



Skin-Melanocytic tumors - Printer Friendly Version

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Primary references - Skin-Melanocytic tumors chapter

[AJCC Cancer Staging Manual \(6th Ed\)](#)

[American Journal of Dermatopathology](#), January 2000 to October 2008

[American Journal of Surgical Pathology \(AJSP\)](#), January 2000 to November 2008

[Archives of Pathology and Laboratory Medicine \(Archives\)](#) [free full text, no registration always], January 1999 to November 2008

[BMC Dermatology](#) [free full text & no registration always] March 1988 to 24 October 2008

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[Human Pathology \(Hum Path\)](#), January 2000 to November 2008

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Rosai, J: Ackerman's Surgical Pathology (9th Ed), Mosby, 2004

Sternberg, S: Diagnostic Surgical Pathology (4th Ed); Lippincott Williams & Wilkins, 2004

Websites: [PathoPic](#)

Journal search: review all abstracts plus search PubMed for each topic below in November 2008

Dermoscopy - Skin-Melanocytic tumors chapter

Also called dermatoscopy

See also discussion under particular entities

Method of skin examination using an optical instrument with a light source; allows visualization of pigmentation patterns and skin structures deeper than can be seen with naked eye; link between clinical and histologic examination, permitting an earlier diagnosis ([Int J Dermatol 2008;47:712](#))

Useful to analyze pigmented skin lesions - benign lesions tend to have symmetrical dermoscopic structures and colors but malignant lesions tend to have irregular and atypical dermoscopic structures ([J Dermatol 2006;33:513](#))

Improves the ability of primary care physicians to accurately triage lesions suggestive of skin cancer ([J Clin Oncol 2006;24:1877](#))

Standardized reporting system has been recommended ([J Am Acad Dermatol 2007;57:84](#))

ABCDE criteria are commonly used: asymmetry, irregular borders, multiple colors, diameter >6 mm, enlarging lesion

CASH algorithm (color, architecture, symmetry, homogeneity) may also be useful ([J Am Acad Dermatol. 2007;56:45](#))

Nevus type varies by skin type in white people ([Arch Dermatol 2007;143:351](#))

Atypia may be due to radiation therapy in area of a nevus ([Dermatol Surg 2006;32:100](#))

Recommended to use alcohol based gel as immersion fluid to prevent nosocomial infections ([Dermatol Surg 2006;32:552](#))

Image collections / lectures: [Dermoscopy.org](#), [DermLectures.com](#), [Dermoscopy Atlas](#)

Dermoscopes: [DermLite](#), [DermaGenius](#)

References: [eMedicine](#)

Nevi

Nevi-general - Skin-Melanocytic tumors chapter

Definition: congenital circumscribed growth of the skin, usually refers to mole or benign melanocytic abnormality

See also [Eye-Conjunctiva](#)

Nevus (singular) also spelled naevus

Means birthmark in Latin

Also called melanocytic, nevocellular or pigmented lesion

Most common melanocytic tumor

Usually clinically evident between ages 2-6 years; most whites have 20-30 nevi; can estimate total body count 13-14 year olds by examining lateral arms ([Am J Epidemiol 2007;166:472](#))

Nevi common on head, neck and trunk, compared to extremities for melanoma

Mostly occur in skin, but also mucosal membranes covered by squamous epithelium

May be neoplastic since many are clonal

Existence of freckles, lentiginos (small, pigmented, flat or slightly raised spots with a clearly defined edge, but no nests of melanocytes) and melanocytic nevi increases chance of having melasma ([BMC Dermatol 2008 Aug 5;8:3](#))

Often accompanied by keratinous cysts, abscess, folliculitis

Incidental microscopic aggregates of nevi cells occur in 1% of skin excisions ([Am J Dermatopathol 2008;30:45](#)); also occur in clusters in lymph node capsules, particularly in axilla (see [Lymph Nodes](#) chapter)

Atypia may occur due to radiation therapy ([Dermatol Surg 2006;32:100](#))

Large numbers of nevi are risk factor for melanoma ([Int J Cancer 2008 Sep 12 \[Epub ahead of print\]](#))

Increasing numbers of nevi are associated with neonatal phototherapy ([Arch Dermatol 2006;142:1599](#)), sun exposure on hot holidays ([J Invest Dermatol 2005;124:56](#)), number of nevi in parents ([Cancer 2003;97:628](#)), although this does not necessarily mean these factors are risk factors for melanoma

Patterns associated with benign behavior: lentiginous hyperplasia (single cell melanocytic growth along dermoepidermal junction), nested proliferation, pagetoid proliferation (discohesive single cell growth throughout entire epidermis—seen in Spitz nevi and acral nevi, as well as melanoma), melanocyte nuclei smaller than in adjacent keratinocytes, transdermal elimination of melanin pigment

Color: due to Tyndall effect (scattering of light as it hits melanin granules, [Wikipedia](#)); melanin in stratum corneum appears black, melanin in reticular dermis appears slate-gray or blue

Nevi may regress due to lymphocytic infiltration (see [halo nevus](#))

Dermoscopy: nevus type varies by skin type in white people ([Arch Dermatol 2007;143:351](#))

Nevi-general - Skin-Melanocytic tumors chapter

Case reports: melanocytic intranuclear inclusions due to molluscum contagiosum ([J Cutan Pathol 2008;35:782](#)), nodal nevus cells associated with dermatopathic lymphadenopathy ([Diagn Cytopathol 2004;31:180](#))

Treatment: excise new lesions in adult, giant congenital nevi, nevi causing chronic mechanical irritation, itching, bleeding, ulceration or oozing of serum; nevi with rapid growth, deepening pigmentation, pigmentation beyond outline of lesion, flat areas of depigmentation or erythema; don't excise using cautery (distorts tissue); skin graft may be required for large nevi ([Mil Med 2008;173:105](#)); shaving may be acceptable for facial lesions ([Int J Dermatol 2004;43:533](#))

May recur with incomplete excision (shave biopsy), usually within 3 months; recurrent nevus may resemble melanoma due to irregular scarring, lentiginous melanocytic hyperplasia, basilar keratinocytic hyperpigmentation, nuclear enlargement and prominent nucleoli

Clinical: papule or macule, tan-brown, uniformly pigmented, small (0.6 cm or less); often erosion or ulceration if adjacent to a hair follicle, with a granulomatous response or scale crust

Micro: may have sclerotic changes resembling melanoma ([J Cutan Pathol 2008;35:995](#)), myxoid changes, amyloid deposition, elastosis, psammoma bodies, metaplastic bone, cytoplasmic vacuoles or oncocyctic changes ([Am J Dermatopathol 2002;24:468](#)); may cause acantholytic changes in overlying epidermis; plasma cells in 6% ([Acta Dermatovenerol Croat 2008;16:158](#))

Micro: type A cells - in superficial dermis; pigmented epithelioid cells with well defined cell boundaries, abundant eosinophilic to amphophilic cytoplasm containing coarse melanin granules, uniform round/oval nuclei slightly smaller than that of adjacent keratinocytes, finely dispersed chromatin, delicate nuclear membrane, no/small distinct eosinophilic nucleoli

type B cells - in intermediate dermis; cells more lymphoid than epithelioid; decreased cytoplasm with no melanin, smaller and slightly hyperchromatic nuclei with dispersed chromatin and no nucleoli

type C cells - in deep dermis; spindled, fibroblast-like or schwannian cells with oval nuclei and bland chromatin; single cell infiltration of superficial reticular collagen

maturation - deeper portion of lesion has smaller cells with less pigment and less atypia; deep cells grow in smaller sized nests or single cells; may resemble neural tissue

traumatized nevi - features include parakeratosis (92%), dermal telangiectasias (61%), ulceration (51%), dermal inflammation (49%), melanin within stratum corneum (24%), dermal fibrosis (25%), pagetoid spread of melanocytes limited to the site of trauma (20%) or away from areas of trauma (8%) ([Am J Dermatopathol 2007;29:134](#))

Positive stains: MelanA in type A and B but not type C cells

Molecular: BRAF mutations in 75% of congenital and acquired nevi ([Am J Dermatopathol 2007;29:534](#)), have clonal genetic changes ([Hum Path 2002;33:191](#))

Videos: [DermLectures.com](#); [recurrent nevi](#)

Acral nevi - Skin-melanocytic tumors chapter

Defined as either (a) lesion of volar or dorsal hands/feet or (b) only volar (palm/sole) hands/feet

Present in 4-9% of population, usually elderly patients

May resemble early acral melanoma, although melanomas are rare at these sites

Clinical: circumscribed, light brown, not palpable, flat to side lighting

Dermoscopy: parallel patterns present ([Dermatology 2008;216:205](#))

Micro: more cellular than most nevi; usually junctional; lentiginous pattern common with moderate melanin pigment; often low level pagetoid, single cell migration into stratum spinosum; possible transepidermal elimination of pigmented nevus cells within stratum granulosum; large, oval, vertically oriented junctional nests surrounded by retraction artifact; nevus cells mature to lesional base

DD: dysplastic nevi (have anastomosing rete ridges, cytological atypia and well-formed lamellar fibroplasia, [Histopathology 1995;27:549](#))

References: [Mod Path 2006;19 Suppl 2:S4](#)

Ankle nevi - Skin-melanocytic tumors chapter

Cases with atypical features typically occur in women (73%), have moderate-severe architectural abnormalities in 100%, mild-moderate atypia in 78%, but do not recur ([AJSP 2007;31:1130](#))

Auricular nevi - Skin-melanocytic tumors chapter

Often 6 mm or more

May be symmetric with pagetoid spread and moderate/marked atypia with nucleoli, but no mitotic figures or apoptotic melanocytes ([Am J Dermatopathol 2005;27:111](#))

May have irregularity of nesting pattern; nests may be poorly circumscribed with lateral extension of junctional component beyond the dermal component; also elongation of rete ridges with bridging between them ([J Cutan Pathol 2005;32:40](#))

Flexural skin nevi - Skin-melanocytic tumors chapter

Flexural sites: axilla, umbilicus, inguinal creases, pubis, scrotum and perianal area

Micro: lentiginous and nested patterns of junctional proliferation similar to nevi of genital skin; confluence of enlarged nests with variation in size, shape and position at dermoepidermal junction; diminished cohesion of melanocytes ([J Cutan Pathol 2000;27:215](#))

DD: dysplastic nevi (cytologic atypia present, stromal alterations)

Genital nevi - Skin-melanocytic tumors chapter

Rare, often large and irregularly shaped

Usually young women in vulva, also children

Benign behavior with only rare recurrence ([AJSP 2008;32:51](#))

Atypical melanocytic nevi of genital type: young women, symmetric lesions with well demarcated lateral margins, prominent junctional component with round/fusiform nests, retraction artifact, cellular dyscohesion or single cells, mild/moderate atypia, benign appearing dermal component with maturation and dense eosinophilic fibrosis in superficial dermis; no nuclear atypia in superficial dermis, no mitotic figures, do not recur after excision ([J Cutan Pathol 2008;35:24](#))

Micro: irregular nests and lentiginous melanocytic hyperplasia resembling melanoma, often retraction artifact or cellular dyscohesion; mild to severe atypia, but maturation always present; may have dermal fibrosis; no/rare mitotic figures

DD: dysplastic nevus (has eosinophilic and lamellar fibroplasia,

Head and trunk nevi - Skin-melanocytic tumors chapter

Clinical: papular, usually compound nevi in children / young adults, evolve into flesh colored dermal nevi with age

Micro: nevus cells commonly in lower third of reticular nevus; scalp nevi often have prominent neural component

DD: congenital nevus (present at birth, > 1.5 cm, nevus cells within epithelium of skin appendages)

Active nevus - Skin-Melanocytic tumors chapter

Terminology not in widespread use

Commonly before age 20 years

Solitary, small, very dark and papular nevus with prominent junctional component, melanocytic hyperplasia, intraepidermal melanin

Often increased cellularity, dermal inflammation, prominent nucleoli and occasional mitotic figures

Benign behavior

References: [Arch Dermatol 1983;119:35](#)

Balloon cell nevus - Skin-Melanocytic tumors chapter

Most melanocytes are large, pale with foamy or finely vacuolated cytoplasm but no atypia

Positive stains: melanocytic markers

DD: blue nevi, balloon cell melanoma (has radial growth phase, mitoses, and other types of melanoma cells in vertical growth component)

Becker's nevus - Skin-Melanocytic tumors chapter

Also called pigmented hairy epidermal nevus, Becker's melanosis

Present in 0.5% of young men ([Ann Dermatol Venereol 1981;108:41](#))

First described by Becker in 1948 ([Arch Dermatol 1948;60:155](#))

Associated with high androgen receptors ([J Am Acad Dermatol 1984;10:235](#), [J Am Acad Dermatol 2008;59:834](#))

May be associated with hypoplasia of ipsilateral breast ([Arch Iran Med 2006;9:68](#)), aplasia of ipsilateral pectoralis major muscle, limb shortening, lipoatrophy ([Clin Exp Dermatol 2002;27:27](#)), spina bifida, scoliosis

May occur with melanoma, although no known increased risk ([Dermatologica 1991;182:77](#))

Case reports: bilateral nevus in 18 year old man ([Indian J Dermatol Venereol Leprol 2008;74:73](#)),

with segmental naevus depigmentosus ([Australas J Dermatol 2007;48:224](#)), hypopigmented pityriasis versicolor developing on pre-existing Becker's naevus ([Indian J Dermatol Venereol Leprol 2002;68:43](#))

Treatment: none, laser ([Br J Dermatol 2005;152:308](#))

Clinical: sharply demarcated, unilateral, hyperpigmented, tan macule in teenager boy on back, shoulder or chest, hypertrichosis in 50%

Micro: increased epidermal pigmentation, mild acanthosis, hyperkeratosis, regular elongation of rete ridges; variable hypertrichosis; areas associated with smooth muscle hamartoma have more pronounced smooth muscle bundles irregularly dispersed within the dermis and unrelated to either hair follicles or vascular channels; does not actually contain nevus cells

References: [eMedicine](#)

Blue nevus - Skin-Melanocytic tumors chapter

Common type

See also [Eye-Conjunctiva](#)

No relationship to blue rubber bleb nevus syndrome ([eMedicine](#))

All variants (common, atypical, cellular, epithelioid, malignant) are uncommon

May be due to arrested migration of immature melanocytes in dermis

May evolve from ordinary non-blue nevi ([Ann Diagn Pathol 2007;11:160](#))

Associated with neurocutaneous melanosis

Usually small lesions of head, neck or upper extremity of young adults, particularly women

Blue color due to the Tyndall effect of selective absorption of parts of the light spectrum by deeply located (dermal) melanin pigment, which is usually abundant.

Case reports: plaque-like tumors ([AJSP 2000;24:92](#)), subungual tumor ([J Am Acad Dermatol](#)

[2008;58:1021](#)), poliosis (patch of gray/white hair) overlying a nevus with blue nevus features

([Dermatol Online J 2008;14\(2\):20](#)), persistent tumor ([J Am Acad Dermatol 2004;50:S118](#)), with

satellitosis ([J Eur Acad Dermatol Venereol 2001;15:570](#)), multiple blue nevi of penis ([J Cutan Pathol](#)

[2004;31:185](#)), involvement of nodal capsule #1 ([AJCP 1984;81:367](#)); #2 ([Pathologica 1992;84:547](#))

Clinical: heavily pigmented, solitary, < 1 cm, slightly elevated or dome-shaped

Dermoscopy: homogeneous, structureless pigment pattern with various colors (blue, white-blue, brown, black, polychromatic, [J Cutan Pathol 2007;34:543](#)); acral tumors may simulate melanoma ([Dermatology 2007;214:174](#))

Micro: ill defined deep dermal proliferation of spindled melanocytes with abundant pigment and melanophages, dissecting dermal collagen and often extending into subcutis; no junctional or superficial dermal involvement

Positive stains: S100, HMB45, MelanA/Mart1, other melanocytic stains; variable CD34

DD: benign fibrous histiocytoma (hemosiderin pigment, no melanin), dermatofibrosarcoma protuberans, metastatic melanoma

References: [eMedicine](#)

Atypical cellular blue nevus - Skin-Melanocytic tumors chapter

Atypia insufficient for definitive diagnosis of malignancy

Treat conservatively with excision

Experienced dermatologists frequently disagree on this diagnosis ([AJSP 2008;32:36](#))

Case reports: 37 year old woman with thigh mass ([J Dermatol 2000;27:730](#)), presenting as vascular lesion of back ([Ann Pathol 2000;20:228](#))

Micro: infiltrative margin or asymmetry, cellular atypia, prominent nucleoli, mitotic rate of less than 2 per square millimeter

References: [J Cutan Pathol 1998;25:252](#)

Cellular blue nevus - Skin-Melanocytic tumors chapter

Buttock and sacrococcygeal areas are most common; also scalp, face, dorsal hands and feet

Benign, but rarely recurs or involves regional lymph nodes

Melanomas may arise from cellular blue nevus

Amelanotic tumors have atypical clinical appearance

Note: no specific features separate benign and malignant blue nevi, even "metastases", since benign cellular blue nevi may involve lymph node parenchyma and sinuses in a metastatic-like pattern; as a result, some are best classified as having "uncertain biologic behavior"

Case reports: [Case of the Week #7](#); nevus cells in sentinel lymph node ([Eur J Dermatol 2008;18:586](#)), eyelid tumors ([J Am Acad Dermatol 2008;58:257](#)), with pilonidal cyst ([J Cutan Pathol 2007;34:942](#)), 14 year old boy with giant, infiltrative, facial tumor ([J Clin Pathol 2007;60:82](#)), 31 year old man ([Indian J Dermatol Venereol Leprol 2001;67:200](#)), 28 year old woman with intracranial extension ([J Clin Neurosci 2000;7:453](#))

Treatment: excision

Clinical: large (> 1.5 cm) with intense pigmentation

Micro: well circumscribed collection of interweaving fascicles with increased cellularity and extension into subcutis; heavily pigmented spindle cells alternate with clear cells; have pushing margins and variable fasciculation and neural structures; no/minimal atypia; no junctional activity, no epidermal invasion, no peripheral inflammation, no necrosis, no/rare mitotic figures; scalp lesions may have intracranial extension

"Ancient" blue nevi show stromal changes of large dilated vessels with pseudoangiomatous features, hyaline angiopathy, myxoid changes, sclerosis or hyalinization of stroma, variable edema, similar to ancient melanocytic nevi ([Am J Dermatopathol 2008;30:1](#))

Variants include desmoplastic, amelanotic ([AJSP 2002;26:1493](#)) or with balloon cell change

Positive stains: HMB45, MelanA/Mart1, variable S100, CD34 ([J Cutan Pathol 2001;28:145](#))

Negative stains: no/low Ki-67

Molecular: no chromosomal aberrations ([AJSP 2005;29:1214](#))

DD: blue melanoma (scalp or heel lesion with marked nuclear atypia, numerous mitotic figures, some atypical, and necrosis; variable epithelioid tumor cells)

Epithelioid blue nevus - Skin-Melanocytic tumors chapter

Very rare

May be part of Carney complex, which includes cardiac myxoma, psammomatous melanotic schwannoma, multicentric blue nevi, endocrine overactivity ([Orphanet J Rare Dis 2006 Jun 6;1:21](#)); may also occur by itself ([Am J Dermatopathol 2000;22:473](#))

May be a low grade melanoma; 60% have nodal metastases, but clinical course is otherwise indolent

May involve genital mucosa ([Br J Dermatol 2001;145:496](#))

Case reports: 2 year old boy with congenital giant melanocytic nevus on back and no evidence of Carney complex ([Am J Dermatopathol 2002;24:30](#)); involving oral mucosa ([Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:429](#))

Micro: poorly circumscribed but symmetric heavily pigmented dermal lesion; short fascicles, small nests and single cells; composed of both (a) heavily pigmented and globular melanocytes and (b) lightly pigmented and polygonal or spindle melanocytes; no/rare mitotic figures; usually no maturation and no dermal fibrosis

Malignant blue nevus - Skin-Melanocytic tumors chapter

Very rare

Melanoma arising in background of cellular or common blue nevus or resembling a blue nevus

Often in children or in scalp

May be present for many years before rapid growth occurs

Highly aggressive ([AJSP 2001;25:316](#)); may recur locally, extend into brain (if from scalp or eyelids), metastasize and cause death

Case reports: 5 year old girl ([Croat Med J 2005;46:463](#)), 11 year old girl with malignant blue nevus of left ear, associated with large nevus at same location and 2 intracranial melanocytic tumors ([Hum Path 2004;35:1292](#)), 41 year old man ([Am J Dermatopathol 2003;25:21](#)), 55 year old man with scalp lesion, nodal and distant cutaneous metastases ([Am J Dermatopathol 2007;29:88](#)), with nodal metastases ([J Cutan Pathol 2008;35:651](#)), scalp tumor with distant skin metastases ([Am J Dermatopathol 2007;29:88](#)), in keloid scar ([J Plast Reconstr Aesthet Surg 2008 Jan 7 \[Epub ahead of print\]](#))

Treatment: excise and examine carefully

Micro: expansile asymmetric nodule with benign component OR low power benign features plus infiltrative borders, necrosis, mitoses or atypical cytologic features; may have epithelioid features with large hyperchromatic nuclei, prominent nucleoli and cytoplasmic melanin

Note: no specific features separate benign and malignant blue nevi, even "metastases", since benign cellular blue nevus may involve lymph node parenchyma and sinuses in a metastatic-like pattern; some blue nevi are best classified as having "uncertain biologic behavior"

DD: "animal/equine" melanoma - infiltrative, aggregates along follicles, cells resemble melanophages but all cells are melanoma cells after bleaching

Cockarde nevus - Skin-Melanocytic tumors chapter

Also called cockade nevus

Appears to be rare; few recent publications

Concentric (targetoid) pattern of pigmentation, with central papule (pink to brown/black) surrounded by clear zone, then outer stippled pigment

Zonation may be due to failure of melanin synthesis ([Acta Derm Venereol 1980;60:360](#))

Micro: central lesion is junctional or compound nevus, intermediate zone is unremarkable, outer zone has multiple junctional melanocytic nests

References: [Pediatr Dermatol 1988;5:250](#)

Combined nevus - Skin-Melanocytic tumors chapter

Uncommon; two different types of melanocytic proliferation in the same pigmented lesion

Usually common blue nevus of penetrating type and acquired nevus ([Pathology 2004;36:419](#)); rarely includes Spitz nevus, which are difficult to classify by dermoscopy ([J Cutan Pathol 2004;31:600](#))

Mean age 30 years, usually trunk, head and neck, upper extremity

Clinical diagnosis is often melanoma, particularly at dermoscopy ([Dermatology 2007;214:174](#), [Dermatol Surg 2006;32:1176](#))

Case reports: common blue nevus and pigmented epithelioid melanocytoma ([J Am Acad Dermatol 2008;58:1021](#)), compound nevus and spindle cell Spitz nevus ([J Dermatol 2000;27:233](#)), with melanoma in situ ([Am J Dermatopathol 1991;13:169](#))
References: [AJSP 1991;15:1111](#)

Compound nevus - Skin-Melanocytic tumors chapter

Only rarely undergoes malignant transformation

Case reports: 17 year old woman with pigmented lesion on mons pubis ([Archives 2003;127:e391](#)), compound nevus combined with Spitz nevus ([J Dermatol 2000;27:233](#))

Clinical: elevated or dome shaped, less pigmented than junctional nevi

Micro: features of both junctional and intradermal nevi (i.e. epidermal and dermal components); junctional component is similar to junctional nevus, with nests regularly distributed at bases of rete ridges, occasional lentiginous pattern, no pagetoid spread, no atypia, and tendency to diminish with patient age; dermal component consists of nests (may be very large) or linear pattern of melanocytes, cells are small with scant cytoplasm and regular nuclei, cells mature with depth by becoming more slender / spindled with less pigment; dermal melanocytes or nests are separated by collagenous stroma; often clusters of chronic inflammatory cells at base of nevus; mucin in < 1% ([Am J Dermatopathol 2008;30:236](#))

Congenital nevus - Skin-Melanocytic tumors chapter

1-2% of newborns ([Dermatology 2007;214:227](#)), 17% of Italian children ages 12-17 years, usually 6-15 mm

Congenital usually refers to presence at birth, may also refer to clinical appearance or histologic pattern

Usually larger than acquired nevi; may grow rapidly

Associated with higher number of common melanocytic nevi and family history of melanoma, but not with sun exposure ([Br J Dermatol 2008;159:433](#))

May be associated with infantile hemangioma ([J Am Acad Dermatol 2008;58:S16](#))

Proliferative nodules in these nevi are often p53+ (67%) and c-kit+ (97%), but are usually benign and may regress ([AJSP 2004;28:1017](#))

Associated with nevus cells in lymph nodes ([Am J Dermatopathol 2002;24:1](#))

Overall risk of melanoma is 0.7% ([Br J Dermatol 2006;155:1](#))

Acral lesions resemble melanoma clinically

Agminate nevi: means "clustered"; includes nevus spilus (flat mole), a discrete, hyperpigmented foci on a hyperpigmented macular background due to nests of nevus cells within superficial dermis associated with minimal basilar keratinocyte hyperpigmentation

Neuronevus: congenital nevi with prominent neural features

Case reports: with benign proliferative nodule ([J Am Acad Dermatol 2008;59:518](#)), with subsequent melanoma ([Archives 2003;127:e343](#), [J Plast Reconstr Aesthet Surg 2007 Dec 8 \[Epub ahead of print\]](#)), halo congenital nevus in 56 year old woman with vitiligo ([Australas J Dermatol 2008;49:229](#)), with smooth muscle hamartoma ([J Cutan Pathol 2008;35:83](#)), congenital panfollicular nevus ([J Cutan Pathol 2007;34:14](#)), rapid severe repigmentation after curettage and dermabrasion ([Br J Dermatol 2007;156:1251](#))

Treatment: early surgical removal, laser resurfacing in neonates ([Br J Dermatol 2006;154:889](#))

Clinical: often large, irregular in contour and pigmentation, hair bearing

Dermoscopy: globules (83%), hypertrichosis (79%), and reticular networks (71%) ([Arch Dermatol 2007;143:1007](#))

Micro: tends to involve reticular dermis, subcutis, skin adnexa, arrector pili muscles and nerves with single cell permeation of collagen; also neural differentiation with Wagner-Meissner-like corpuscles; frequent proliferative nodules

Lesions of infants may have pagetoid melanocytic proliferation

Proliferative nodules: dermal nodules of large epithelioid or spindled melanocytes that merge with surrounding nevus cells; often prominent nucleoli, cellular areas, focal hemorrhage and ulceration, but no necrosis, no destructive growth, minimal inflammation and 0-4 mitotic figures/10 HPF; lesions mature and regress over time

Molecular: lesions present at birth usually have NRAS but not BRAF mutations; those with congenital type histologic features but not present at birth more commonly have BRAF but not NRAS mutations ([J Invest Dermatol 2007;127:179](#))

DD: glomus tumor, melanoma

References: [eMedicine](#)

Giant congenital nevus - Skin-Melanocytic tumors chapter

Also called giant pigmented nevus or giant hairy nevus

May be defined as surface area of 144 cm² or larger

2-42% risk of malignant transformation, with 6-14% lifetime risk of melanoma, often extracutaneous

Dermatomal, "bathing suit" or "garment" configuration; may involve entire scalp, extremity, most of trunk or placenta

May have satellite nevi, including within mucosal membranes

Scalp lesions are often in thickened folds of skin resembling cerebrum, may involute in first 2 years of life ([J Am Acad Dermatol 2008;58:508](#))

Truncal nevi may develop symptomatic neurocutaneous melanosis (meningeal or cerebral melanosis), which is lethal in 1/3 ([J Am Acad Dermatol 2006;54:767](#))

May give rise to melanoma of skin or CNS or related neuroectodermal tumors (malignant peripheral nerve sheath tumor, cutaneous malignant melanotic neurocristic tumor, rhabdomyosarcoma, liposarcoma)

Case reports: newborn with neurocutaneous melanosis ([J Neuroradiol 2007;34:272](#)), part of SCALP syndrome ([J Am Acad Dermatol 2008;58:884](#)), neonatal patient with proliferative nodules ([Clin Exp Dermatol 2008;33:125](#)), ulcerated and sclerotic lesion ([Clin Exp Dermatol 2007;32:529](#)), desmoplastic giant congenital nevus with progressive depigmentation ([J Am Acad Dermatol 2007;56:S10](#))

Treatment: possibly none for newborn scalp lesions; excision may require careful planning and several stages ([Plast Reconstr Surg 2008;121:1674](#)); often split-thickness skin grafting ([Ann Plast Surg 2008;60:283](#)); laser surgery if inoperable ([Clin Exp Dermatol 2007;32:159](#))

Micro: similar to congenital nevus; deeper nevus cells may be E-cadherin negative, contributing to their motility ([J Dermatol Sci 2008;52:21](#))

Connective tissue nevus - Skin-Melanocytic tumors chapter

A hamartoma, not a melanocytic lesion

See [Skin-Nonmelanocytic tumors](#) chapter

Deep penetrating nevus - Skin-Melanocytic tumors chapter

First reported in 1989 ([AJSP 1989;13:39](#))

Uncommon lesion

Usually face, neck, shoulder, less than 1 cm

May be confused diagnostically with melanoma ([J Plast Reconstr Aesthet Surg 2007;60:1252](#))

Case reports: skin of cheek ([Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:e49](#)), linear arrangement of multiple deep penetrating nevi ([Arch Dermatol 2003;139:1608](#))

Treatment: simple excision; only rarely recurs ([Histopathology 2003;43:529](#))

Micro: nevus whose dermal component extends into reticular dermis or subcutis; cellular, nested or fascicular, with abundant pigment and mild atypia; usually inconspicuous junctional component; no/rare mitotic figures, no/rare inflammation; may be combined with other nevi

DD: vertical growth phase of melanoma (mitotic figures and marked atypia, ATM immunostaining may differentiate, [Cancer Epidemiol Biomarkers Prev 2007;16:2486](#))

References: [Arch Dermatol 1993;129:328](#)

Dermal nevus - Skin-Melanocytic tumors chapter

Definition: all melanocytes are within the dermis

Also called intradermal nevus

Most common adult type of nevus; represents the final stage in progression from junctional to compound to dermal nevus

Seen mainly after adolescence

Melanomas only rarely arise from intradermal nevi ([Dermatology 1998;196:425](#))

Rarely has cerebriform appearance ([Cutis 2004;73:254](#)), and these nevi may be congenital

Case reports: prominent schwannian differentiation ([Am J Dermatopathol 2002;24:39](#)), osseous metaplasia/Osteo-nevus of Nanta ([Dermatol Online J 2007;13\(4\):16](#))

Clinical: flat, pedunculated or papillary; often hairy; flesh colored or lightly pigmented (usually become lighter over time); pigmentation may be in flecks up to 1 cm

Dermoscopy-nonpigmented lesions: brown pigment (78%) white areas (53%), comma shaped vessels (50%), hair (47%), hairpin vessels (22%), comedolike openings (22%), dotted vessels (19%) ([Dermatol Surg 2007;33:1120](#))

Micro: small nests of melanocytes in upper dermis, often around pilosebaceous units, with variable pigmentation and cellularity; may have multinucleated melanocytes; deeper portion is usually less pigmented and less cellular and may have Wagner-Meissner corpuscles (representing neural portion of nevus); mucin in 3% in stroma and within nests of nevus cells ([Am J Dermatopathol 2008;30:236](#)); rarely nevus giant cells, balloon cells, infiltration by fat cells or osseous metaplasia; no junctional component

Can also be classified as Unna's pattern (purely adventitial lesion confined to expanded papillary dermis and often to perifollicular dermis, usually neck, trunk or limbs) or Miescher's pattern (melanocytes diffusely infiltrate adventitial and reticular dermis in wedge shaped pattern, usually on face) ([Am J Dermatopathol 2007;29:141](#))

Divided / kissing nevus - Skin-Melanocytic tumors chapter

Also called split ocular nevus

Rare type of congenital nevus usually involving upper and lower eyelids of one eye

May also appear after birth

May involve penis ([Clin Exp Dermatol 2004;29:471](#))

Treatment: surgery for cosmetic reasons and to prevent later malignant change ([In Vivo 2007;21:137](#), [J Plast Reconstr Aesthet Surg 2007;60:260](#)); may decline treatment

Dysplastic nevus - Skin-Melanocytic tumors chapter

Also called atypical nevus, nevus with architectural disorder, Clark's nevus; overlaps with active nevus

Controversial; may be intermediate step in pathway between benign nevus and melanoma ([J Clin Pathol 2005;58:453](#))

Better defined in dysplastic nevus syndrome (multiple dysplastic nevi and two family members with melanoma)

Rosai believes solitary nevus with dysplastic features should be treated as clinically benign

Develop in teenager years and into adulthood; atypical nevi of scalp of adolescents resemble those in genitalia, with apparent benign behavior ([J Cutan Pathol 2007;34:365](#))

Relative risk of 46x for melanoma in one study of Dutch patients with 5+ atypical nevi ([J Am Acad Dermatol 2007;56:748](#))

Higher risk for melanoma with more severe atypia ([Mod Path 2003;16:764](#))

May occasionally be associated with neurofibroma ([J Cutan Pathol 2007;34:837](#))

Punch biopsy NOT recommended ([Australas J Dermatol 2005;46:70](#))

Case reports: agminated dysplastic nevi ([Arch Dermatol. 2001;137:917](#)), melanoma arising in dysplastic nevus with intradermal sebocyte-like melanocytes ([Am J Dermatopathol 2007;29:566](#)), multiple eruptive dysplastic nevi and in situ melanomas appearing shortly after completion of chemotherapy ([Pediatr Dermatol 2007;24:135](#)), pointillist dysplastic nevus ([Arch Dermatol. 2005;141:763](#))

Clinical: atypical due to size > 5 mm, irregular borders, variegated appearance

Dermoscopy: pigment patterning often disrupted with brown dots, frequently erratically placed; nevi often irregular in shape, asymmetric, with variable coloration and borders that vary from sharply to poorly defined

Micro: compound nevi with marked lentiginous proliferation of melanocytes at dermoepidermal junction extending at least 3 rete ridges beyond lateral margins of dermal component; nests have cytologic and architectural atypia, including irregular sizes and shapes and bridging of adjacent rete ridges, which are themselves irregular; dermis is fibrotic with perivascular infiltrate and vascular dilation; usually mild/moderate cytologic atypia (nuclear hyperchromasia, prominent nucleoli, dusty melanin pigment); melanocytes are spindled and parallel to surface or epithelioid; epidermolytic hyperkeratosis present but not specific ([Am J Dermatopathol 2002;24:23](#))

Mild atypia: at high power, nuclei of melanocytes are condensed, oval/ellipsoid, hyperchromatic, indented, no/small nucleoli; perinuclear halo common; no/minimal pagetoid upward migration of melanocytes; no mitotic figures in dermal component

Moderate atypia: at high power, nevus nuclei are variable in size and chromatin, although some have "mild atypia" plus small nucleoli; enlarged cytoplasm compared to melanocyte, no halo; few but normal mitotic figures in upper dermal part of nevus

Severe atypia: usually asymmetrical but still well circumscribed in epidermis; usually nests of nevus cells, not individual cells; some central upward migration of individual nevus cells; crowded nests in dermis; enlarged nuclei, often bizarre hyperchromatic nuclei mixed with small nuclei, prominent nucleoli; no confluent atypia as seen with melanoma, frequent mitoses in junctional component but not in deep dermal component

Note: grading is not consistent between pathologists ([Br J Dermatol 2006;155:988](#))

Children: may want to downgrade atypia since ordinary childhood nevi have large nests and large nevus cell size, as well as focal atypia

Pagetoid upward migration at periphery may suggest upgrading to melanoma in situ

Mitotic figures at base of dermal component suggests invasive melanoma

Positive stains: Ki-67 index intermediate between benign nevi and melanoma ([Appl Immunohistochem Mol Morphol 2007;15:160](#))

Molecular: usually diploid; often mutations in CDKN2A ([Cancer. 2002;94:3192](#)), 24% have high risk mucosal HPV by PCR ([Br J Dermatol 2005;152:909](#))

EM: cases with severe dysplasia share several features with radial growth phase melanomas, including: large cell size, bizarre shaped and pleomorphic nuclei, well developed Golgi, abundant and deranged mitochondria, aberrant melanosomes with deranged structures and irregular melanization

DD: in situ melanoma arising in a compound nevus (atypia limited to epidermis, consumption of epidermis present, [Am J Dermatopathol 2007;29:527](#), be cautious if partial excision-[J Cutan Pathol 2005;32:405](#)), common nevus with some dysplastic features ([Am J Dermatopathol 2000;22:391](#))

References: [eMedicine](#)

Epidermolysis bullosa nevus - Skin-Melanocytic tumors chapter

Definition: large acquired melanocytic nevi that occur in patients with hereditary epidermolysis bullosa

First described in detail in 2001 ([J Am Acad Dermatol 2001;44:577](#))

Resembles melanoma, but benign behavior

Melanocytic growth factors in blister fluid may promote proliferation, migration and melanogenesis of disconnected melanocytes ([Acta Derm Venereol 2003;83:332](#))

Case reports: large nevus in toddler ([Arch Dermatol 2007;143:1164](#)), 2 infants with recessive dystrophic epidermolysis bullosa ([Clin Exp Dermatol 2005;30:636](#)), similar findings in childhood vulvar pemphigoid ([Dermatology 2006;213:159](#))

Clinical: asymmetrical, irregularly pigmented (initially very dark, then loses pigment), foci of stippled pigmentation and scarring

Dermoscopy: some features of melanoma are common - irregular pigmentation (96%), multicomponent pattern (87%), atypical pigment network (74%), irregular dots/globules (70%), atypical vascular pattern (30%); other features associated with melanoma progression are rare - irregular streaks, blue-white veil, regression structures (blue-white areas), black dots ([Br J Dermatol 2005;153:97](#))

Micro: features of persistent melanocytic neoplasm

Hair follicle nevus - Skin-Melanocytic tumors chapter

A hamartoma, not a melanocytic lesion

See [Skin-Nonmelanocytic tumor](#) chapter

Halo nevus - Skin-Melanocytic tumors chapter

Also called leukoderma acquisitum centrifugum, Sutton's nevus ([Am J Dermatopathol 2003;25:349](#))

Nevus surrounded by zone of hypopigmented skin

Usually due to regression caused by cell mediated immunity, or less commonly humoral immunity or granulomatous inflammation ([Am J Dermatopathol 2008;30:233](#)); in contrast to melanoma, there is no fibrosis ([J Cutan Pathol 2007;34:301](#))

Trunk of young patients; may be single or multiple

Seen in 18% of Turner's syndrome patients ([J Am Acad Dermatol 2004;51:354](#))

Note: classify based on nevus cell population because halo phenomenon occurs in various nevus types ([J Cutan Pathol 1995;22:342](#))

Treatment: observation, excision (for cosmetic reasons), laser for facial lesions to induce repigmentation ([J Cosmet Laser Ther 2007;9:245](#))

Micro: residual melanocytes with heavy infiltration by lymphocytes and histiocytes that destroy pigment containing cells

DD: lymphoma, melanoma, dermatitis

References: [eMedicine](#)

Ito's nevus - Skin-Melanocytic tumors chapter

First described by Minor Ito in 1954 ([Tohoko J Exper Med. 1954;60:10](#))

Usually affects Orientals, also Hispanics, blacks, Native Americans

Different entity from Hypomelanosis of Ito, a neurocutaneous disorder ([J Child Neurol 2000;15:635](#))

Often occurs with nevus of Ota in same patient, but is much less common

Similar to nevus of Ota except for location; Ito's nevus is found in shoulder, side of neck and supraclavicular areas, within the distribution of the lateral (also called posterior) supraclavicular nerve and lateral cutaneous brachial nerves

Case reports: with nevus of Ota ([Indian J Dermatol Venereol Leprol 2004;70:112](#))

Clinical: macule with irregular blue-gray pigmentation

Treatment: laser for lightening pigment (cosmetic purposes)

Micro: deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen in reticular dermis; overlying epidermis is normal

References: [eMedicine](#)

Junctional nevus - Skin-Melanocytic tumors chapter

Melanocytic proliferation restricted to basal epidermis (junctional area)

Earliest stage of intraepidermal melanocytic proliferation

All ages, usually non-sun exposed areas, such as palms and soles ([J Am Acad Dermatol 2007;56:825](#))

Melanomas may arise from junctional nevi

Lentigo simplex: also called lentigo, lentiginos; often in acral sites; precursor lesion to nevi, with proliferation of melanocytes (but no nests) in epidermal basal layer along rete ridges ([DermNet NZ](#))

Multiple lentiginos: associated with Peutz-Jeghers syndrome, centrofacial lentiginosis, Moynahan's syndrome, LEOPARD syndrome, Carney's syndrome, xeroderma pigmentosum

Case reports: with mastocytoma ([Am J Dermatopathol 2004;26:478](#))

Treatment: none needed, excision (cosmetic reasons), laser for flat lesions ([Br J Dermatol 2003;148:80](#))

Clinical: small, flat or slightly elevated, nonhairy, deeply pigmented

Dermoscopy: regular pigmented network of brown and uniform color, more prominent in the center, with gradual fading to the borders (reticular pattern); may have black or brown globules and dots regularly distributed inside the lesion (usually in central region)

Micro: rounded nests of melanocytes / nevus cells on epidermal side of dermoepidermal junction, originating from tips of rete ridges; variable lentiginous melanocytic hyperplasia

Lentiginous nevus - Skin-Melanocytic tumors chapter

See also [speckled lentiginous nevus](#)

Often benign mole with increase in size, formation of irregular borders or peripheral change in color

May be due to “reactivation” of radial proliferation

Benign, but complete excision is recommended

Acral lesions resemble dysplastic nevus due to elongation of rete ridges, continuous proliferation of melanocytes at dermoepidermal junction, single scattered melanocytes or less commonly small clusters within the upper epidermis, poor or absent lateral circumscription, melanocytes with abundant pale cytoplasm and round/oval, sometimes hyperchromatic nuclei and prominent nucleoli present at the dermoepidermal junction; however they lack anastomosing rete ridges, cytological atypia and well-formed lamellar fibroplasia ([Histopathology 1995;27:549](#))

Clinical: usually 5 mm or less

Micro: “shoulder” area of lentiginous junctional melanocytic proliferation beyond lateral border of underlying dermal nevus; elongation of rete ridges with small nests of melanocytes at tips of rete; often mild lymphohistiocytic infiltrate with pigment incontinence; no atypia, no pagetoid spread, no dermal fibrosis

DD: lentiginous (no nests, may be nevi if examine serial sections, [Am J Dermatopathol 1985;7 Suppl:5](#)), dysplastic nevi, superficial spreading melanoma (pagetoid lateral spread, mitotic activity in deep dermis, no maturation, [Mod Path 2005;18:1397](#))

Note: atypia often present in childhood acral lesions ([Pediatr Dev Pathol 1998;1:388](#))

Meyerson's nevus - Skin-melanocytic tumors chapter

Also called halo dermatitis ([Br J Dermatol 1988;118:125](#))

First described in 1971 ([Arch Dermatol 1971;103: 510](#))

Usually trunk and proximal upper extremities

Eczematous halos may also develop around atypical nevi ([J Am Acad Dermatol 1996;34:357](#))

Case reports: 12 year old with 7 nevi exhibiting Meyerson phenomenon ([Dermatol Online J 2008;14\(2\):28](#))

Treatment: wait (may regress) or excision; do not recur or progress to melanoma ([Australas J Dermatol 2008;49:191](#))

Clinical: solitary, pruritic, erythematous eruption encircling a pre-existing pigmented nevus

Micro: epidermal spongiosis and dermal inflammation (CD3+ lymphocytes) associated with a usual type junctional or compound nevus; at most mild atypia, no regression (by definition)

Mongolian spot - Skin-Melanocytic tumors chapter

Congenital disorder, present at birth in most neonates from Asia, East-Africa, Turkey; also Native-Americans;

Incidence of 60-70% in Iran, Nigeria and Taiwan ([Pediatr Dermatol 2006;23:61](#), [Niger J Med 2001;10:121](#), [Chang Gung Med J 2007;30:220](#)), usually regresses over several years, almost always by puberty, but may persist ([Int J Dermatol 2005;44:43](#))

Ill defined area of blue discoloration, up to several centimeters, in lumbosacral region; may also occur at other sites

Usually not present in children with blond hair ([Turk J Pediatr 2006;48:232](#))

Extensive Mongolian spots may be associated with inborn errors of metabolism ([Pediatr Neurol 2006;34:143](#), [Br J Dermatol 2003;148:1173](#))

Case reports: darker pigmented Mongolian spot superimposed on another Mongolian spot ([Pediatr Dermatol 2008;25:233](#)), facial lesion ([J Dermatol 2007;34:381](#))

Treatment: wait for regression, laser ([Lasers Med Sci 2007;22:159](#))

Micro: normal at low power; high power shows occasional deep dendritic melanocytes with melanin granules dissecting bundles of dermal collagen; no associated melanophages

DD: bruises from child abuse

References: [eMedicine](#), [Wikipedia](#)

Naevus sebaceous of Jadassohn - Skin-Melanocytic tumors chapter

A hamartoma, not a nevus

See [Skin-nonmelanocytic tumors](#) chapter

Ota (nevus of Ota) - Skin-Melanocytic tumors chapter

Also called oculodermal melanosis

First described by Ota in 1939 ([Tokio Med J 1939;63:1243](#))

Uncommon hamartoma in periorbital and temporal skin

Usually Orientals, also Hispanics, blacks, Native Americans

60% have lesions at birth, 87% female, 60% have dermal and ocular involvement ([Indian J Dermatol Venereol Leprol 2008;74:125](#))

Tends to persist and extend locally, becoming increasingly prominent with age, puberty and postmenopausal state

Associated with ipsilateral glaucoma, intracranial melanocytosis; rarely with cutaneous, ocular or intracranial melanoma ([Cutis 2008;82:25](#)), vascular nevus ([J Am Acad Dermatol 2008;58:88](#))

Type IA: Mild orbital type: distribution over upper and lower eyelids, periocular and temple region

Type IB: Mild zygomatic type: pigmentation in infrapalpebral fold, nasolabial fold and the zygomatic region

Type IC: Mild forehead type: involvement of forehead alone

Type ID: Involvement of ala nasi alone

Type II: Moderate type: distribution over upper and lower eyelids, periocular, zygomatic, cheek and temple regions

Type III: Involves scalp, forehead, eyebrow and nose

Type IV: Bilateral

Reference: Tanino, [Jpn J Dermatol 1939;46:435](#)

Hori's nevus: acquired bilateral nevus of Ota-like macules ([J Am Acad Dermatol 1984;10:961](#), [Dermatol Online J 2005;11\(4\):1](#)); usually Chinese women with family history, become more confluent and gray over time ([Br J Dermatol 2006;154:50](#))

Sun's nevus: acquired unilateral nevus of Ota

Case reports: with iris melanoma ([Surv Ophthalmol 2008;53:411](#)), 47 year old light-skinned non-Asian woman ([Dermatol Online J 2007;13\(3\):19](#)), bilateral with oral mucosa involvement ([Indian J Dermatol Venereol Leprol 2002;68:104](#)), acquired Ito's nevus in Caucasian elderly woman ([J Cutan Pathol 2007;34:640](#)), acquired bilateral nevus ([Dermatol Online J 2005;11\(4\):1](#))

Treatment: (a) cosmetic coverup products; (b) multiple sessions of laser photothermolysis to avoid darkening and extension, beginning early after diagnosis ([Dermatol Surg 2007;33:455](#)); (c) combined skin abrasion and carbon dioxide snow method ([Plast Reconstr Surg 1996;97:544](#)); cryosurgery and microsurgery **not** recommended due to scarring; chemical bleaching **not** recommended due to depigmentation

Clinical: macule with irregular blue-gray pigmentation in distribution of 1st and 2nd division of trigeminal nerve

Micro: deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen in reticular dermis

References: [eMedicine](#)

Phacomatosis pigmentokeratolica - Skin-Melanocytic tumors chapter

Rare syndrome defined by organoid nevus (occasionally with sebaceous differentiation), speckled lentiginous nevus and other extracutaneous anomalies

May be caused by twin-spot phenomenon (2 different mutant patches involving 2 adjacent or corresponding areas of the body, [Arch Dermatol 1998;134:333](#), [Am J Med Genet 1999;85:355](#))

Case reports: malignant degeneration of both nevus components ([Pediatr Dermatol 2005;22:44](#))

Phacomatosis pigmentovascularis - Skin-Melanocytic tumors chapter

Rare syndrome of widespread, aberrant and persistent nevus flammeus (vascular nevus, capillary malformation) and extensive pigment abnormalities

Divided into three main types:

Phacomatosis cesioflammea (blue spots [caesius = bluish gray] plus nevus flammeus) - also called types IIa/IIb; includes nevus of Ota; most common type ([J Am Acad Dermatol 2008;58:88](#)); often associated with Sturge-Weber and Klippel-Trenaunay syndromes

Phacomatosis spilorozea (nevus spilus [speckled lentiginous nevus] plus pale-pink telangiectatic nevus) - also called types IIIa/IIIb

Phacomatosis cesiomarmorata (blue spots plus cutis marmorata telangiectatica congenita) - also called type V

Subtypes: a - cutaneous involvement only, b - cutaneous and system involvement

Case reports: cutis tricolor coexistent with cutis marmorata telangiectatica congenita ([Eur J Dermatol 2008;18:394](#))

References: [Arch Dermatol 2005;141:385](#)

Pigmented spindle cell nevus - Skin-Melanocytic tumors chapter

Also called Reed's nevus

Often recent onset, on proximal extremities or trunk of young adults ([AJSP 1984;8:645](#))

Clinically resembles melanoma

Treatment: conservative but complete excision; does not recur

Clinical: < 1 cm, solitary, deeply pigmented, well-circumscribed maculopapule

Micro: symmetric with cytologic maturation; nests and fascicles of spindle melanocytes along dermoepidermal junction and within dermal papillae; may be junctional or compound; expansive not infiltrative growth pattern; extends no deeper than reticular dermis; nevus cells typically contain abundant melanin pigment, may be associated with melanophages; nuclei are monotonous, resemble normal keratinocytes and may have small nucleoli; often has architectural or cytologic atypia ([Hum Path 1991;22:52](#)); variable lymphocytic infiltrate at base of lesion; variable transepidermal elimination of junctional nests; no/rare mitotic figures

Note: hypopigmented variant is similar, but without abundant melanin ([J Cutan Pathol 2008;35 Suppl 1:87](#))

DD: superficial spreading melanoma ([Dermatol Online J 2004;10\(2\):5](#)), Spitz nevus

References: [J Am Acad Dermatol 1993;28:565](#)

Speckled lentiginous nevus - Skin-Melanocytic tumors chapter

Also known as Nevus spilus

Relatively common cutaneous lesion characterized by multiple darkly spotted light-brown macules or papules within a pigmented patch

Congenital ([Arch Dermatol 2001;137:172](#)) or acquired

Slight potential to develop into melanoma

Macular variant: tan-brown background with dark flat speckles in relatively even distribution resembling polka dots; associated with phacomatosis pigmentovascularis

Papular variant: light-brown macule superimposed by multiple melanocytic nevi in the form of papules or nodules that show a more uneven distribution reminiscent of a star map; small dark macules may be present; associated with phacomatosis pigmentokeratocica or speckled lentiginous nevi syndrome ([Dermatology 2006;212:53](#))

Case reports: with melanoma ([Int J Dermatol 2006;45:1362](#))

Treatment: excision of speckles or entire lesion

Micro: macular variant - 'jentigo' pattern (lentiginous pattern plus nests of melanocytes at dermal-epidermal junction) in the darker speckles and by some nests of melanocytes at the dermoepidermal junction at the tips of the papillae, but background pigmentation has microscopic features of lentigo

papular variant - dermal or compound melanocytic nevi

References: [Cutis 2007;80:465](#), [eMedicine](#)

Spitz nevus - Skin-Melanocytic tumors chapter

Also called spindle and epithelioid cell nevus, benign juvenile melanoma

First described by Sophie Spitz in 1948 ([AJSP 1948;24:591](#))

Usually occurs before puberty, but 2/3 at age 20+ years in one study ([Am J Dermatopathol 2005;27:469](#))

Usually single, but may also be multiple and clustered (agminate) or multiple and disseminated

Benign, but may recur if incompletely excised or even if "clinically removed" ([AJSP 2002;26:654](#))

May involve regional lymph nodes, particularly in controversial lesions ([AJSP 2002;26:47](#))

Misdiagnosis of melanoma as Spitz nevus is common cause of malpractice claims ([Archives 2006;130:617](#))

Sites: lower extremities, head and neck, trunk most common; tongue lesions may have pseudoepitheliomatous hyperplasia and resemble malignancy ([AJSP 2002;26:774](#))

Case reports: 2 year old boy with multiple clustered lesions on a pigmented macule ([Actas Dermosifiliogr 2008;99:69](#)), 23 year old woman with buccal lesion that metastasized ([Melanoma Res 2008;18:36](#)), 28 year old man with conjunctival tumor ([Bull Soc Belge Ophtalmol 2007;303:63](#)), 32 year old woman with lip lesion ([Clinics 2008;63:140](#)); multiple agminate nevi ([Melanoma Res 1998;8:156](#))

Treatment: complete excision to determine depth and extension with evaluation of margins; clinical followup, particularly of multiple or atypical lesions

Clinical: small, raised, pink/red or brown/black nodule; may resemble hemangioma or pyogenic granuloma; usually 6 mm or smaller

Micro: symmetric with sharp lateral borders, usually compound nevus with prominent intraepidermal component; 5% are junctional, 20% are dermal; composed of spindle cells and epithelioid cells; spindle cells may be arranged in fascicles perpendicular to epidermis, are cigar shaped with large nuclei and prominent nucleoli; epithelioid cells are dispersed individually, are polygonal with abundant eosinophilic cytoplasm, distinct cell borders, large nuclei and prominent nucleoli, variable mitotic figures, occasional multinucleation, often marked atypia, although most cells appear benign; cell maturation occurs in deep portion of tumor; also large and well formed Kamino bodies (eosinophilic hyaline bodies along dermoepidermal junction); may have pagetoid growth, lymphatic invasion, pseudoepitheliomatous hyperplasia, "tubular" growth pattern, plexiform growth pattern, halo reaction, prominent vasculature ([Am J Dermatopathol 2000;22:135](#)), lymphocytic infiltrate; scanty pigmentation

"Consumption of epidermis" (associated with melanoma) in 10%, defined as thinning of epidermis with attenuation of basal and suprabasal layers and loss of rete ridges in areas of direct contact with neoplastic melanocytes ([AJSP 2004;28:1621](#))

Positive stains: S100, HMB45; also WT1 (positive in melanoma and some dysplastic nevi, negative in other benign nevi, [Histopathology 2007;51:605](#)); Kamino bodies are PAS+ (even after predigestion with diastase); also S100A6 ([Mod Path 2003;16:505](#))

Negative stains: low Ki-67 ([J Am Acad Dermatol 2007;56:815](#), [AJCP 2004;122:499](#)); EMA, keratin, myogenic markers; usually CD99 ([J Cutan Pathol 2007;34:576](#))

Molecular: H-RAS occasionally but usually not N-RAS or B-RAF mutations, unlike melanoma ([AJSP 2005;29:1145](#)), but B-RAF mutations found in some classic and atypical Spitz nevi in another study ([Mod Path 2006;19:1324](#))

DD: melanoma (asymmetric, irregular lateral borders, uneven base, pagetoid scatter of melanocytes, uneven nests of melanocytes, lack of maturation, spindle cells not perpendicular to surface, epidermal spread, ulcerated surface, most cells appear malignant)

References: [Mod Path 2006;19 Suppl 2:S21](#), [eMedicine](#)

Atypical Spitz nevus - Skin-Melanocytic tumors chapter

Also called Spitz tumor ([Mod Path 2006;19 Suppl 2:S21](#))

Regional lymph node involvement in up to 1/3 ([Hum Path 2006;37:816](#))

Usually large and deep with pushing borders into dermis and subcutis

Poor prognostic factors include size > 1 cm, tumor extension into subcutis, ulceration, high mitotic index ([Arch Dermatol 1999;135:282](#), [Hum Path 1998;29:1105](#))

Borderline biologic behavior between Spitz nevi and malignant melanoma ([Mod Path 2005;18:197](#))

Case reports: resembling dermatofibroma clinically ([Clin Exp Dermatol 2008;33:309](#))

Treatment: complete excision to determine depth and extension; some recommend sentinel node biopsy, particularly if melanoma is suspected ([Ann Surg Oncol 2008;15:302](#), [Semin Diagn Pathol 2008;25:95](#) but see [Adv Anat Pathol 2008;15:253](#))

Micro: junctional or compound lesion not fulfilling the histopathologic criteria of melanoma but with one of the following features - asymmetry, predominance of single melanocytes over nests in lesions 4 mm or larger, ulceration, large dermal sheets of melanocytes, lack of maturation in dermis, deep dermal mitotic figures, extensive involvement of subcutis, nuclear pleomorphism ([Arch Dermatol 2005;141:1381](#), [Cancer 2003;97:499](#))

Positive stains: S100, HMB45 only at dermoepidermal junction or superficially

Molecular: H-RAS occasionally but usually not N-RAS or B-RAF mutations, unlike melanoma ([AJSP 2005;29:1145](#)); some cases may have copy number loss of the CDKN2A gene, also seen in melanoma ([Br J Dermatol 2007;156:1287](#))

DD: spitzoid melanoma

Desmoplastic Spitz nevus - Skin-Melanocytic tumors chapter

Usually limbs of young adults (not a common site for melanoma)

Micro: resembles classic Spitz nevus (symmetric with inverted wedge shape, infiltration of dermis by relatively bland epithelioid and spindle cells), but dermal fibrosis encircles individual cells and simulates invasion

Angiomatoid variant exists ([Am J Dermatopathol 2000;22:135](#))

Positive stains: HMB45 and MelanA

DD: desmoplastic melanoma (in situ component present, cells resemble fibroblasts with atypia, negative for MelanA and HMB45)

White sponge nevus - Skin-Melanocytic tumors chapter

Rare, typically autosomal dominant disorder due to mutation in mucosal keratins CK4 ([Br J Dermatol 2003;148:1125](#)) and CK13 ([J Dent Res 2001;80:919](#))

Primarily affects nonkeratinized stratified squamous epithelium

First described by Cannon in 1935 ([Arch Dermatol Syphilol 1935;31:365](#))

Case reports: 33 year old with buccal lesion, no family history ([Dermatol Online J 2008;14\(5\):16](#), [link](#))

Treatment: no standard treatment; possibly tetracycline; progression usually stops at puberty; no malignant transformation

Clinical: white to gray, diffuse, painless, spongy and folded plaques on buccal mucosa

Micro: parakeratosis, acanthosis with formation of large blunt rete ridges, spongiosis; extensive vacuolation of suprabasal keratinocytes; dyskeratotic cells exhibit dense peri- and paranuclear eosinophilic condensations, which correspond to tonofilament aggregates; abundant Odland bodies (keratinosome, membrane bound granule in upper stratum spinosum) within keratinocytes, but few are present in the intercellular spaces

Other melanocytic lesions

General - Skin-Melanocytic tumors chapter

Patterns of benign behavior: lentiginous hyperplasia (single cell melanocytic growth along dermoepidermal junction), nested proliferation and pagetoid proliferation (discohesive single cell growth throughout entire epidermis-seen in Spitz nevi and acral nevi, as well as melanoma); melanocyte nuclei are smaller than that of adjacent keratinocytes

Other benign features: symmetric pattern of growth and involution, lateral dimension of dermal component is equal to that of original epidermal component

Maturation: deeper portion of lesion has smaller cells with less pigment, less atypia; deep cells grow in smaller sized nests or single cells; may resemble neural tissue

Case reports: lentiginous hyperplasia associated with hamartoma ([Am J Dermatopathol 2008;30:488](#)) or dermatofibroma ([J Dermatol 1996;23:840](#))

Atypical melanocytic hyperplasia - Skin-Melanocytic tumors chapter

Controversial topic

Atypical hyperplasia ("atypical melanosis") may occur on foot ([Arch Dermatol 1994;130:1042](#), [J Dermatol 2007;34:56](#))

Case reports: associated with esophageal squamous cell carcinoma in situ ([Virchows Arch 2000;437:203](#))

Micro: atypical melanocytes limited to epidermis, often seen at peripheral of classic melanoma

DD: melanoma in situ ([Am J Dermatopathol 1996;18:560](#))

Café-au-lait spot - Skin-Melanocytic tumors chapter

Definition: pigmented birthmark, at least 0.5 mm, flat, round/oval, sharply demarcated, smooth or irregular borders with even pigmentation, long axis is along cutaneous nerve tract; pigment histologically restricted to basal layer of epidermis; usually present at birth

Café au lait is French for coffee with milk, refers to light brown color of lesions

Present in up to 20% of population; also in neurofibromatosis type 1 (any person with 6 or more should be presumed to have neurofibromatosis until proven otherwise), McCune-Albright syndrome, other syndromes ([eMedicine](#))

In children under 5 years, 19% had one, 0.75% had more than 2, more present in African-Americans ([Arch Dis Child 1966;41:316](#))

Case reports: newborn with McCune-Albright syndrome and multiple bilateral café au lait spots ([Pediatr Dermatol 1991;8:35](#))

Micro: basal hyperpigmentation of epidermis; no deeper pigmentation; increased amount of pigment in melanocytes, some have giant pigment granules ([Tohoku J Exp Med 1976;118:255](#))

EM: macromelanosomes

DD: pigmented nevi (deeper pigment clinically, melanocytes not restricted to basal epidermis), mongolian spots (blue pigmentation, larger)

References: [Wikipedia](#)

Ephelis (freckle) - Skin-Melanocytic tumors chapter

Plural - ephelides

Affects sun exposed areas of skin of susceptible individuals (fair skin type and red hair)

Appears in early childhood; fades in winter and reappears in summer

Risk factor for skin cancer

Due to variations in melanocortin-1-receptor gene ([Hum Mol Genet 2001;10:1701](#))

Micro: mild hyperpigmentation of basal keratinocytes, normal architecture

References: [Wikipedia](#)

Hyperpigmentation - Skin-Melanocytic tumors chapter

Definition: common, usually harmless condition, in which patches of skin become darker than normal surrounding skin

Due to melanocyte stimulation from sunlight, heat, post-inflammatory ([eMedicine](#)), drugs ([Merck](#)), hormones, malignancy, metabolic disease, scars, various dermatoses, familial progressive hyperpigmentation ([Eur J Dermatol 2006;16:246](#))

Patches near axilla may be post-inflammatory due to hair plucking ([Int J Cosmet Sci 2006;28:247](#))

Amiodarone may deposit in skin and cause hyperpigmentation ([Arch Dermatol 2008;144:92](#))

Hyperpigmentation can be evaluated with Taylor hyperpigmentation scale ([Cutis 2005;76:270](#))

Age / liver spots are common, due to sun damage on hands or face

Case reports: drugs - bleomycin ([Arch Dermatol 2003;139:337](#)), diltiazem ([Arch Dermatol 2006;142:206](#)), hydroxychloroquine ([J Cutan Pathol 2008;35:1134](#)), imatinib ([Dermatol Online J 2008;14\(7\):7](#)), imipramine ([Dermatol Online J 2007;13\(4\):8](#)), minocycline ([J Clin Rheumatol 2008;14:17](#)); **malignancy** - leukemia cutis ([J Cutan Pathol 2008;35:662](#)); **other** - periungual hyperpigmentation in newborns ([Pediatr Dermatol 2008;25:25](#)), Vitamin B12 deficiency ([Indian J Dermatol Venereol Leprol 2006;72:389](#))

Clinical: skin with darker pigmentation than surrounding healthy skin, due to increased melanin

Treatment: none, bleaching products with hydroquinone, retinol and antioxidants ([Cutis 2008;81:365](#)), laser therapy ([Plast Reconstr Surg 2008;121:282](#))

Note: hydroquinone slows production of melanin so darker areas gradually fade to match surrounding skin; tretinoin and cortisone take 3-6 months to produce improvement
Micro: increased pigmentation of basal keratinocytes, increased transfer of melanin into adjacent keratinocytes; variable melanophages, deposits in dermal cells, apoptotic cells; no atypia
References: [Wikipedia](#)

Linear and whorled nevoid hypermelanosis - Skin-melanocytic tumors chapter

Rare skin disorder, often in first weeks of life, with swirls and streaks of macular hyperpigmentation along lines of Blaschko

Usually not associated with other abnormalities ([Pediatr Dermatol 2007;24:205](#))

Case reports: 20 year old man with widespread involvement associated with scoliosis, unsuccessfully treated with medium depth chemical peel ([Dermatol Online J 2007;13\(3\):23](#)); familial cases ([J Am Acad Dermatol 1994;30:831](#))

Treatment: no satisfactory treatment

Clinical: swirls and whorls of hyperpigmented macules in reticulate pattern along Blaschko's lines ([Wikipedia](#), [image](#))

Micro: epidermal melanosis; no pigment incontinence or melanophages

Melasma - Skin-melanocytic tumors chapter

Also called chloasma

Definition: acquired large areas of darkened skin usually due to hormonal changes (birth control pills, pregnancy), usually on both sides of face

90% women; more common in dark-skinned individuals

In pregnant women, hormones cause "mask of pregnancy" on face and darkened skin on abdomen and elsewhere

Associated with freckles, lentigines and 4+ nevi ([BMC Dermatol 2008 Aug 5;8:3](#))

Patterns: centrofacial, malar, mandibular

Classification: based on level of increased melanin in skin determined by Wood's light examination ([J Am Acad Dermatol 1981;4:698](#))

Epidermal: 70% of cases, increased melanin in basal and suprabasal epidermis; skin pigmentation enhanced under Wood's light; responds best to bleaching agents

Dermal: 10% of cases, increase in melanophages in upper dermis; no enhancement of skin pigmentation under Wood's light, responds poorly to bleaching agents

Mixed: 20% of cases, mixture of epidermal and dermal features; patchy enhancement of skin pigmentation under Wood's light

Indeterminate: 2% of cases; not possible to characterize pigmentation pattern

Treatment (to lighten skin): avoid sunlight, broad spectrum (UVA + UVB) sunscreen; also topical hydroquinone, tretinoin, azelaic acid, Vitamin C; new reports suggest combination therapy with laser ([J Cosmet Laser Ther 2008;10:167](#)), pidobenzene 4% ([Dermatol Ther 2008;21 Suppl 1:S18](#)), chemical peels ([Dermatol Surg 2008;34:1032](#)), ellagic acid containing products ([J Dermatol 2008;35:570](#)), Mequinol 2%/tretinoin 0.01% topical solution for men ([Cutis 2008;81:179](#)); often relapses when treatment stops

Micro: mild lymphohistiocytic infiltrate in 75%; increase in amount of epidermal melanin, but no increase in number of melanocytes; melanocytes are larger with prominent dendrites ([Am J Dermatopathol 2005;27:96](#))

EM: more melanosomes in keratinocytes, melanocytes and dendrites

DD: post inflammation pigmentation, pigmented contact dermatitis

References: [eMedicine](#)

Paraganglioma-like dermal melanocytic tumor - Skin-Melanocytic tumors chapter

Very rare (8 of 30,000 consultation cases in one series)

First described in 2004 ([AJSP 2004;28:1579](#))

75% females, mean age 35 years (range 18-53 years)

Case reports: 60 year old man ([Cases J 2008;1:48](#))

Clinical: dermal nodule, mean 1 cm

Micro: nested growth pattern similar to paraganglioma, composed of clear to amphophilic oval cells separated by delicate fibrous strands; no/mild nuclear atypia; 1-4 MF/10 HPF; no melanin; normal epidermis, no junctional activity

Positive stains: S100 (100%), HMB45 (100%), microphthalmia transcription factor (100%), MelanA (50%)

Negative stains: keratin, smooth muscle actin

Molecular: no t(12;22)

DD: clear cell sarcoma (centered in fascia and tendons, rare in dermis, high grade with prominent nucleoli and scattered tumor giant cells, t(12;22)+), melanoma (high grade, no nesting pattern)

Solar lentigo - Skin-Melanocytic tumors chapter

Also called solar lentiginos, age spots

Benign melanocytic proliferation due to sun exposure ([Br J Dermatol 2007;156:1214](#))

Sun exposed skin of elderly (90% of whites age 60+); also truck drivers on sun-exposed face ([J Dermatol 2008;35:146](#))

Multiple lesions, often poorly circumscribed

Multiple large solar lentigos on the upper back and shoulders suggest prior severe sunburn, a risk factor for melanoma ([Dermatology 2007;214:25](#))

Treatment: laser ([J Am Acad Dermatol 2006;54:S262](#)), intense pulsed light ([Dermatol Surg 2007;33:449](#)), cryotherapy, trichloroacetic acid ([J Eur Acad Dermatol Venereol 2008;22:316](#))

Clinical: macular hyperpigmentation, often > 1 cm

Dermoscopy: sharply demarcated border and finger-print like structures

Micro: elongation of rete ridges and increased pigmentation; pigmentation may be irregular; also elastosis, telangiectasia, variable chronic inflammatory infiltrate in dermis; may have transepidermal elimination of melanin pigment

DD: lentigo maligna (clusters of MelanA+ cells at dermoepidermal junction, versus scattered for solar lentigo, [J Cutan Pathol 2008;35:931](#)), actinic keratosis

References: [eMedicine](#)

Vitiligo - Skin-Melanocytic tumors chapter

Definition: partial or complete loss of pigment producing melanocytes within the epidermis

Affects 1% of world's population; more noticeable in dark skinned individuals

Usually hands/wrists, axilla, perioral, periorbital, anogenital skin

An autoimmune disorder associated with pernicious anemia, Addison's disease, Hashimoto's thyroiditis

Perilesional skin up to 5 cm from vitiligo spot is still lighter than normal ([Photodermatol Photoimmunol Photomed 2008;24:314](#))

Associated with polymorphisms in COX2 gene ([J Dermatol Sci 2008 Nov 10. \[Epub ahead of print\]](#)), mutations of autoimmune regulator gene ([Br J Dermatol 2008;159:591](#))

May cause severe psychological distress

Patterns: focal (only a few areas), segmented (one side of the body only), generalized (most common, both sides of body), trichrome-3 shades of skin color in same patient

Treatment: laser skin ablation, phototherapy, 5 FU ([Photodermatol Photoimmunol Photomed 2008;24:322](#)), topical steroids or immunomodulators ([J Dermatol 2008;35:503](#)); hydroxyacetone ([Dermatol Online J 2008;14\(8\): 23](#))

Clinical: asymptomatic, flat, well-demarcated zones of pigment loss

Micro: difficult to diagnose, decreased melanocytes (use S100 or MelanA and control biopsy from adjacent normal skin, [Am J Dermatopathol 2008;30:112](#))

EM: no melanocytes

DD: albinism (melanocytes present, but no melanin due to defect in tyrosinase enzyme)

References: [Wikipedia](#), [eMedicine](#)

Melanoma

Melanoma in situ - Skin-melanocytic tumors chapter

Cases in sun damaged skin may resemble benign lichenoid keratosis ([Hum Path 2003;34:706](#))

Lentigo maligna type is characterized by pagetoid spread, confluence, and nesting of atypical melanocytes; associated with invasive lentigo malignant melanoma ([Hum Path 2000;31:705](#))

Hutchinson's sign: periungual extension of brown-black pigmentation from longitudinal melanonychia [pigmented stripe within length of nail bed] onto the proximal and lateral nailfolds

Case reports: melanoma in-situ arising within seborrheic keratosis ([Cases J 2008;1:263](#)), vitiligo-like in situ disease ([Am J Dermatopathol 2008;30:451](#)), involving epidermal inclusion cyst, with adjacent invasive disease ([Am J Dermatopathol 2007;29:564](#))

Treatment: Mohs micrographic surgery ([Dermatol Surg 2008;34:660](#)); evaluation of entire margin is recommended ([Dermatol Surg 2007;33:1434](#)); Imiquimod cream 5% as a nonsurgical alternative ([Cutis 2007;79:149](#))

Dermoscopy: blue-whitish veil (78%), gray-blue areas (76%), black dots (73%), irregular extensions and branched streaks (62%) ([Cancer 2001;91:992](#)); parallel ridge pattern identifies early acral lesions ([Arch Dermatol 2005;141:1413](#))

Micro: atypical melanocytes in epidermis with no dermal invasion; usually epidermal effacement (absences of rete ridges in some foci, [J Drugs Dermatol 2007;6:708](#))

DD: ankle nevi ([AJSP 2007;31:1130](#)), seborrheic keratosis with clear basal cells ([J Am Acad Dermatol 2006;54:132](#))

Melanoma-invasive-General - Skin-Melanocytic tumors chapter

Incidence increasing worldwide

48,000 cases and 9,200 deaths in US in 2000

Usually due to sun (UV light) exposure

Physiology: cytotoxic T lymphocytes have difficulty killing melanoma cells due to delayed or ineffective apoptosis ([J Cell Mol Med 2008 Nov 8 \[Epub ahead of print\]](#))

Clinical warning signs: change in color of pigmented lesion, enlargement of existing mole, itching or pain in preexisting mole, development of new pigmented lesion in adult life, irregular borders in pigmented lesion, variegation of color in pigmented lesion

Sites: head and neck, lower extremities (particularly in women); also oral and anogenital mucosa, esophagus, meninges, eye; rarely subungual ("melanotic whitlow"), palm, sole

Populations at higher risk: whites with fair skin, red hair, tendency to burn or freckle from sun exposure, large number of melanocytic nevi, xeroderma pigmentosum, familial dysplastic nevi, melanosis, vitiligo, frequent sunburns at any age ([Ann Epidemiol 2008;18:614](#)), 5-10% familial ([Surg Clin North Am 2008;88:897](#)), possibly neurofibromatosis type I

Blacks and Hispanics in US have low risk, their common melanoma sites are palms, soles, nail beds or mucous membranes; often poorer prognosis ([Cancer Control 2008;15:248](#))

Usually occurs after puberty, occasionally children - all have same morphology

Self assessment often inaccurate ([Public Health 2008;122:1433](#))

Clinical features: 5% are multiple, although prognosis is related to type and stage of largest lesion, not number of lesions; must distinguish multiple lesions from "hot nevi" / nevus activation

Regression: partial regression is common, total regression may occur after metastasis ([Am J Dermatopathol 2008;30:178](#))

Metastases: regional lymph nodes, liver, lungs, GI tract, bone, CNS, heart (50% at autopsy), skin (satellite tumors are considered intralymphatic metastases within 2 cm of primary tumor, in transit metastases if >2 cm from primary tumor but before the first echelon of regional lymph nodes), other sites

Metastasis are occasionally S100 negative, but can still be identified as melanoma due to (a) negative workup for carcinoma, lymphoma and sarcoma, (b) HMB45+, MART1+, (c) clinical history of melanoma ([Hum Path 2005;36:1016](#))

Metastases may arise from unrelated clones ([AJSP 2007;31:1029](#))

Molecular analysis can distinguish a second primary from metastatic disease ([AJSP 2007;31:637](#))

Survival: overall 5 year survival is 60%, but behavior is variable, with occasional late deaths or long survival even with widespread satellite nodules

Poor prognostic factors: increased Breslow (vertical) thickness in primary tumor, high stage (TNM), male gender, high mitotic rate, ulceration ([AJSP 2006;30:1396](#)), microscopic satellites (tumor nests 50 microns or larger and separated from main tumor mass), deeper level of invasion for T1 tumors, higher % tumor area/volume in sentinel node, positive nonsentinel lymph nodes ([Ann Surg Oncol 2008 Nov 1 \[Epub ahead of print\]](#))

possible poor prognostic factors: patient age, site of primary melanoma, angiotropism (migration of melanoma cells along external surface of blood vessels, [AJSP 2008;32:1396](#)), tumor lymphangiogenesis ([Mod Path 2005;18:1232](#)), increased density of dendritic leukocytes in nodal paracortex ([Mod Path 2004;17:747](#))

For patients with localized melanoma, most important prognostic factors are tumor thickness and ulceration

For patients with nodal metastases, most important prognostic factors are number of metastatic nodes, microscopic versus macroscopic tumor and presence or absence of ulceration of primary melanoma

Note: there is excellent agreement between pathologists in assessing tumor thickness, ulcerative state and tumor mitotic rate ([AJSP 2003;27:1571](#))

Case reports: metastasis to basal cell carcinoma ([AJSP 2006;30:133](#)), malignant basomelanocytic tumor with subsequent metastatic melanoma ([AJSP 2004;28:1393](#)), presenting as leptomeningeal melanomatosis ([Hum Path 2003;34:625](#)), with true epithelial component ([Am J Dermatopathol 2007;29:395](#)), myxoid stroma associated with patient use of phototherapy ([Am J Dermatopathol 2008;30:185](#)), angiomatoid periorbital tumor ([Hum Path 2000;31:1520](#)), presentation in 71 year old identical female twins at same time and location ([Am J Dermatopathol 2008;30:182](#)), with dysplastic nevi and sebaceous-type cells ([Am J Dermatopathol 2007;29:566](#)), with incipient follicular lymphoma in axillary node ([Hum Path 2001;32:1410](#)), nipple melanoma resembling Paget's disease ([Dermatol Online J 2007;13\(2\):18](#)), with diffuse cutaneous melanosis ([Dermatol Online J 2007;13\(2\):9](#)), presenting as vitiligo-like patches ([Am J Dermatopathol 2008;30:451](#))

Diagnosis and treatment: punch biopsies for diagnosis are discouraged, since determination of depth may be inaccurate ([Dermatol Online J 2005;11\(1\):7](#)), but may be useful to define margins ([Ann Surg Oncol 2008;15:3028](#)); initial excision is usually down to subcutis with narrow margins, but then need wide local reexcision with 1-2 cm margins; frozen sections for margins only; lymphatic mapping and sentinel node biopsy for staging tumors that have spread to lymph nodes; often nodal block dissection ([ANZ J Surg 2008;78:982](#))

Note: minimal metastatic risk if radial growth phase only; metastatic behavior occurs with vertical growth phase

Treatment for metastatic disease: Interleukin-2 and dacarbazine; possibly adoptive cell therapy with autologous antitumor lymphocytes in lymphodepleted hosts ([J Clin Oncol 2008;26:5233](#)); variable results for adjuvant radiotherapy ([Ann Surg Oncol 2008;15:3022](#), [Cancer Control 2008;15:233](#))

Dermoscopy: more accurate than naked eye examination ([Br J Dermatol 2008;159:669](#))

ABCD rule: asymmetry, border, color and differential structure ([J Am Acad Dermatol 1994;30:551](#))
Black dots represent pigmented cells at dermal-epidermal junction and within epidermis in heavily pigmented columns; brown dots are similar to black dots, but with less pigment; blue dots are due to melanophages surrounding superficial vascular plexus; depigmentation is due to intense fibrosis of papillary dermis; radial streaming and pseudopods are due to cells in nests or centrifugal linear extensions ([Am J Dermatopathol 2006;28:13](#)); blue-whitish veil is associated with melanoma ([Am J Dermatopathol 2001;23:463](#)); dermoscopy is less accurate if no significant pigment, but helpful features include blue-white veil, scarlike depigmentation, multiple blue-gray dots, irregularly shaped depigmentation, irregular brown dots/globules, 5-6 colors and predominant central vessels ([Arch Derm 2008;144:1120](#))

Amelanotic/hypomelanotic lesions: blue-white veil, scarlike depigmentation, multiple blue-gray dots, irregularly shaped depigmentation, irregular brown dots/globules, 5-6 colors and predominant central vessels are suggestive ([Arch Dermatol 2008;144:1120](#))

Micro: classic features are junctional activity with obscured dermoepidermal junction and pagetoid spread individually and in clusters throughout epidermis; prominent melanin pigmentation, invasion of surrounding tissue, large cells with abundant eosinophilic and finely

granular cytoplasm; nuclear pseudoinclusions, folds or grooves; marked atypia with pleomorphic nuclei with large eosinophilic nucleoli; frequent mitotic figures

4 major subtypes: acral lentiginous, lentigo maligna, nodular, superficial spreading (see below)
Lack of a junctional component suggests a metastases, although epidermal component may have regressed or not been sampled, or melanoma may have developed from an intradermal nevus
Consumption of epidermis: usually (86%) present; thinning of epidermis with attenuation of basal and suprabasal layers and loss of rete ridges in areas of direct contact with neoplastic melanocytes; variable clefts separating epidermis and dermis, edema, telangiectasias ([AJSP 2004;28:1621](#)); is associated with increased Breslow depth and ulceration ([Am J Dermatopathol 2007;29:527](#))

Lymphatic invasion identified in 5% on H&E but 33% using podoplanin and S100 ([Hum Path 2008;39:901](#))

Subepidermal cleft present in 24% ([Hum Path 2005;36:412](#))

Angiotropism is suggestive of epidermotropic metastatic disease versus recurrent disease ([Am J Dermatopathol 2006;28:429](#))

Rarely paradoxical maturation occurs, but still have areas of cells with abundant cytoplasm and large nuclei, more mitotic figures, more confluence, high Ki-67 rate ([AJSP 2000;24:1600](#))

Rarely CD68+ osteoclast-like giant cells ([Am J Dermatopathol 2005;27:126](#)), signet-ring cells ([Am J Dermatopathol 2003;25:418](#)), lipoblast like cells ([Archives 2003;127:370](#))

Regressed melanoma: dense lymphocytic infiltration similar to spontaneously disappearing nevi, variable melanin-laded macrophages; may be complete or incomplete with residual tumor cells present

Variable microscopic features:

Growth patterns: pseudoglandular, pseudopapillary, peritheliomatous (around blood vessels), hemangiopericytoma-like, Spitz nevus-like, trabecular, verrucous, nevoid

Cell type: epithelioid, spindled or bizarre

Size: lymphocytes to multinucleated giant cells

Cytoplasm: eosinophilic, basophilic, foamy, signet ring, rhabdoid, oncocytic or clear

Stroma: desmoplastic, myxoid, bone or cartilage, osteoclast-like giant cells

Epithelium: pseudoepitheliomatous hyperplasia

Other differentiation: Schwann cells, ganglion cells, other neural structures

Cytology: metastases may have spindle cells resembling malignant peripheral nerve sheath tumor ([Diagn Cytopathol 2008;36:754](#))

Positive stains (distinguish melanocytes from non-melanocytes, but not malignant cells from benign cells)

S100: nuclear and cytoplasmic staining, 90%+ sensitive but not specific (although usually negative in tumors considered in the differential)

HMB45: cytoplasmic and weak nuclear staining ([Mod Path 2008;21:1121](#)), less sensitive but more specific than S100; negative in desmoplastic melanoma

MelanA/Mart1: sensitive, but also stains steroid-producing cells in ovary, testis, adrenal cortex

Tyrosinase: sensitive, but also stains peripheral nerve sheath and neuroendocrine tumors

Microphthalmia transcription factor: sensitive, but also stains dermatofibroma and smooth muscle tumors; negative in spindle cell / desmoplastic melanoma

NKI-C3 and NSE: nonspecific

PHH3 and Ki-67: may distinguish melanoma from nevi ([Am J Dermatopathol 2008;30:117](#));

another marker is SM5-1 ([Am J Dermatopathol 2005;27:401](#))

Azure blue counterstaining may be preferable to bleaching ([Mod Path 1999;12:1143](#))

Other positive stains: Fontana-Masson (detects melanin granules), vimentin; variable staining for Cam 5.2, CEA, EMA, alpha-1-antichymotrypsin, CD68

Negative stains: p53

Electron microscopy: melanosomes and premelanosomes; may be useful if stains are not confirmatory; may have well developed microvilli similar to adenocarcinoma

Molecular: main altered pathways include (a) RAS-RAF-MEK-ERK, (b) p16(INK4A)-CDK4-RB and (b) ARF-p53 ([APMIS 2007;115:1161](#)); 20% of melanoma prone families have point mutation in CDKN2A locus at 9p21 which encodes p16(INK4a) and p14(ARF) ([Br J Cancer 2008;99:364](#)); 10%

of cases may be familial due to CMM1 gene at 1p36; microsatellite instability seen in pediatric melanoma (43%), adult melanoma (30%), nevi (9%) ([Am J Dermatopathol 2005;27:279](#))

DD: nevi (particularly Spitz nevi-desmoplastic type, halo nevi, activated and dysplastic nevi, vulval nevi and recurrent nevi after incomplete excision; features relatively specific for melanoma include absence of maturation, suprabasal melanocytes; also atypia, size >6 mm, mitotic figures, dermal lymphocytes and asymmetry, necrosis, asymmetrical melanin and melanin in deep cells ([Melanoma Res 2008;18:253](#)), benign fibrous histiocytoma, hemangioma, pigmented seborrheic keratosis, pigmented basal cell carcinoma, atypical fibroxanthoma (HMB45, MelanA and S100 usually negative but see [Am J Dermatopathol 2007;29:551](#)), granular cell tumor (negative for HMB45 and MelanA, [Am J Dermatopathol 2007;29:22](#)); amelanotic tumors resemble pyogenic granuloma

Helpful features of melanoma that differentiate from benign lesions (from Rosai): poor circumscription of intraepidermal component, lateral extension of individual melanocytes, transepidermal migration of melanocytes, pleomorphism of tumor cells, asymmetry, lack of maturation of dermal tumor cells, atypia, mitotic figures in melanocytes (particularly atypical ones), melanocytes with clear cytoplasm and finely dispersed chromatin, individual melanocyte necrosis (compared to eosinophilic hyaline bodies in Spitz nevi), band like chronic inflammatory infiltrate in dermis

References: [Wikipedia](#), [eMedicine](#)

Acral lentiginous melanoma - Skin-Melanocytic tumors chapter

Acral: relating to or affecting the peripheral parts, such as limbs, fingers, ears

Usually palms and soles, subungual, mucocutaneous oral and nasal cavity, or anus

More common in blacks and Asians; 10% of melanomas in whites

Often advanced at diagnosis because thickened, hyperkeratotic epidermis overlies and hides the primary lesion; often initially misdiagnosed ([J Am Acad Dermatol 2003;48:183](#))

Older age than other variants (66 vs. 52 years), associated with other malignancies, less often associated with sunburn

May evolve slowly over years; mean 1 year to diagnosis in foot/ankle lesions ([J Foot Ankle Res 2008;1:11](#))

Rarely are multiple ([Dermatol Surg 2007;33:1](#))

Median disease free survival is 10 years ([Br J Dermatol 2006;155:561](#))

Poor prognostic factors: high mitotic rate, microsatellites ([Br J Dermatol 2007;157:311](#))

Case reports: initially treated as plantar wart ([Dermatol Online J 2006;12\(4\):3](#), [link](#))

Clinical: in situ cases show longitudinal pigmented streak in nail plates, black pigmentation on proximal or lateral nail fold, irregular border or variegated pigmentation on sole or thumb ([Am J Dermatopathol 2004;26:285](#)); invasive cases show densely pigmented macules with irregular borders; mean 3 mm, usually ulcerated (74%) ([Cancer Causes Control 2008 Aug 29 \[Epub ahead of print\]](#))

Dermoscopy: may have parallel ridge pattern (band-like pigmentation on ridges of skin markings is specific)

Micro: intraepidermal lentiginous component is similar to lentigo maligna, but intraepidermal melanocytes are bizarre, epidermis is markedly hyperplastic, papillary dermis is widened and inflamed

Early lesions may show proliferation of solitary melanocytes in crista profunda intermedia, the epidermal rete ridge underlying the ridge of the skin marking ([Am J Dermatopathol 2006;28:21](#))

Nail lesions show confluent stretches of solitary melanocytes, multinucleation, lichenoid inflammatory reaction and florid pagetoid spread ([AJSP 2008;32:835](#))

Positive stains: S100 and HMB45 ([Int J Dermatol 2003;42:123](#))

DD: melanocytic nevi

Lentigo maligna melanoma - Skin-Melanocytic tumors chapter

Also called melanoma arising in Hutchinson's freckle, actinic melanosis, melanoma on sun damaged skin

5-15% of (invasive) melanoma; increasing prevalence, particularly among men age 65+ years ([J Invest Dermatol 2005;125:685](#))

Slow growing lesion of sun exposed skin of elderly whites, often cheek; partial regression is common

Similar behavior to other melanoma subtypes when depth of invasion is considered, but unusual to die of disease

Possible origin from progenitor stem cell (strongly CD133+ and CD34+) in outer root sheath of the mid-lower hair follicles ([Dermatol Ther 2008;21 Suppl 1:S1](#))

Note: lentigo maligna (a subtype of melanoma in situ), by definition, does NOT infiltrate into dermis, but lentigo maligna melanoma has at least single cell infiltration into papillary dermis

Case reports: present (in retrospect) in 22 year old woman ([Dermatology 2008;217:66](#)); **collision tumors:** - with basal cell carcinoma ([Am J Dermatopathol 2005;27:319](#)), with Merkel cell carcinoma ([J Cutan Pathol 2008;35:203](#))

Treatment: excision with careful margin control ([J Am Acad Dermatol 2008;58:142](#)); staged excision for peripheral margin control using permanent sections is required because frozen sections are unreliable ([Plast Reconstr Surg 2007;120:1249](#)); possibly radiation ([Surg Clin North Am 2003;83:323](#)); possibly imiquimod without ([Ann Plast Surg 2008;61:419](#)) or with surgery ([Dermatol Surg 2008;34:147](#)); possibly cryotherapy

Clinical: flat, tan to black with irregular hyperpigmentation, > 2 cm

Dermoscopy: annular-granular pattern, asymmetric pigmented follicular openings, dark rhomboidal structures, homogeneous areas

Micro: atypical melanocytes in basal layer, individually and in nests (theques); cells are often spindled, pleomorphic and have cytoplasmic retraction; dermis shows solar elastosis; also epidermal atrophy, actinic damage, basilar keratinocyte hyperpigmentation

DD: desmoplastic melanoma (may arise secondary to lentigo maligna)

References: [eMedicine](#)

Nodular melanoma - Skin-Melanocytic tumors chapter

15-30% of melanoma patients

Affects all body surfaces, but usually legs and trunk

Rapid growth; comprises 34% of thick (2 mm+) melanomas ([Arch Dermatol 2005;141:745](#))

Median age 63 years; screening methods have had little impact on this subtype ([Cancer 2008 Nov 5 \[Epub ahead of print\]](#))

Higher risk for metastases due to vertical growth phase, but differs from "vertical growth melanoma" ([J Dermatol 2008;35:643](#))

May recur even in sentinel lymph node negative patients ([Surgeon 2006;4:153](#))

Case reports: 25 cm tumor ([Dermatol Online J 2007;13\(2\):7](#)), metastatic amelanotic tumor during pregnancy ([Medicina \(Kaunas\) 2008;44:467](#)), with Spitz nevus like features ([J Dermatol 2007;34:821](#))

Clinical: smooth nodule covered by normal epidermis, elevated blue-black plaque or ulcerated polypoid mass; usually no lateral flat component

Dermoscopy: nonspecific global dermoscopic patterns of globules, blue-white veil, atypical vessels and structureless areas ([Arch Dermatol 2008;144:1311](#))

Micro: no radial growth phase; no in situ melanoma; occasionally monster cells ([Am J Dermatopathol 2005;27:208](#))

Molecular: B-RAF and N-RAS mutations in 25-30% ([J Invest Dermatol 2005;125:312](#))

DD: primary dermal melanoma (no in situ component, ulceration, regression, associated nevus, [Arch Dermatol 2008;144:49](#))

Superficial spreading melanoma - Skin-Melanocytic tumors chapter

Traditionally considered the most common type of melanoma (50-75%), but lentigo maligna may be more common in patients with extensive sun exposure ([J Am Acad Dermatol 2008;58:1013](#))

Usually affects light skinned individuals, young adults to elderly, often trunk and extremities

Recently diagnosed tumors are thinner with less ulceration than in the past ([Cancer 2008 Nov 5 \[Epub ahead of print\]](#))

Risk factors: extensive sun exposure during childhood, family history of melanoma, large numbers of benign nevi, dysplastic nevi
Recommended to evaluate vertical growth phase as prognostic factor for thin (< 0.76 mm) tumors ([AJSP 2003;27:717](#))

Case reports: 77 year old man with tumor in vertical growth phase with microscopic satellite nodule ([Archives 2003;127:e365](#))

Clinical: variegated, black, brown, tan, blue, pink or white; slightly elevated, flat and irregular margins, often with an indentation or notch; may have white areas of tumor regression or nodular areas of deep dermal invasion

Dermoscopy: multi-component pattern, asymmetry and multiple colors; also atypical reticular pattern (irregular holes and thick lines) with a sharp demarcation, blue-white veil, irregular linear vessels, central ulceration, irregularly distributed dots

Micro: classified based on radial growth component (has nothing to do with level of dermal invasion); noninvasive areas have uniform atypical melanocytes with nests and pagetoid cells; also transdermal migration, apoptosis of individual melanocytes, pigmented parakeratosis

Molecular: Exon 15 BRAF mutations in 29% ([J Invest Dermatol 2005;125:575](#))

Desmoplastic melanoma - Skin-Melanocytic tumors chapter

Also called desmoplastic neurotropic melanoma if neuroma-type features with prominent nerve involvement ([Adv Anat Pathol 2005;12:92](#))

First described in 1971 ([Cancer 1971;28:914](#))

Rare variant of spindle cell melanoma seen in older adults in sun-exposed skin

Mean age 71 years, 72% in head, often nonpigmented

Easily misdiagnosed; only 27% are initially diagnosed as melanoma ([Am J Dermatopathol 2008;30:207](#))

76% survival at 5 years ([Ann Surg Oncol 2006;13:728](#)), may be similar to melanomas with similar thickness ([J Clin Oncol 2005;23:6739](#)), although have fewer positive sentinel lymph nodes than classic melanoma ([Cutis 2007;79:390](#), [Cancer 2006;106:900](#))

Poor prognostic factors: mixed subtype ([AJSP 2004;28:1518](#), [Ann Surg Oncol 2005;12:207](#)), possibly N-cadherin expression ([Hum Path 2006;37:899](#))

Case reports: young woman with scalp cyst ([Univ of Pittsburgh Case #378](#)), 81 year old man with scalp lesion ([The Internet Journal of Dermatology 2008;6\(2\)](#)), collision tumor with squamous cell carcinoma on lip ([J Cutan Pathol 2008;35:473](#)), osteogenic tumor of foot ([J Cutan Pathol 2007;34:423](#))

Treatment: wide local excision with careful attention to margins ([Cancer 2005;104:1462](#)); may recur if positive margins ([Cancer 2008;113:2770](#)); possibly adjuvant radiotherapy to reduce recurrence ([ANZ J Surg 2008;78:273](#))

Clinical: often nonpigmented and mistaken for nonmelanocytic lesion, such as scar; usually advanced thickness at presentation ([Br J Dermatol 2005;152:673](#))

Dermoscopy: features of regression (white scar like areas, peppering); also multiple colors, linear irregular vessels or milky-red areas ([Br J Dermatol 2008;159:360](#))

Micro: a type of nodular (vertical growth) melanoma; poorly circumscribed; focal fascicular pattern of scanty spindle cells with prominent desmoplastic stroma; tumor cells may have minimal atypia; solar elastosis (82%), amelanotic (71%), deep invasion, perineural infiltration (35%), lymphoid aggregates at periphery (37%), may grow in peripheral nerve sheath pattern; may be pure or combined with classic melanoma (pure have better prognosis, [Am J Surg Pathol 2004;28:1518](#))

Cytology: clean background; aggregates of pleomorphic spindle cells mixed with fibrous stroma and single cells; fine, wispy and delicate cytoplasm at nuclear poles, nuclei are elongated and plump with irregular contours, deep grooves and folds, dark coarse chromatin with variably prominent nucleoli ([Cytojournal 2007;4:18](#)); compared to other melanomas, is less cellular and less often has intranuclear cytoplasmic inclusions and mitotic figures ([Am J Clin Pathol 2008;130:715](#))

Positive stains: S100 (strong, [Melanoma Res 2006;16:347](#)), may have high Ki-67 index; possibly NGFR ([Am J Dermatopathol 2006;28:162](#)), KBA.62 ([Hum Path 2008;39:1136](#)), clusterin ([J Invest Dermatol 2005;124:412](#))

Negative stains: HMB45 and MelanA (usually, but may have focal staining of epithelial cells in junctional component or superficial dermis, [Am J Dermatopathol 2004;26:452](#)), MITF (usually, [Am J Dermatopathol 2001;23:185](#), [Am J Surg Pathol 2002;26:82](#)), tyrosinase (usually)

Molecular: V599E BRAF mutation not present ([Cancer 2005;103:788](#))

DD: hypertrophic scar, sclerotic or nonpigmented blue nevi (strongly MelanA+, [Am J Dermatopathol 2004;26:452](#)), atypical fibroxanthoma, spindle squamous cell carcinoma, peripheral nerve sheath tumor (usually S100A1 negative, [J Cutan Pathol 2008;35:1014](#)), neurofibroma, fibromatosis, basal cell carcinoma

Follicular melanoma - Skin-Melanocytic tumors chapter

Definition: deep seated follicular structure with malignant melanocytes extending downward along follicular epithelium and permeating parts of follicle as well as adjacent dermis

Rare; only one published report

Often age 60+ years on head (nose, cheek neck), develops within 1-2 years

Treatment: excision, not shave biopsy ([Am J Dermatopathol 2004;26:359](#))

Clinical: less than 0.5 cm; resembles comedo or pigmented cyst

DD: lentigo maligna

Lentiginous melanoma - Skin-Melanocytic tumors chapter

First described in 2005 ([Mod Path 2005;18:1397](#))

Elderly patients

May remain in situ for prolonged periods before invasion

May be an analogue of lentigo maligna on non-severely sun-damaged skin ([J Cutan Pathol 2007;34:296](#))

May recur locally

Micro: lentiginous proliferation of melanocytes at dermoepidermal junction both as single cells and as small nests with areas of confluent growth, extending to edges of biopsy; prominent atypia of melanocytes and invasion may be evident only at excision; variable dermal fibrosis; no solar elastosis

DD: lentiginous nevus or dysplastic nevus

Minimal deviation melanoma - Skin-Melanocytic tumors chapter

Also called borderline melanocytic lesion

First described by Reed ([Semin Oncol 1975;2:119](#))

Controversial topic-concept is not universally accepted

Cells are more atypical than nevi but less atypical than classic melanoma

Usually on trunk of adults in 20's and 30's ([Cancer Treat Rev 2002;28:219](#))

Better prognosis than other melanomas, even with infiltration of reticular dermis ([Hum Pathol 1986;17:796](#))

Clinical: plaque or nodule, fleshy, dark brown or blue-black, up to 1 cm; may resemble an epidermal cyst

Micro: expansive nodule in vertical growth phase that fills papillary dermis and may extend into reticular dermis; usually uniform cells with mild to moderate atypia that resemble nevus cells but are moderately enlarged with irregular chromatin and increased N/C ratios; growth displaces surrounding structures and remnants of residual benign nevus are often present; equivalent to at least a level III melanoma due to extent of dermal invasion; may have perineural invasion and mitotic figures, but usually does not invade subcutaneous fat, no necrosis, no maturation

Variants: Spitz, halo nevus-like ([Am J Surg Pathol 1990;14:53](#)), spindle cell ([Pediatr Pathol 1988;8:401](#)), desmoplastic, small cell, dermal

Positive stains: Ki-67 and p53 values are intermediate between compound or Spitz nevi and superficial spreading melanoma ([Mod Path 2003;16:525](#))

DD: nevoid melanoma (more mitotic figures, usually no residual nevus)

References: [Mod Path 2006;19 Suppl 2:S41](#)

Nevoid melanoma - Skin-Melanocytic tumors chapter

Definition: rare variant characterized by morphologic features of nevus
Behavior similar to other melanomas; may recur or metastasize causing death ([Am J Dermatopathol 2001;23:167](#))

Key to diagnosis is high index of suspicion

Case reports: metastatic tumor to sentinel lymph node in 4 year old child ([J Cutan Pathol 2003;30:647](#)), multiple primary nevoid melanomas in HIV/AIDS patient ([J Am Acad Dermatol 2002;47:S172](#))

Clinical: tan nodule 1 cm or larger on trunk or proximal limbs of young adult

Micro: resembles compound or dermal nevus at low power, with symmetrical dome shaped or verrucous and papillomatous features, sharp lateral demarcation, inconspicuous junctional component, no pagetoid growth; high power shows relatively bland and monomorphic cells resembling classic nevus or epithelioid cells in Spitz nevus; however, there is subtle pleomorphism and impaired maturation with depth; focal sheetlike growth pattern, nucleoli in tumor cells at base of lesion; multiple dermal mitoses

Positive stains: HMB45 (strong throughout, [J Cutan Pathol 1995;22:502](#))

DD: minimal deviation melanoma (at most moderate atypia, at least level III due to dermal invasion, remnants of existing nevi usually present, usually few mitotic figures), nodular melanoma (high grade atypia, intraepidermal atypia), melanoma arising in dermal nevus (residual nevus present, often tumor extension into deep reticular dermis and fat)

References: [Hum Pathol 1995;26:171](#), [Arch Dermatol Res 1985;277:362](#)

Pigmented epithelioid melanocytoma - Skin-Melanocytic tumors chapter

Definition: melanoma with prominent pigment synthesis

Rare low grade variant of melanoma, first described under this name in 2004 ([AJSP 2004;28:31](#))

Mimics melanocytic neoplasms in gray horses and laboratory animals, although appears to have different molecular origin than equine melanomas ([AJSP 2007;31:1764](#))

Includes lesions previously described as epithelioid blue nevus of the Carney complex ([AJSP 1996;20:259](#))

Median age 27 years, with wide range

Extremities are most common site, although numerous sites are affected

Does not appear to be related to sun exposure

Nodal metastases in 46%, but death from disease is rare

Case reports: [Case of the Week #113](#), 27 year old man with sentinel node metastasis and balloon cell change ([Am J Dermatopathol 2001;23:341](#)), 28 year old woman with positive sentinel node biopsy ([Am J Dermatopathol 2004;26:290](#)), subungual tumor with blue nevus ([J Am Acad Dermatol 2008;58:1021](#))

Treatment: conservative re-excision and sentinel lymph node sampling

Clinical: resembles combined nevus

Micro: sheets and nodules of heavily pigmented epithelioid or spindled melanocytes in deep dermis; variable atypia but no consistent high grade features; may have ulceration, a combined nevus or rarely necrosis; after bleaching, cells have abundant gray, slate-like cytoplasm, round nuclei, prominent nuclear membrane, prominent nucleoli; rarely 2 nucleoli or cytoplasmic inclusions; no/rare mitotic figures, no atypia

case of the week - low power - #1; medium power - #2; #3; #4; high power - #5; #6; #7

Positive stains: MiTF, NKI/C3, NSE, p53, CD68

Negative stains: HMB45, MelanA, R1alpha ([AJSP 2007;31:1764](#))

Molecular: associated with loss of protein kinase A regulatory subunit type 1alpha (R1alpha), coded by the PRKAR1A gene, which is lost in both sporadic cases and patients with Carney complex ([AJSP 2007;31:1764](#))

EM: abundant cytoplasm with numerous single and rare compound melanosomes; frequent aberrant melanosomes; large indented nucleus with prominent nuclear membrane, central nucleolus, peripheral chromatin

DD: blue nevus (no pigmented and epithelioid cells), nodular melanosis (pigmented cells are actually pigment laden macrophages)

Primary dermal melanoma - Skin-Melanocytic tumors chapter

Definition: melanoma subtype confined to dermis or subcutis

Prolonged survival ([Arch Dermatol 2004;140:99](#)) compared to melanoma of similar thickness, but may recur or develop metastases

Micro: melanoma confined to dermis or subcutis; mean Breslow depth is 1 cm; no in-situ component, regression or ulceration; no associated nevus

DD: primary nodular melanoma, cutaneous metastatic melanoma

References: [Arch Dermatol 2008;144:49](#)

Subungual melanoma - Skin-Melanocytic tumors chapter

Uncommon; difficult to diagnosis clinically and pathologically

Median age 59-66 years; common sites are great toe and thumb

Often delay in diagnosis because lesion is attributed to trauma; most (73%) cases are AJCC stage II/III, acral lentiginous subtype (66%), Clark level IV/V (79%) ([AJSP 2007;31:1902](#))

Sentinel node metastases in 24%

Case reports: 86 year old man with post-traumatic amelanotic tumor ([Dermatol Online J 2008;14\(1\):13](#)), regressed tumors with positive sentinel nodes ([Dermatol Surg 2006;32:577](#)), with osteocartilaginous differentiation ([Skeletal Radiol 2003;32:724](#)), amelanotic tumor resembling pyogenic granuloma ([J R Coll Surg Edinb 2002;47:638](#))

Treatment: wide local excision, may require amputation ([Am J Surg 2008;195:244](#)) although conservative approach for thumb lesions has been advocated ([J Plast Reconstr Aesthet Surg 2007;60:635](#))

Micro: usually not circumscribed; have prominent lentiginous growth with more single cells than nests, moderate to severe atypia, haphazard and dense pagetoid intradermal spread; also ulceration (33%), tumor infiltrating lymphocytes

DD: lentigo

Miscellaneous

Sentinel node biopsy for melanoma - Skin-Melanocytic tumors chapter

Sentinel lymph node is defined as first extracutaneous target of lymphogenous tumor cell spread and the potential source of subsequent lymph node metastases and distant metastases

Lymphatic mapping and sentinel lymph node biopsy are widely used for staging

Recommendations: use for thick ([Semin Diagn Pathol 2008;25:86](#)) and thin melanomas (1 mm thick or less, [Arch Surg 2008;143:892](#))

Tumor in sentinel node by H&E predicts recurrence ([Mod Path 2007;20:427](#)), usually leads to dissection of lymph nodes in affected nodal basin ([Ann Surg Oncol 2008;15:1566](#)), which reduces recurrence ([Curr Treat Options Oncol 2008 Nov 8 \[Epub ahead of print\]](#))

Measuring antimony (originating from antimony sulfide colloid) can confirm sentinel nature of node ([Mod Path 2004;17:1191](#))

Predictors of positive sentinel nodes: Breslow thickness > 1 mm ([Int J Surg 2008;6:205](#)); lymphatic invasion using D2-40, ulceration ([Arch Dermatol 2008;144:462](#)), younger age ([Ann Surg Oncol 2008;15:630](#))

Predictors of positive nonsentinel nodes in sentinel node positive patients (occurs in 20-35%): amount of tumor in sentinel node, Breslow thickness of primary melanoma, density of dendritic WBCs in sentinel node paracortex ([Mod Path 2004;17:747](#)); also perinodal intralymphatic tumor ([Ann Surg Oncol 2008;15:1723](#)), depth of invasion in sentinel node ([Ann Surg Oncol 2008;15:1202](#))

S100 and NKI-C3 are most sensitive stains for nodal metastases, but are nonspecific; MART1 is most specific ([AJSP 2001;25:1039](#))

S100 and MART1 together are recommended ([Hum Path 2004;35:217](#))

Intraoperative touch imprints may be accurate ([Anticancer Res 2008;28:465](#))

Patients with triple negative (H&E, S100/HMB45, RT-PCR) nodes have a markedly improved survival ([Mod Path 2008;21:438](#))

Micrometastasis: single metastasis < 2 mm not associated with metastases in non-sentinel nodes ([J Surg Oncol 2008;98:46](#))

RT-PCR: prognostic significance of metastatic disease in histologically negative nodes is controversial (significant-[APMIS 2008;116:199](#), not significant-[Mod Pathol 2007;20:427](#))

Recommended protocols for sentinel nodes:

(a) 3 levels at 250 micrometer intervals, each level has 1 section stained with H&E, S-100 and HMB-45 ([AJSP 2005;29:305](#))

(b) 2 H&E sections, S100 and HMB45 ([AJSP 2003;27:1197](#))

DD: benign nevus cells (usually in capsule, also parenchyma, no atypia, MART1+, S100+, HMB45-, Ki-67 neg, [AJSP 2002;26:1351](#), [AJSP 2003;27:673](#)), histiocytes (no atypia), tattoo pigment ([Dermatol Online J 2005;11\(1\):14](#))

References: [eMedicine](#)

Breslow's system for tumor thickness - Skin-Melanocytic tumors chapter

Measure tumor thickness with ocular micrometer at right angles to surface of adjacent normal skin, from (a) top of granular layer of overlying epidermis OR from ulcer base over deepest point of invasion to (b) deepest invasive tumor cells

Traditional categories are 0 to 0.76 mm, 0.76 to 1.50 mm and greater than 1.50 mm

5 year disease free survival is 98% for first group, 44-63% for third group, intermediate for middle group

New staging systems use 1 mm increments

Frozen section measurements may be accurate ([Histopathology 1999;34:257](#))

An important prognostic factor ([Cancer 2000;88:589](#))

References: [Wikipedia](#)

Clark's levels of invasion - Skin-Melanocytic tumors chapter

Used to define subcategories of T1 melanomas (1 mm or less in thickness) ([J Natl Cancer Inst 1989;81:1893](#))

NOT useful for melanoma of palm or sole

Clark's levels are related to incidence of nodal metastases but only consider primary tumor, not nodes or metastases

Less prognostic significance than T classification ([J Craniofac Surg 2007;18:1353](#))

Less reproducible than Breslow's system ([J Pathol 1991;163:245](#)); also not always uniform due to variation in depth of skin layers

5 year disease free survival is 100% with level II, 88% with level III, 66% with level IV, 15% with level V

Must recognize that deep collection of malignant melanocytes may be attached to a pilosebaceous unit

Definition of Clark's levels:

I: not penetrating basement membrane (in situ)

II: in papillary dermis (difficult to differentiate II versus III ([SEER](#)))

III: filling the papillary dermis and stopping at the interphase between the papillary and reticular dermis

IV: in the reticular dermis

V: in the subcutaneous tissue

Melanoma – features to report - Skin-Melanocytic tumors chapter

Specimen type / procedure

Tumor location

Histologic subtype

Tumor size

Tumor thickness (Breslow)

Tumor depth (Clark's levels)

Margin of excision (distance from tumor) - lateral and deep

Tumor mitotic rate

Number of nodes examined, number with melanoma

Also: ulceration, regression, precursor lesion, angiolymphatic invasion, host lymphocytic response, mitotic index, characteristics of radial growth phase and vertical growth phase

Synoptic reports: more complete than non-synoptic reports; recommendations include free text option, tailoring to each institution and regular updates ([Histopathology 2008;52:130](#))

Staging of melanomas - Skin-Melanocytic tumors chapter

Primary difference between clinical and pathologic stage grouping is whether regional lymph nodes are staged clinically (including radiologic exam) or pathologically (after excision)

Clinical staging: perform after complete excision of tumor, microstaging (pathologic exam to determine Breslow thickness and Clark level of invasion) and assessment of metastases

Note: significant survival differences are noted based on clinical versus pathologic staging

Pathologic staging: uses clinical staging information plus pathologic examination of regional lymph nodes and pathologic confirmation of metastases

Primary tumor (T) - Melanoma - Skin-melanocytic tumors chapter

TX: primary tumor cannot be assessed (e.g. shave biopsy or regressed melanoma)

T0: no evidence of primary tumor

Tis: melanoma *in situ*

T1: melanoma 1.0 mm or less in thickness with or without ulceration

T1a: melanoma 1.0 mm or less in thickness and level II or III, no ulceration

T1b: melanoma 1.0 mm or less in thickness and level IV or V or with ulceration

T2: melanoma 1.01 - 2.0 mm in thickness with or without ulceration

T2a: melanoma 1.01 - 2.0 mm in thickness, no ulceration

T2b: melanoma 1.01 - 2.0 mm in thickness, with ulceration

T3: melanoma 2.01 - 4.0 mm in thickness with or without ulceration

T3a: melanoma 2.01 - 4.0 mm in thickness, no ulceration

T3b: melanoma 2.01 - 4.0 mm in thickness, with ulceration

T4: melanoma greater than 4.0 mm in thickness with or without ulceration

T4a: melanoma greater than 4.0 mm in thickness, no ulceration

T4b: melanoma greater than 4.0 mm in thickness, with ulceration

Notes: ulceration means absence of intact epidermis overlying the primary melanoma, as assessed by histologic examination

Regional lymph nodes (N) - Melanoma - Skin-melanocytic tumors chapter

NX: regional lymph nodes cannot be assessed

N0: no regional lymph node metastasis

N1: metastasis in one lymph node

N1a: clinically occult (microscopic) metastasis

N1b: clinically apparent (macroscopic) metastasis

N2: metastasis in 2-3 regional nodes or intralymphatic regional metastasis without nodal metastases

N2a: clinically occult (microscopic) metastasis

N2b: clinically apparent (macroscopic) metastasis

N2c: satellite or in-transit metastasis without nodal metastasis

N3: metastasis in four or more regional nodes, or matted metastatic nodes, or in-transit metastasis or satellite(s) with metastasis in regional node(s)

Satellite metastases: defined arbitrarily as intralymphatic metastases occurring within 2 cm of the primary melanoma

In-transit metastases: defined arbitrarily as intralymphatic metastases occurring more than 2 cm from the primary melanoma but before the first echelon of regional lymph nodes

Regional nodal metastases: disease confined to one nodal basin or two contiguous nodal basins

Note: HMB45 or MelanA positive isolated cells in sentinel nodes appear to have no prognostic significance, at least short term ([AJSP 2007;31:1175](#))

Distant metastasis (M) - Melanoma - Skin-melanocytic tumors chapter

MX: distant metastasis cannot be assessed

M0: no distant metastasis

M1: distant metastasis

M1a: metastasis to skin, subcutaneous tissues or distant lymph nodes

M1b: metastasis to lung

M1c: metastasis to all other visceral sites or distant metastasis at any site associated with an elevated serum lactic dehydrogenase (LDH)

Clinical stage grouping - Melanoma - Skin-melanocytic tumors chapter

0 : Tis N0 M0

IA : T1a N0 M0 ()

IB : T1b N0 M0 or T2a N0 M0

IIA : T2b N0 M0 or T3a N0 M0

IIB : T3b N0 M0 or T4a N0 M0

IIC : T4b N0 M0

III : Any T, N1-N3, M0

IV : Any T, any N, M1

Note: clinical staging includes microstaging of the primary melanoma and clinical/radiologic examination for metastases

Stages I/II: no evidence of metastases; stage I are considered low risk for metastases / mortality, and stage II are considered intermediate risk

Stage III: regional metastases to lymph nodes, satellite metastases or in-transit metastases; no substaging is done

Stage IV: distant metastases

Pathologic stage grouping and 5 year survival - Melanoma - Skin-melanocytic tumors chapter

0 : Tis N0 M0

IA : T1a N0 M0 (95%)

IB : T1b N0 M0 or T2a N0 M0 (89-91%)

IIA : T2b N0 M0 or T3a N0 M0 (77-79%)

IIB : T3b N0 M0 or T4a N0 M0 (63-67%)

IIC : T4b N0 M0 (45%)

IIIA : T1-T4a, N1a or N2a, M0 (67%)

IIIB : T1-T4b, N1a or N2a, M0 or T1-T4a, N1b or N2b, M0 or T1-T4b, N2c, M0 (52-54%)

IIIC : T1-T4b, N1b or N2b, M0 or any T, N3 M0 (24-28%)

IV : Any T, any N, M1

Stages I/II: no evidence of metastases (regional or distant); stage I are considered low risk for metastases / mortality, and stage II are considered intermediate risk

Stage III: regional metastases to lymph nodes, satellite metastases or in-transit metastases; stage IIIA are considered to have intermediate risk for distant metastases / survival, stage IIIB to have high risk and stage IIIC to have very high risk

Stage IV: distant metastases

Notes: increased complexity of AJCC 2002 system did not improve its predictive ability over the simpler AJCC 1997 ([Cancer 2006;106:163](#))

References: [CA Cancer J Clin 2004;54:131](#), [Cancer Control 2002;9:9](#), [Staging Tool](#)

End of Skin-Melanocytic tumors chapter

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