Once the sclerosant is injected, it causes irritation and inflammation of the vein endothelium. This inflammation along with compression of the vein causes the vein to scar closed. Sclerotherapy may be used alone or along with surgical treatment to remove the varicosity [7].

Sclerosants (Table 11.5)

Indications
1. Treatment of spider veins.
2. Small varicose veins (1–3 mm) when there is no major reflux.
3. Treatment of veins <3 mm that remain after surgery or larger veins 3–4 mm that are not due to underlying disease of perforating veins.

Protocol:
- Aspirin for primary prevention or anti-inflammatory drugs should be discontinued 1 week before treatment.

Table 11.5 Characteristics of selected sclerosing agents

Agent	Type	FDA approved	Ulcer risk	Allergenicity	Vessel size
Hypertonic saline	Hyperosmolar	No	High	Lowest	Small
Sodium tetradecyl sulfate	Detergent	Yes	High	Low	Small-medium
Polidocanol	Detergent	Yes	Low	Low	Small-medium
Hypertonic saline + Dextrose	Hyperosmolar	No	Low	Lowest	Small
Sodium morrhuate	Detergent	Yes	High	High	Small
Ethanolamine	Detergent	Yes	Low	Low	Small
Chromated glycerin	Chemical Irritant	No	Low	High	Smallest
Polyiodinated iodine	Chemical Irritant	No	High	Highest	Large

Adapted from Bolognia, Chapter 155, 2012 [7]

- If indicated by history, consider a prior Duplex ultrasound scan to map out the path of superficial, perforator and deep veins.
  1. No anesthetic is required.
  2. Clean the area with 70% isopropyl alcohol or chlorhexidine.
  3. The sclerosant is injected directly into the vein, starting with larger veins.
  4. Compression is applied to the treated area after treatment.
  5. Compression stockings need to be worn for 1–3 weeks after the procedure.
- Repeated treatments may be necessary at 6- to 12-week intervals to achieve up to 85% success at 3 years.

Contraindications [8]

1. Pregnancy
2. Age > 75 years in some cases
3. Sedentary patients who may be at increased risk for deep vein thrombosis
4. Patients with underlying medical history including diabetes, kidney disease, liver disease, cancer, heart disease, lung disease or bleeding disorders
5. Peripheral arterial disease (PAD) or decreased blood flow to the legs
6. Recent or acute phlebitis, superficial vein thrombosis or deep vein thrombosis
7. Veins that are connected to major veins (saphenous veins) that have reflux (incompetence)
   - Very fine vessels may be too small to inject, in which case a vascular laser or intense pulsed light treatment may be more suited.

Complications and side effects [9]:

1. Pain, swelling and redness
2. Bruising (usually fades over 2–3 weeks after treatment)
3. Matting around the treated area
4. Hyperpigmentation at the site or along the line of the vein
5. Ulceration
6. Microthrombi in the vein: can treat with a microthrombectomy (using a small blade or needle to create a hole into the vein)
7. Superficial vein thrombosis or phlebitis
8. Deep vein thrombosis (DVT)
9. Severe allergic response to the chemical agents (does not occur with hypertonic saline)

Platelet Rich Plasma (PRP)

Mechanism of action:

The basis of PRP is the suggestion that biological growth factors from the plasma can promote healing and rejuvenation in tissues.

Available data are largely based on case series.
Evidence on efficacy is controversial since there are no large scale, randomized, double blinded, placebo controlled trials.
There are numerous protocols in the current literature that describe the optimal conditions for centrifugation.
Protocols have been optimized with respect to different variables of the process, such as volume and sampling of processed whole blood, number of spins, time period of centrifugation, and range of centrifugal acceleration.
PRP is autologous and immunologically neutral, posing no danger of allergy, hypersensitivity or foreign-body reaction.

Process with sterile technique

1. Venous blood sampling in anticoagulated vacutainer tubes. Can keep whole blood up to 4 hrs before starting the PRP protocol.
2. Differential centrifugation of blood: according to manufacturer's protocol. Once centrifuged, PRP needs to be used immediately, within 10 minutes.
3. PRP Extraction. Cellular constituents sediment at different phases based on different specific gravities:
   I. Platelet poor plasma
   II. Platelet rich concentrate
   III. Separator Gel
   IV. Red blood cell and granulocyte mixture

Injection of PRP

- Inject **intradermally** into the desired site using a 30 G needle the platelet rich concentrate.
- Recommended to inject 0.5 ml/cm^2 into each injection point

Dermatologic applications [10]:

1. Facial rejuvenation: wrinkles, photodamage and discoloration (can be combined with other treatment modalities)

2. Hair loss disorders: male pattern alopecia, telogen effluvium and female pattern alopecia
3. Scars: post-traumatic and acne scarring (can be combined with centrifuged fat tissue and fractional laser resurfacing)
4. Ulcers: venous and arterial leg ulcers, diabetic foot ulcers and pressure ulcers
5. Burns: first and second degree thermal burns
6. Wounds: superficial injuries, cuts, abrasions and surgical wounds

Absolute Contraindications:
1. Critical thrombocytopenia
2. Hypofibrinogenemia
3. Acute and chronic infections
4. Chronic liver disease
5. Anti-coagulation therapy

Risks and side effects:
Injection sites reactions: pain, inflammation and infection.

Microneedling

Mechanism of action:
A minimally-invasive non-surgical procedure that involves the use of a microneedling device to create controlled skin injury through micro-holes, triggering the body to form new collagen and elastin in the papillary dermis.

Indications:
1. Scars
2. Stretch marks
3. Rejuvenation and tightening
4. Fine lines and wrinkles
5. Dyspigmentation

Procedure Pearls:

1. Use topical anesthetic cream.
2. Apply appropriate ingredients or serums uniformly on the treated region. The numerous micro-holes obtained due to the action of the needles will favor the deep penetration of the active ingredients into the skin.
3. Section the face into 5 parts: forehead, cheeks, chin/upper lip and nose.
4. Can be done manually with a rolling device (also referred to as a dermaroller) or with a stamping device.
5. Depth can range from 0.20 to 3.0 mm (Table 11.6)
6. Use a steady and slow treatment pace while exerting a constant pressure.
7. Change the direction of each pass and repeat until pinpoint bleeding is observed (Fig. 11.2).

   Avoid contact with the lips and eye contour (mainly the eyelids) as the skin is thinner in these particular areas.
8. After the entire treatment is complete, provide cooling and apply a non-allergenic moisturizer.

Table 11.6 Example of proposed depth of microneedling per facial area or indication

Region	Thin skin (mm)	Thick skin (mm)
Forehead	0.25–0.5	0.5–0.75
Glabella	0.25–0.5	0.5–1.0
Nose	0.25	0.5
Periorbital	0.25	0.5
Cheek Bone	0.5	0.5–1.0
Cheek and Chin	0.5–1.0	1.0–2.0
Perioral	0.25	0.5–0.75
Scarring (face)	1.0–1.25	1.5–2.0
Stretch Mark	1.0–1.5	1.5–2.0

Adapted from the Dermapen® brochure [11]
Cases are individualized, use pinpoint bleeding as a guide of treatment end point

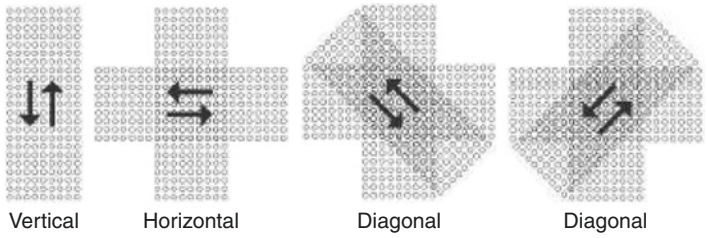

FIGURE 11.2 Microneedling pass directions

Post-Operative Treatment:
– Avoid sun exposure for 72 h. Sunscreen may be applied 24 h after treatment.
– Although no consensus exists, it is typically advised to avoid makeup for 2 days and skin products for 5 days.
– Immediate results can be seen after one treatment; however, offer patients several treatments to see maximum results.

Expectations:
- Day 1: Severity of erythema and presence of pinprick bleeding will depend on treatment depth.
- Day 2: Erythema persists comparable to a moderate sunburn. Edema may be more noticeable on the second day.
- Day 3: Skin can be slightly pink or normal color.

Relative Contraindications:
1. Bleeding disorder
2. Anticoagulant agents
3. Active infection at treatment site
4. Propensity to form keloid scars

Treatment Considerations:
1. If the patient has a history of herpes labialis, give antiviral prophylaxis

2. Topical retinoids may be discontinued 24 h prior to treatment
3. Caution in darker skin types as they may be prone to post-inflammatory hyperpigmentation

Risks:
1. Prolonged erythema and edema
2. Infection
3. Milia
4. Acneiform eruption
5. Post inflammatory dyspigmentation

Microneedling with radiofrequency:
This combines microneedling with the release of radiofrequency currents from the needle tips, producing thermal zones in the dermal structural components and accessory glands without damaging the overlying epidermis. Radiofrequency energy and heat is delivered deeper with minimal epidermal injury and heating.

Chemical Peels

Mechanism of action:
A peel, chemical or acid, removes layers of skin (Table 11.7). Depending on the chemical type and strength, the stratum corneum through the papillary dermis may be removed. This leads to regeneration of new epidermal skin with a more uniform color. Neocollagenesis in the dermis improves skin texture.

– The deeper the peel, the higher the risks and recovery time.

Indications for chemical peels:
1. Photodamage
2. Acne scars

Table 11.7 Characteristics of different chemical peels

Depth of peel	Depth in the skin	Peel used	Downtime
Light superficial Superficial	Stratum corneum Only the epidermis	Alpha hydroxy acids: lactic acid, mandelic acid and 35–70% glycolic acids Beta hydroxy acid: Salicylic acid Trichloracetic acid (TCA) 10–30% Jessner's formula (14% lactic acid, 14% salicylic acid and 14% resorcinol)	Erythema and peeling 1–4 days
Medium	Down to the papillary dermis or upper reticular dermis	35% TCA (in combination with Jessner's) 70% glycolic acid or lactic acid	Peeling 4–7 days Erythema up to 2 weeks
Deep[a]	Through the papillary dermis extending down to the reticular dermis	Phenol 88% Baker Gordon Phenol formula (88% phenol diluted with water, septisol and crouton oil)	Peeling for 2 weeks Erythema and edema may last for 2 months

[a]Need cardiac monitoring, conscious sedation and local anesthetics. Also, local blocks are recommended

3. Dyspigmentation
4. Rhytides

Procedure:

1. Consider priming the skin for 2–4 weeks prior to peel by application of depigmenting agents such as hydro-

quinone and the use of sunscreens. Retinoids and hydroquinone can be discontinued 3–5 days before the procedure. Patients with a history of recurrent herpes infection should be prophylactically treated with antiviral therapy.
2. Wash and degrease the skin with alcohol or acetone.
3. Apply solution over the desired area using gauze, cotton tip applicator, sponge or brush.
   - Amount of chemical and number of passes determines the depth and concentration of peel.
   - Sensitive areas (i.e. around the eyes and bony prominences) should only be treated by those experienced.
4. Neutralize alpha-hydroxy peels with sodium bicarbonate.
5. Use ice packs or a fan for comfort. Apply cool compresses to treated skin.
6. Over-the-counter pain-relieving medication, such as ibuprofen, naproxen sodium and acetaminophen, may help reduce any discomfort for medium and deep peels.

Relative contraindications
1. Cigarette smoking
2. Poorly controlled diabetes
3. Immunocompromised status
4. Recent facelift or laser resurfacing
5. Pregnancy or lactation

Risks and side effects:
1. Viral or bacterial infections
2. Scarring
3. Milia and acneiform eruptions
4. Hyperpigmentation or hypopigmentation

Lasers

Light amplification by stimulated emission of radiation (LASER)

Definitions:

- J = Joules Measures of energy
- W = Watts = Measure of power (W = J/s)
- Fluence = J/cm^2
- Irradiance = Power Density = W/cm^2
- Thermal Relaxation Time = Time for structure to cool to ½ its temperature to which it was heated.

Mechanism of action:

Lasers differ by their medium: gas, liquid or solid. When a medium gains energy and becomes excited from a power source, the atoms involved convert their stored energy into light by releasing a photon. This process is called "stimulated emission" [12]. Each medium releases light at a specific wavelength. This light is amplified and has the following characteristics:

1. Monochromatic (the light is of a single wavelength)
2. Coherent (the light beam waves are in phase)
3. Collimated (the light beams travel in parallel)

The structures in the skin that are to be targeted by the light, and that will absorb the light, are called chromophores. Each chromophore maximally absorbs light at a certain wavelength of light. Light energy from a laser is absorbed by a given chromophore, it get excited, "heated" and destroyed (selective thermolysis) [13].

There are 4 main chromophores in the skin (Fig. 11.3):

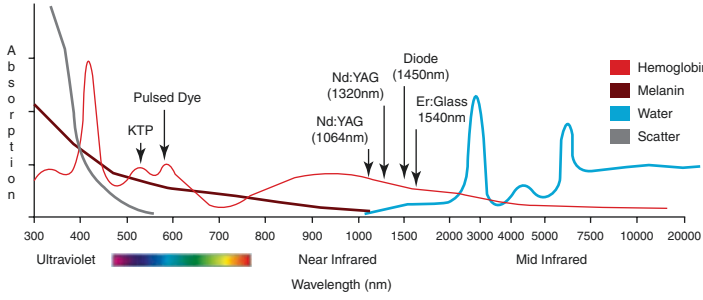

Figure 11.3 Absorption spectra of different chromophores. Different chromophores preferentially absorb light of different wavelengths

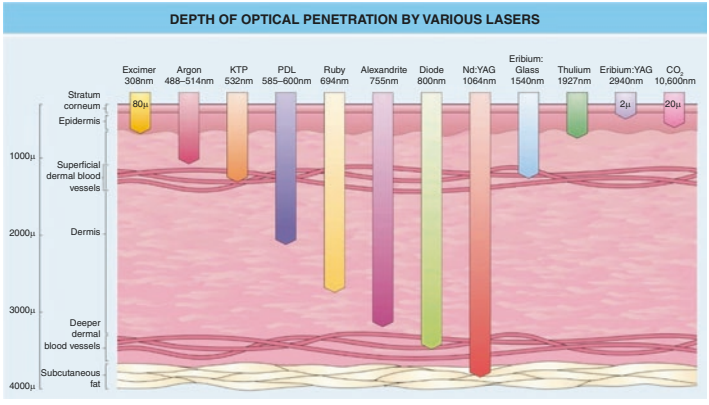

FIGURE 11.4 Depth of penetration of different lasers.

1. Hemoglobin (endogenous chromophore)
2. Melanin (endogenous chromophore)
3. Water (endogenous chromophore)
4. Tattoo pigment (exogenous chromophore)

In general, the depth of penetration increases with longer laser wavelengths (Fig. 11.4).

Cooling:
Objective is to minimize heat of normal skin, i.e. the superficial epidermis. This is achieved by selectively cooling these superficial layers and preventing their thermal injury.

In darker skinned individuals, epidermal melanin competes with the laser's chromophore making patients at risk for burning, pain, blistering, and subsequent dyspigmentation.

Epidermal cooling can be achieved by contact or non-contact cooling mechanisms such as cryogen, aqueous gel or air cooling.

Applications (Tables 11.8 and 11.9):

Table 11.8 Characteristics of different lasers available

Laser	Wavelength (nm)	Chromophore	Indications
Excimer	308	Protein	Psoriasis Vitiligo
Argon	508–514	Melanin Hemoglobin	Vascular and pigmented lesions
Pulsed dye (short)	510	Melanin	Pigmented lesions
KTP (potassium titanyl phosphate)	532	Melanin Hemoglobin	Pigmented and superficial vascular lesions
QS Nd:YAG (frequency doubled)	532	Epidermal pigment Tattoo pigment (Red, orange and yellow)	Superficial pigmented lesions
Pulsed dye (PDL)	584–595	Hemoglobin	Vascular lesions Hypertrophic scars Verrucae
Long pulsed Ruby	694	Melanin	Hair removal (skin type I, II)
QS Ruby	694	Melanin Tattoo pigment (Blue, black and green)	Pigmented lesions (epidermal and dermal) Nevus of Ota
Long pulsed Alexandrite	755	Melanin	Hair removal (skin type I, II) Leg veins
QS Alexandrite	755	Melanin Tattoo removal (Blue and Black)	Pigmented lesions

Table 11.8 (continued)

Laser	Wavelength (nm)	Chromophore	Indications
Picosecond laser (pulse duration 10^{-12})	755 or 1064	Melanin Tattoo removal (lack, green, blue and red)	Pigmented lesions Nevus of Ota Café au lait patches Solar lentigines
Diode	800–810	Melanin Hemoglobin	Hair removal (skin type I, II, III, IV, V) Leg veins
Nd:Yag	1064	Melanin Hemoglobin	Hair removal (skin type II, IV, V) Nonablative dermal remodeling[a] Leg veins
QS Nd:Yag	1064	Melanin Tattoo pigment (blue and black)	Pigmented lesions
Diode (long pulsed)	1450	Water	Non ablative remodeling[a]
Er:Yag	2940	Water	Ablative remodeling[b]
CO_2	10,600	Water	Ablative remodeling

Adapted from Tanzi et al. [13]

[a]Fractional non-ablative lasers target the skin and create microscopic areas of thermal injury called "microthermal zones" (MTZs). The intervening areas of untreated/unheated skin serve to re-epithelialize the skin [13]. This process induces collagen remodeling

[b]Ablative lasers target the whole epidermis and superficial dermis, leading to their complete ablation. This process induces collagen remodeling

Table 11.9 Tattoo colors with their respective pigments and laser treatments

Tattoo color	Pigments used	Lasers used
Red	Mercuric sulfide Cadmium selenide Sienna	Nd:Yag (freq doubled) PDL
Green	Chromates Malachite Ferro-ferric cyanide Phthalocyanine dyes Curcuma	QS Ruby QS Alexandrite Picosec Laser
Black Dark-blue	Carbon Iron Oxide Logwood	QS Ruby QS Alexandrite QS Nd:YAG Picosec Laser
Light blue	Cobalt	
Yellow	Cadmiun sulfide	PDL Picosec Laser
Brown	Iron oxide[a]	
White	Titanium dioxide[a]	

[a]Pulsed (Q-switched or picosecond) laser treatment should be avoided in tattoos that are suspected of containing iron oxide or titanium dioxide inks (e.g., white, tan, brown, or rust pigments in cosmetic tattoos) because of the high risk of ink darkening. The paradoxical reaction is attributed to the chemical reduction of rust-colored ferric oxide to black ferrous oxide or white titanium^{4+} to blue titanium^{3+} dioxide [15]

Pulsed laser systems have a mechanism that stores the generated energy and releases it as high energy pulses in ultrashort pulse durations with long intervening time period between each pulse (0.1–1 s). Pulses may be either long-pulsed with pulse durations ranging from 450 ms to 40ms, or very short-pulses (5–100 ns) such as the quality-switched lasers (Q-switched) [14].

Q-switched lasers with very short pulse durations are ideal for selective destruction of melanin, without dissipation of heat to the surrounding tissues.

Ophthalmologic complications:
Types of ocular injuries are wavelength specific (Table 11.10).

Lasers in the ultraviolet or infrared range damage the cornea and the lens due to their high aqueous concentration. Lasers in the visible range of the electromagnetic spectrum penetrate deeper and damage the retina and choroid due to melanin and hemoglobin absorption of the energy. In addition, lasers such as Nd:YAG, alexandrite and diode can damage both lens and retina though a photoacoustic and thermal mechanism [16].

Laser protective eyewear or goggles have different colored lenses that filter light. They have specific wavelength of rejection which should match the emission spectrum of the specific laser in use.

Corneal eye shields are designed to fit directly on the patient's eyes, just like contact lenses. When treating the areas around the eyes, laser-impenetrable metal ocular shields must be worn for the duration of treatment.

Table 11.10 Ophthalmologic complications from different lasers

Wavelengths	Absorbed by	Method of Injury
UVB & UVC (100–300 nm)	Cornea- Photokeratitis	Sunburn
UVA (315–400 nm)	Lens- Cataract	PUVA
Visible (400–1400 nm)	Retina (melanin, photoreceptors) Pigmented retinal epithelium- Retinal damage	Ruby PDL Argon Diode Alexandrite Nd:YAG
Infrared (>1400 nm)	Cornea	CO2 Erbium: YAG

Contraindications:
1. Cancer
2. Pregnancy
3. History of epilepsy (particularly photosensitive epilepsy)

Risks and side effects:
1. Pain, erythema, edema
2. Purpura
3. Blistering
4. Infection (herpes simplex virus reactivation, bacterial infection)
5. Postinflammatory dyspigmentation
6. Scarring

Soft Tissue Fillers

Introduction
Facial soft tissue augmentation requires an in-depth knowledge of anatomy, ability to select the appropriate patient/filler/site, and proper technique in order to obtain an optimal outcome.

Types of fillers
A. Non-Permanent fillers – Hyaluronic acids (HA) (Table 11.11)
Mechanism of action: HA, when injected into the dermis, binds to water leading to a temporary increase in volume.
B. Semi-Permanent and Permanent fillers (Table 11.12)
- **Mechanism of action:** permanent fillers are biosynthetic polymers combined with different carriers, such as gel beads or liquids.
- **Poly-Lactic acid (PLLA, semi-permanent)** – injection of polymer particles leading to subclinical inflammation and increased volume [1].
- **Polymethylmethacrylate (PMMA)** – mixture of microspheres, bovine collagen and fibroblasts are stimulated leading to new collagen formation.
- **Calcium Hydroxylapatite (CaHA, semi-permanent) –** combination of CaHA microspheres and 70% of methylcellulose leads to collagen stimulation and growth.

C. Summarized Clinical Guide
1. Informed consent is obtained and all questions regarding the procedure including side effects should be answered prior to treatment.
2. Area to be treated is washed, ensuring that all makeup and residues are removed.
3. Treatment area is cleaned with alcohol or chlorhexidine.
4. Injector may use needle(s) that comes with the filler or choose to use cannulas with blunted ends.
5. Injection techniques include threading, serial droplets, fanning, depot, and cross-hatching (Fig. 11.5).
6. Filler should be placed at appropriate dermal level (Fig. 11.6).
7. Aspirate before injection at every injection site.
8. Have all materials and medications at hand if needed for inadvertent arterial injection.
9. Provide patient with contact number to call in case of any concerns or questions.

TABLE 11.11 Available non-permanent fillers and their characteristics

Non-permanent filler	Property/ type	Indications	Depth	Duration
Hyaluronic acid				
Belotero Balance	Non animal Stabilized HA	Moderate to severe facial lines: nasolabial, infra-orbital, perioral and perioral rhytides	Mid to deep dermis	Up to 6 months
Hydrelle	HA and lidocaine	Moderate to severe facial wrinkle	Mid-to deep dermis	Up to 6 months

(continued)

Table 11.11 (continued)

Non-permanent filler	Property/ type	Indications	Depth	Duration
Juvéderm Ultra XC Juvéderm Ultra Plus XC	Hyaluronic Acid with Lidocaine	Moderate to severe facial wrinkle	Mid-to deep dermis	Up to 12 months
Juvéderm Volbella XC	Hyaluronic Acid with Lidocaine	Lips and perioral rhytides	Mid-to deep dermis	Up to 12 months
Juvéderm Vollure XC	Hyaluronic Acid	Correction of moderate to severe facial wrinkles (nasolabial folds)	Mid-to deep dermis	Up to 18 months
Juvéderm Voluma XC	Hyaluronic Acid with Lidocaine	Cheek augmentation to correct volume deficit in mid-face	Deep (subcutaneous and supraperiosteal)	Up to 24 months
Prevelle Silk	Hyaluronic Acid with Lidocaine	Moderate to severe facial wrinkles and folds (nasolabial folds)	Mid-to deep dermis	3–4 months
Restylane Gel	Hyaluronic Acid	Lip augmentation; Moderate to severe facial wrinkles and folds	Mid-to deep dermis	Up to 6 months

Table 11.11 (continued)

Non-permanent filler	Property/ type	Indications	Depth	Duration
Restylane Lyft (formerly known as Perlane)	Hyaluronic Acid with Lidocaine	Moderate to severe facial wrinkles and folds	Deep dermis, superficial subcutis	Up to 6 months
Restylane Silk	Hyaluronic Acid with Lidocaine	Lip augmentation; Perioral rhytides	Dermis	Up to 6 months
Restylane-L	Hyaluronic Acid with Lidocaine	Moderate to severe facial wrinkles and folds; Lip augmentation	Mid-to deep dermis	6 months
Restylane Refyne	Hyaluronic Acid with Lidocaine	Nasolabial folds and marionette lines	Mid-to deep dermis	Up to 12 months
Restylane Defyne	Hyaluronic Acid with Lidocaine	Nasolabial folds and marionette lines	Mid-to deep dermis	Up to 12 months
Human or animal derived collagen				
Cosmoderm 1, Cosmo-plast	Human Collagen	Wrinkles and acne scars	Superficial to papillary dermis	3–4 months
Fibrel	Porcine Collagen	Correction of depressed cutaneous scars	Dermis	3–4 months

(continued)

Table 11.11 (continued)

Non-permanent filler	Property/ type	Indications	Depth	Duration
Hylaform (Hylan B Gel)	Modified HA (animal derived)	Moderate to severe facial wrinkle and folds	Mid-to deep dermis	Up to 6 months
Zyderm Collagen Implant	Bovine collagen with Lidocaine	Correction of contour deficiencies	Dermis	3–4 months
Zyplast ®	Bovine collagen with Lidocaine	Correction of contour deficiencies	Mid-to deep dermis	3–4 months

Table adapted from Carruthers et al., 2015 [17] and FDA website [18]

Table 11.12 Available semi-permanent and permanent fillers and their characteristics

Semi-permanent and permanent filler	Composition	Indications	Depth	Duration
PLLA (Sculptra)[a]	Poly-L-lactic acid	Midface Lower face Jaw line Facial lipoatrophy Nasobabial folds and other facial wrinkles	Subdermal	1–2 years
PMMA (Bellafill)[b]	Polymethyl-methacrylate	Midface Jawline Nasolabial fold	Mid-Deep Dermis	Years to Permanent

Table 11.12 (continued)

Semi-permanent and permanent filler	Composition	Indications	Depth	Duration
CaHA (Radiesse and Radiesse +)[c]	Calcium hydroxylapatite microspheres suspended in gel	Moderate to severe facial fold and wrinkles	Subdermal	~15 months

PLLA[a] Poly-latic acid, *PMMA*[b] Polymethilmethacrylate, *CaHA*[c] Calcium Hydroxylapatite
Table adapted from Carruthers et al. (2015) [17]

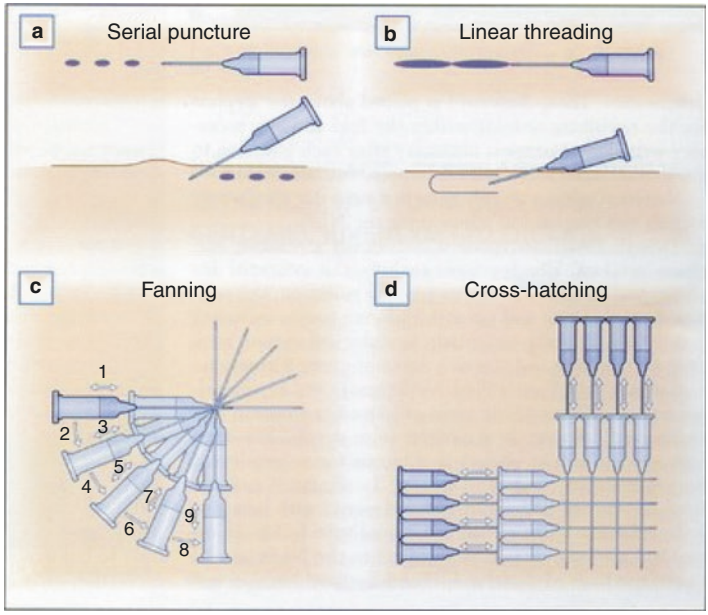

Figure 11.5 Filler techniques of injection (**a**) Serial puncture; (**b**) threading; (**c**) Fanning; (**d**) Cross-hatching. (https://www.sandine-zartaux.com/en/zartaux-dermamed/54-zartaux-dermafill-plus.html)

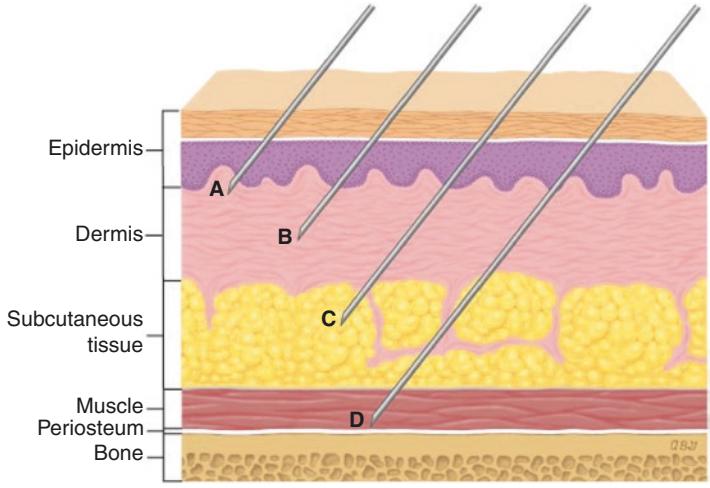

Figure 11.6 Depth and angle of injection (**a**) Level of superficial filler; (**b**) Level of mid-dermal filler; (**c**) Level of deep fillers; (**d**) Level of subcutaneous fillers (https://www.drgambhir.com/depth-of-filler-placement.html)

Adverse Events

Complications include swelling, redness, clumping, lumping, nodules, infection, necrosis, and granulomatous reactions.

Impending necrosis

1. Massage area and apply warm compresses
2. Apply 2% nitroglycerin
3. If HA filler: administer hyaluronidase: dose is determined based on amount of product injected. HA sensitivity depends on each product.

Recommendations to avoid adverse events

- Knowledge of facial anatomy
- Appropriate patient and filler selection
- Appropriate technique
- Use the smallest needle that allows for adequate flow
- Check syringe for reflux (aspirate before inject)
- Inject slowly and with small volumes
- Minimize number of injection sites

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Index

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