18th Summer Academy of Dermatopathology | Graz, July 6 - 10, 2026

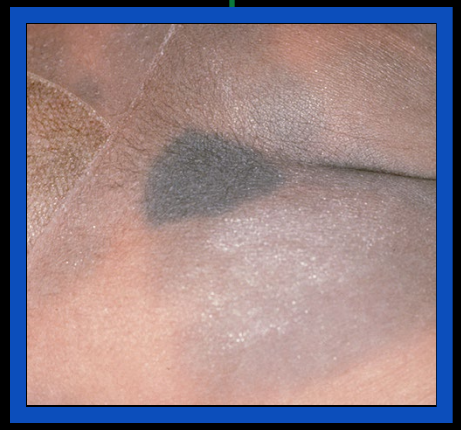
Dermal Melanocytoses and Melanocytomas

Jean Bolognia, MD

Conflict of Interest: Royalties Elsevier

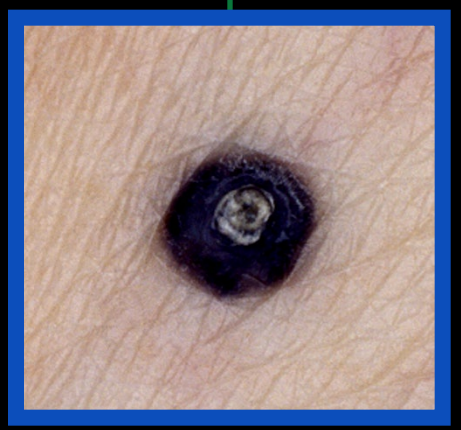
Melanocytoses

Melanocytomas

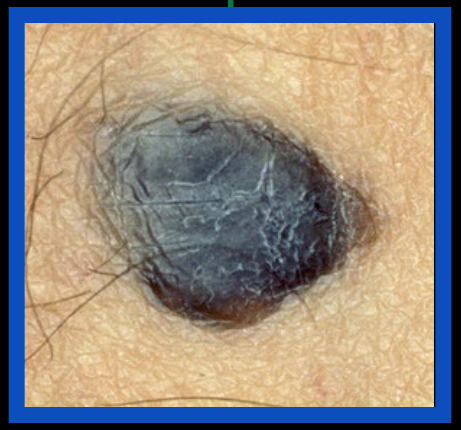


CDM

Nevus of Ota

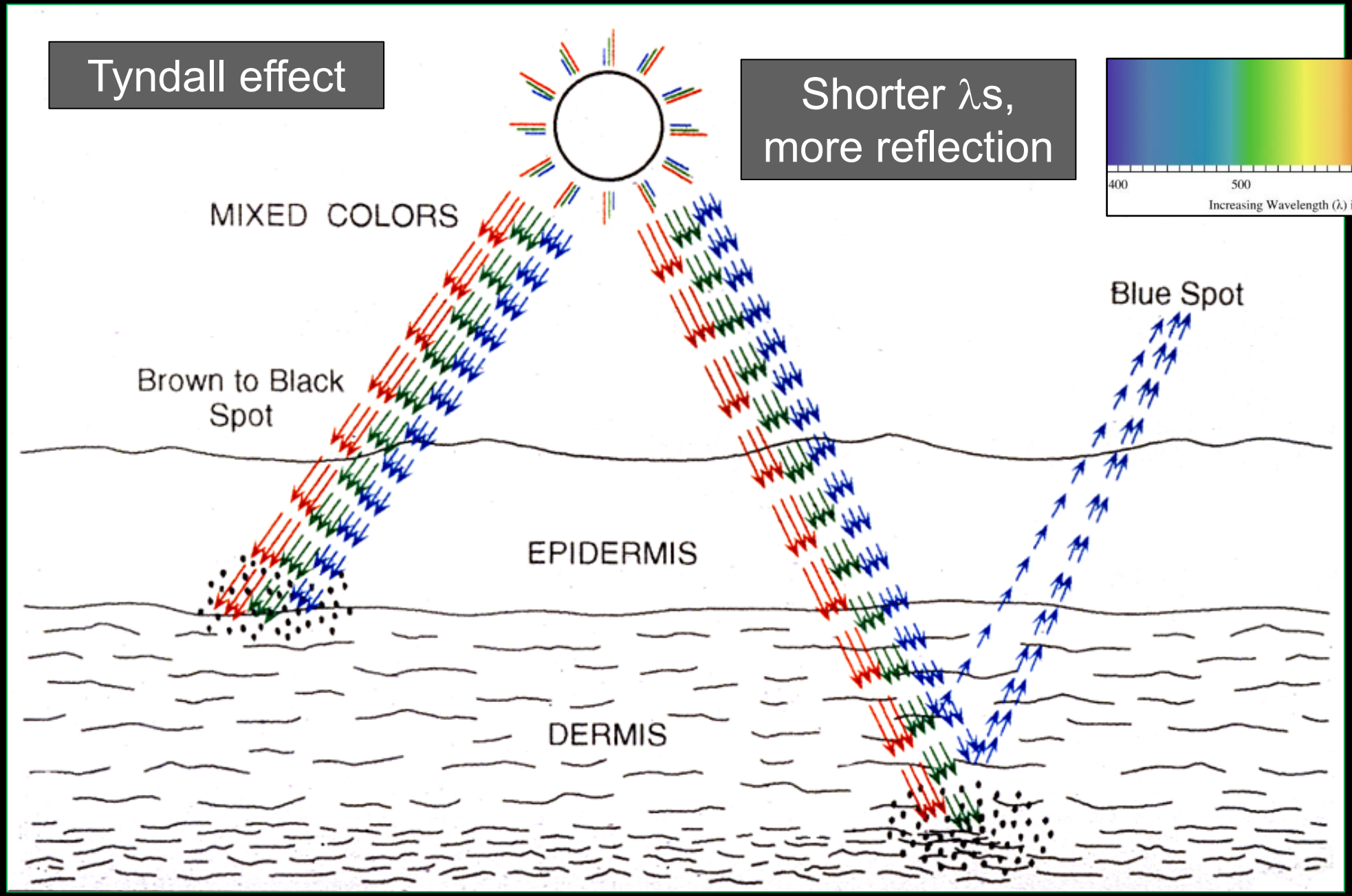


Common blue nevus



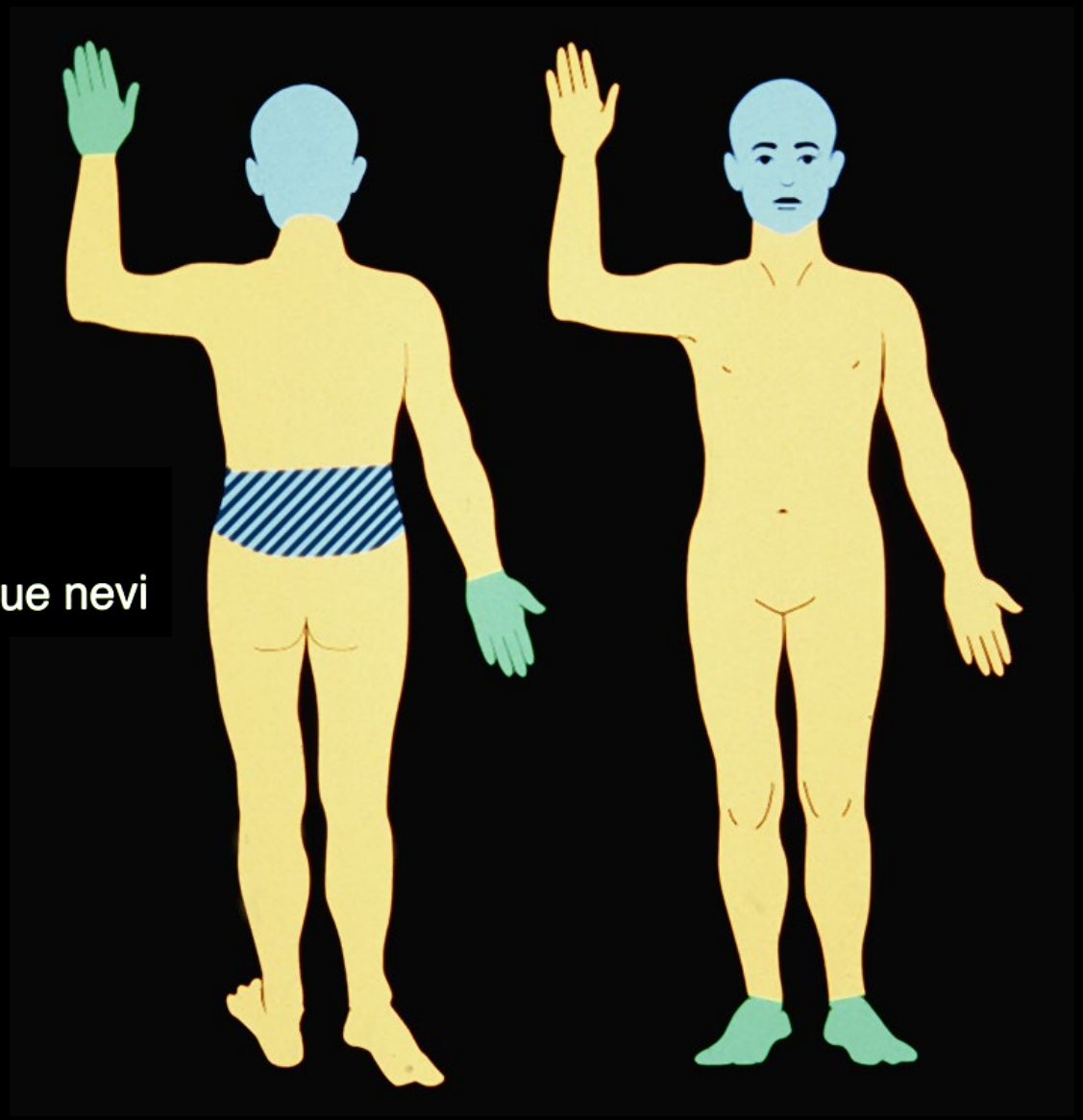
Cellular blue nevus

CDM, congenital dermal melanocytosis – also called circumscribed dermal melanocytosis or sacral spot of infancy; previously referred to as Mongolian spot (Baelz, 1901), child fleck, and “purple tail”


Tyndall effect
Shorter λs, more reflection
400
500
600
700
Increasing Wavelength (λ) in nm →
MIXED COLORS
Blue Spot
Brown to Black Spot
EPIDERMIS
DERMIS

Common blue nevi

Common and cellular blue nevi and nevus of Ota



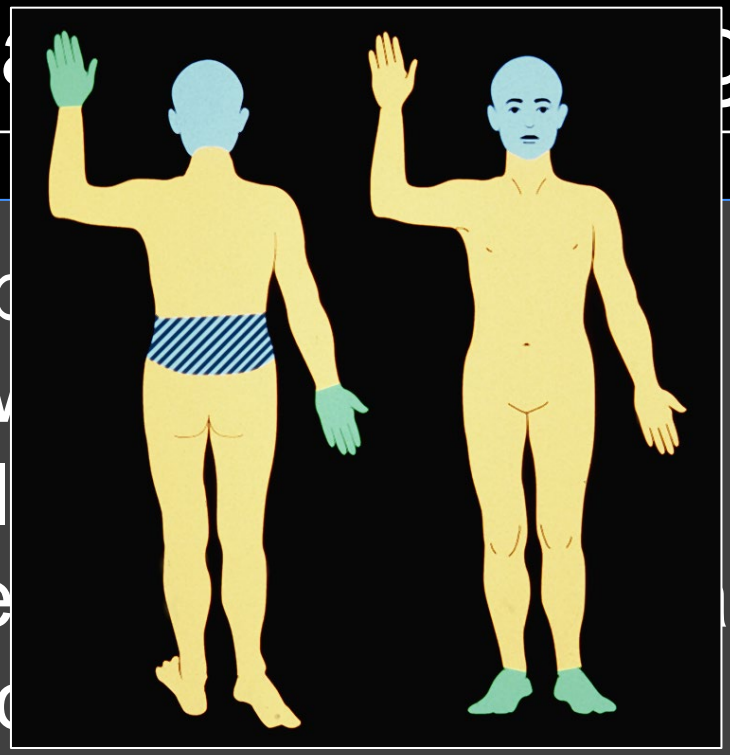
Congenital dermal melanocytosis (CMD) and cellular blue nevi

Dermal Melanocytes during Fetal Life

- Melanoblasts appear in the dermis of the fetus beginning in week 10
- Initial sites: scalp, neck, and sacral region
- Beginning in week 20, there is disappearance of dermal melanocytes
- By birth have disappeared except in the dermis of:
  - scalp
  - sacral region
  - dorsum hands & feet

Zimmerman AA, Becker SW, Jr. Fourth Conference on Biology of Pigment Cells, 1957.

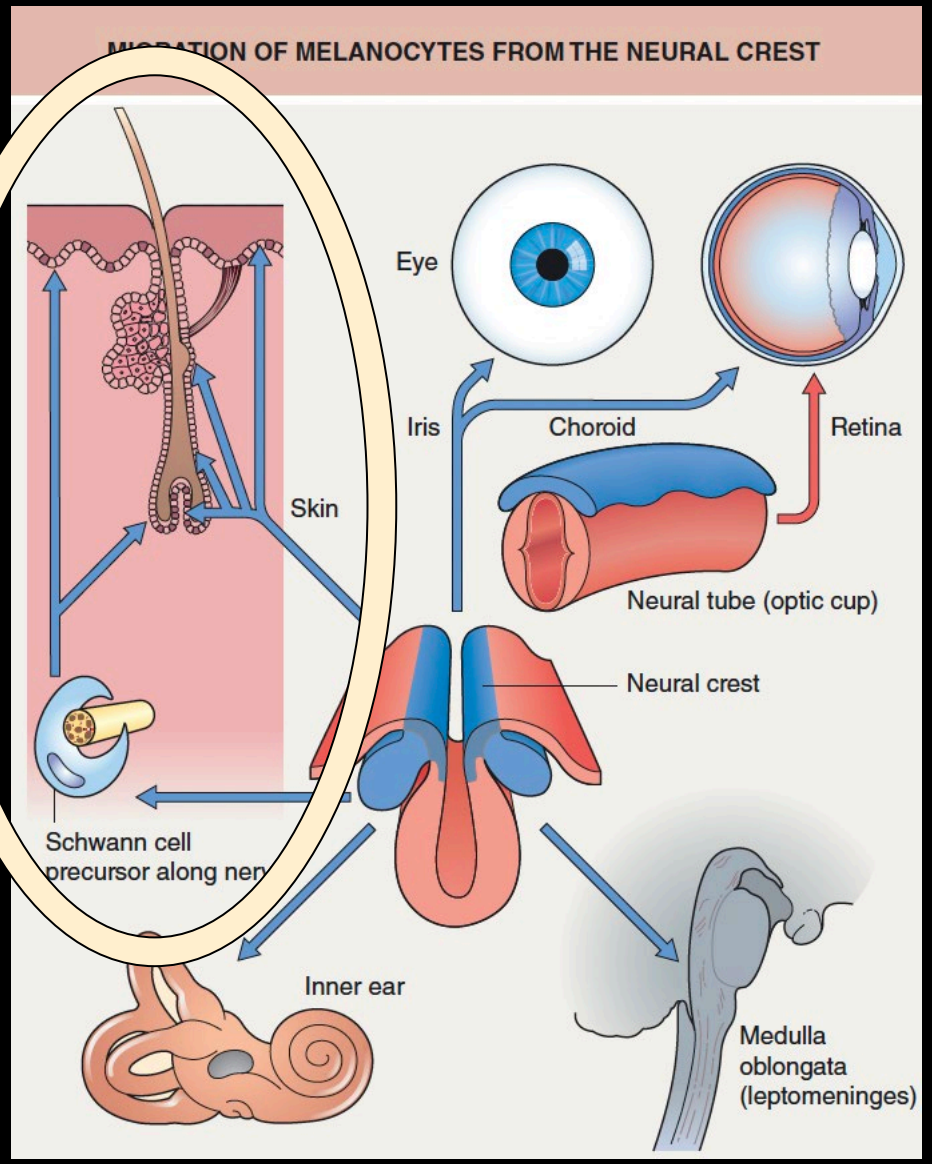
Dermal Mel… …g Fetal Life

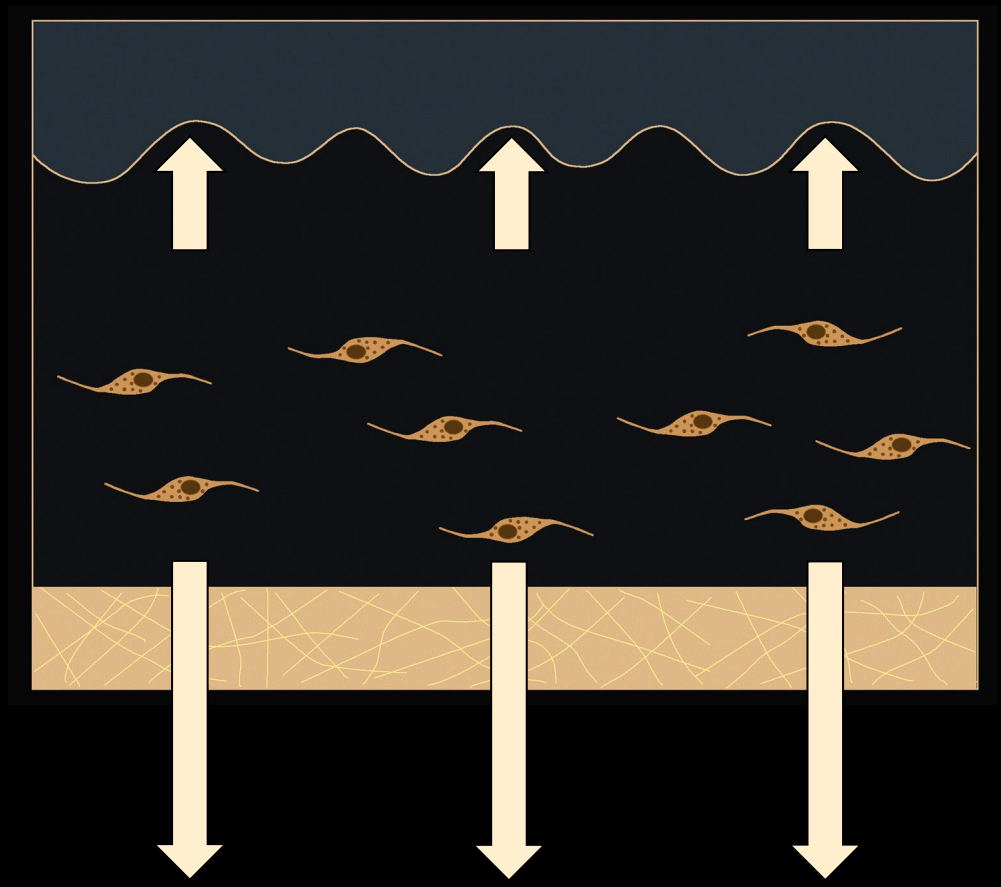


- Melanoblasts ap… …of the fetus beginning in w…
- Initial sites: scal… …region
- Beginning in we… …ppearance of dermal melan…
- By birth have disappeared except in the dermis of:
  - scalp
  - sacral region
  - dorsum hands & feet

Zimmerman AA, Becker SW, Jr. Fourth Conference on Biology of Pigment Cells, 1957.

Zimmerman A. Gordon, Pig Cell Bio, 1959, pp. 159–170.


MIGRATION OF MELANOCYTES FROM THE NEURAL CREST
Eye
Iris
Choroid
Retina
Skin
Neural tube (optic cup)
Neural crest
Schwann cell
precursor along ner
Inner ear
Medulla
oblongata
(leptomeninges)



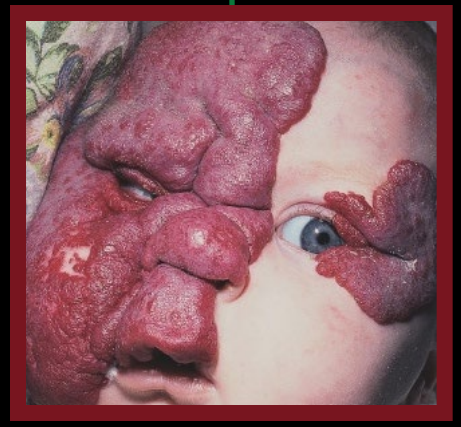
Apoptosis

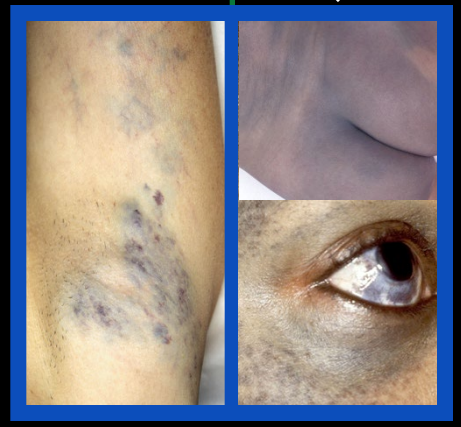
BLUE

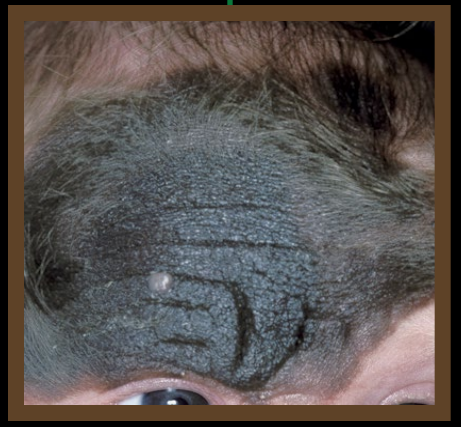
Dermal melanocytosis
nevus fuscocaeruleus
patch blue nevus
Dermal melanocytoma
nevus of Ota-like macules*
nevus of Ota
nevus of Ito
common
Blue nevi
extra sacral**
sacral**
plaque blue nevus
cellular
Density of dermal melanocytes
+
+++

*acquired **congenital dermal melanocytosis

Birthmarks







Melanocytoses

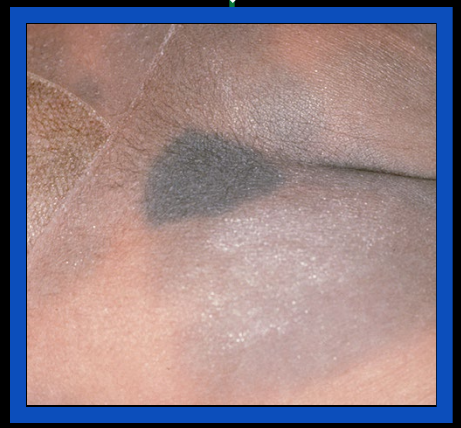
Melanocytomas

Congenital

~65% 1st yr

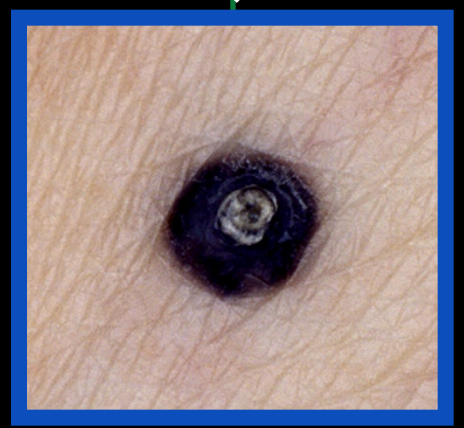
~15%*

~30%*

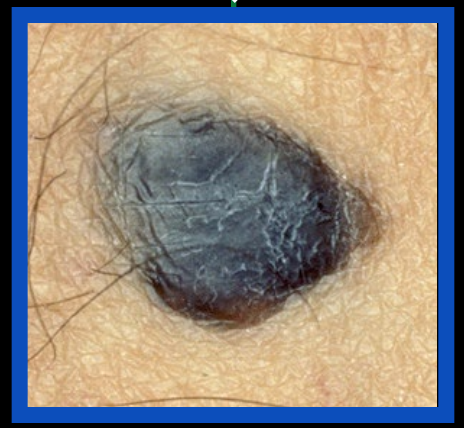


CDM

Nevus of Ota



Common blue nevus



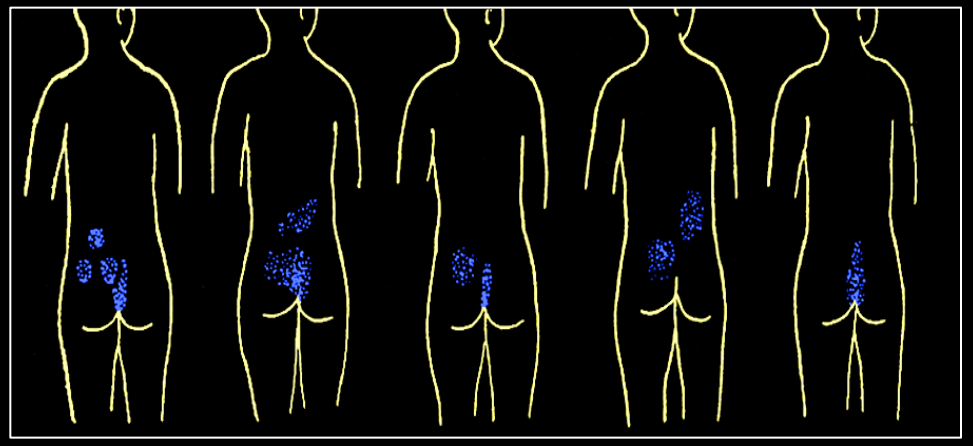
Cellular blue nevus

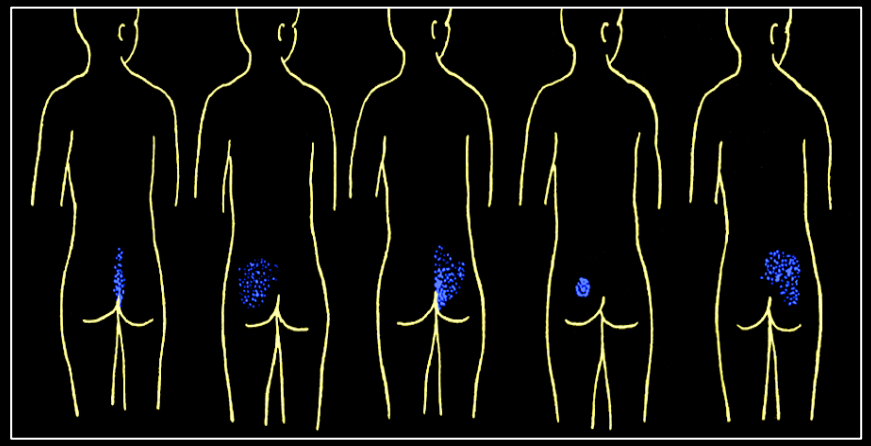
CDM, congenital dermal melanocytosis – also called circumscribed dermal melanocytosis or sacral spot of infancy; previously referred to as Mongolian spot (Baelz, 1901), child fleck, and “purple tail”

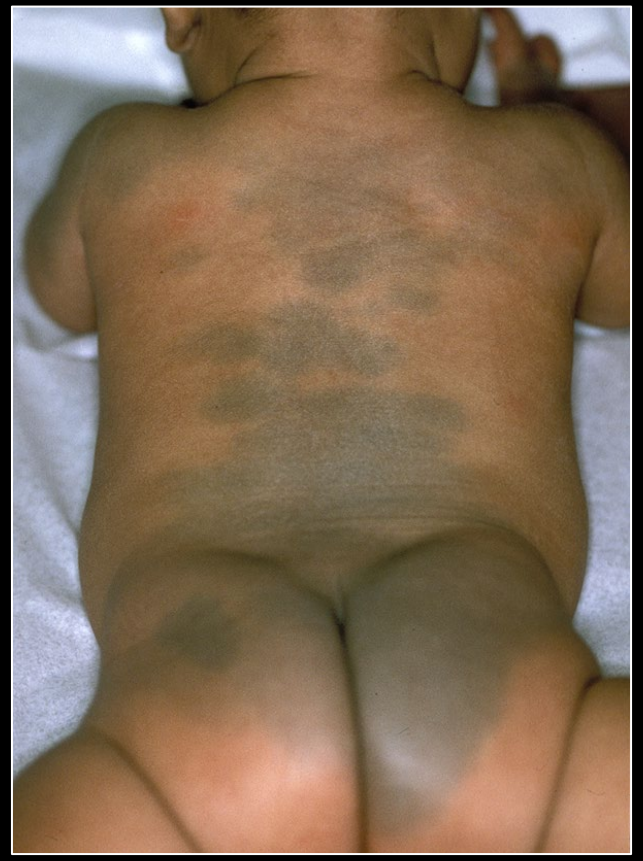
*% congenital

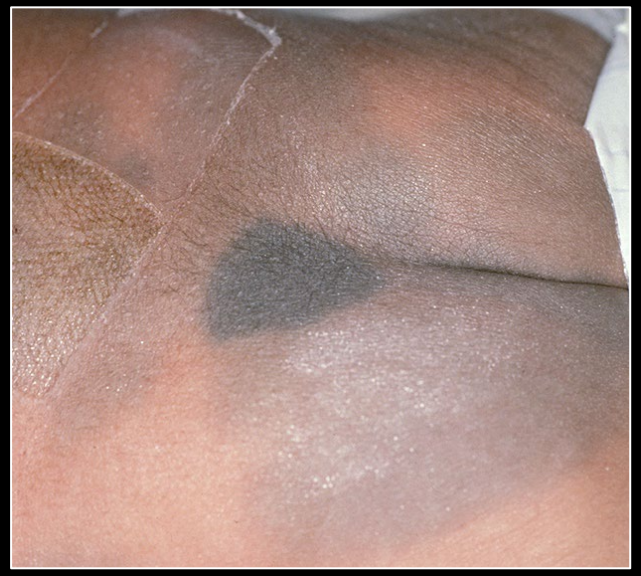
Congenital (Circumscribed) Dermal Melanocytosis

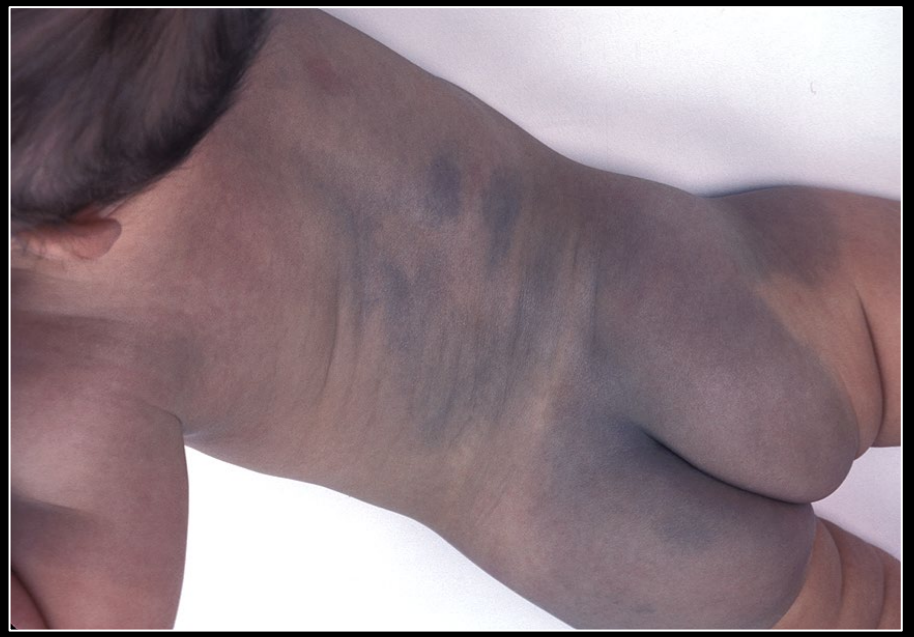
- Usually occupy <5% body surface area (BSA)
- In <5% of patients, involvement is >15% BSA
- Sacrococcygeal and lumbar regions, buttocks > mid/upper back >> extremities >> ventral trunk
- Usually different shades of blue & gray-blue

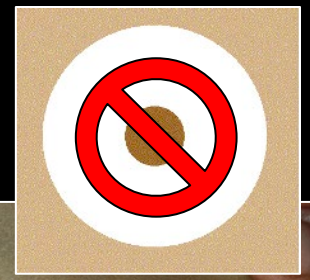


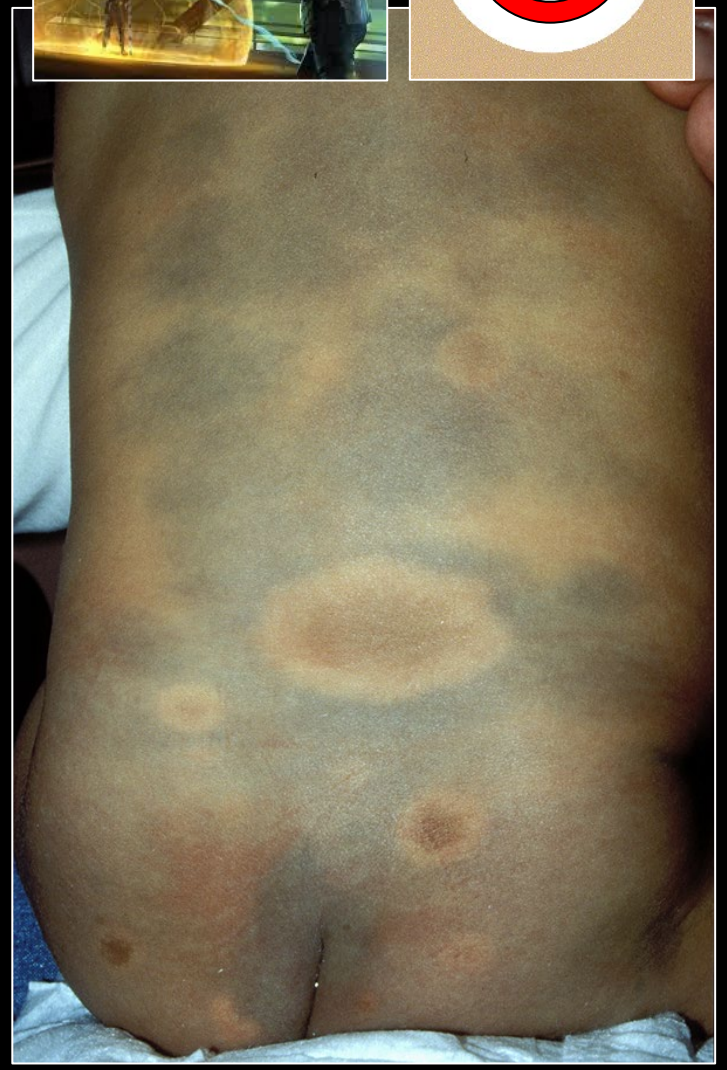




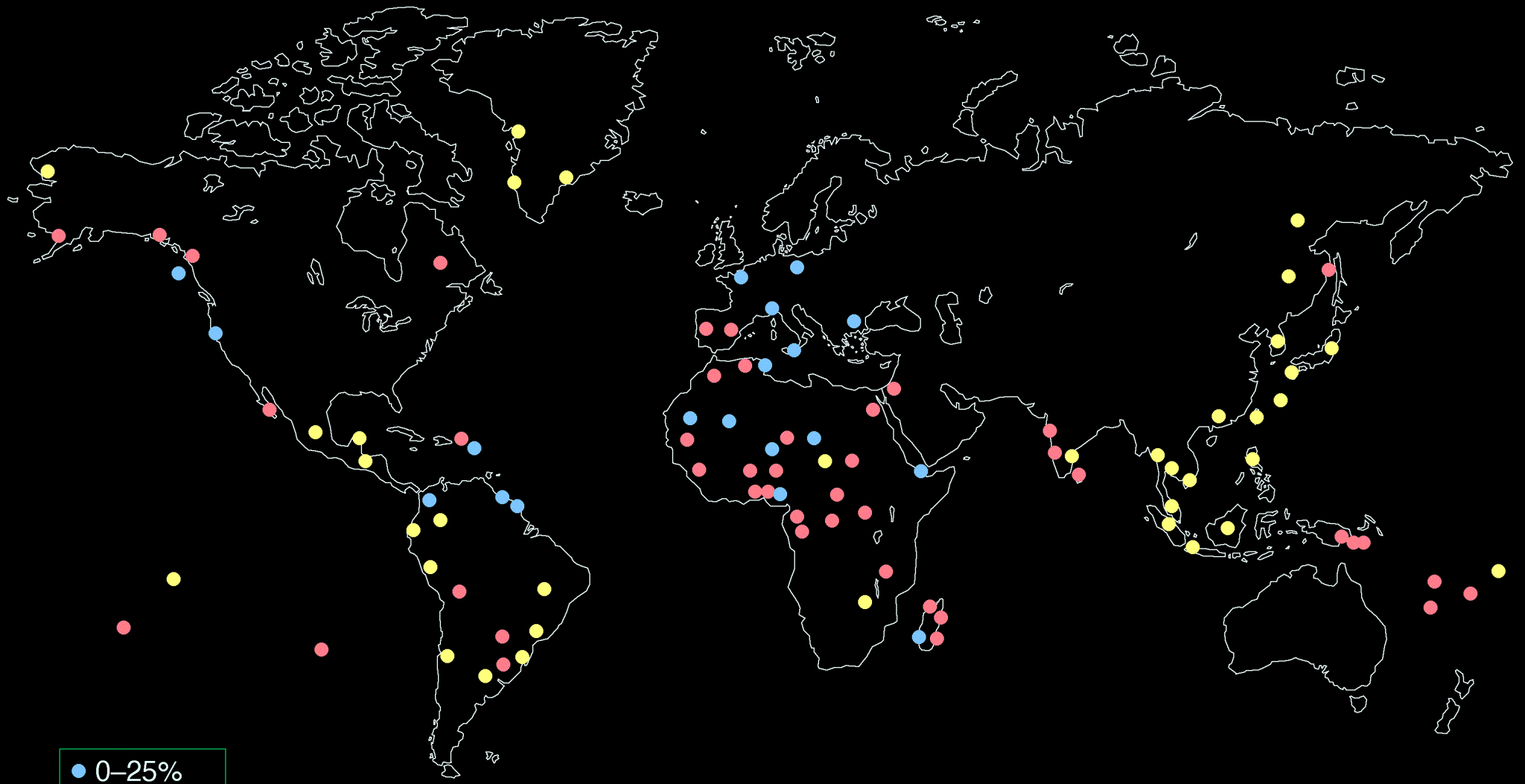








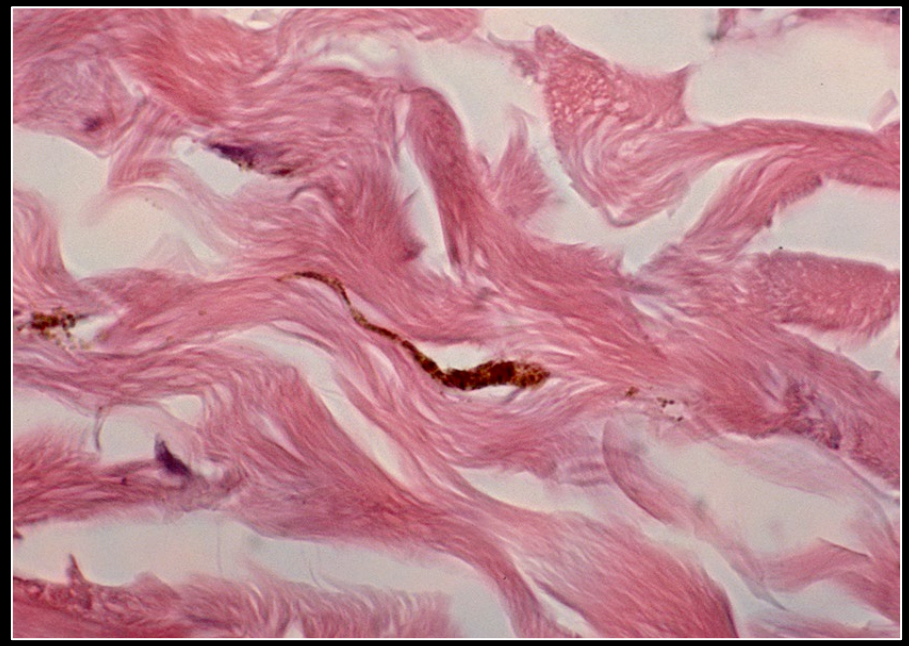
First described in the 1970s



Adapted from Kikuchi I. Biology and DIseases of Dermal Pigmentation, 1982
Uribe MGA. IJD 9:180, 1970
Morooka K. AAJ 3:1371, 1931

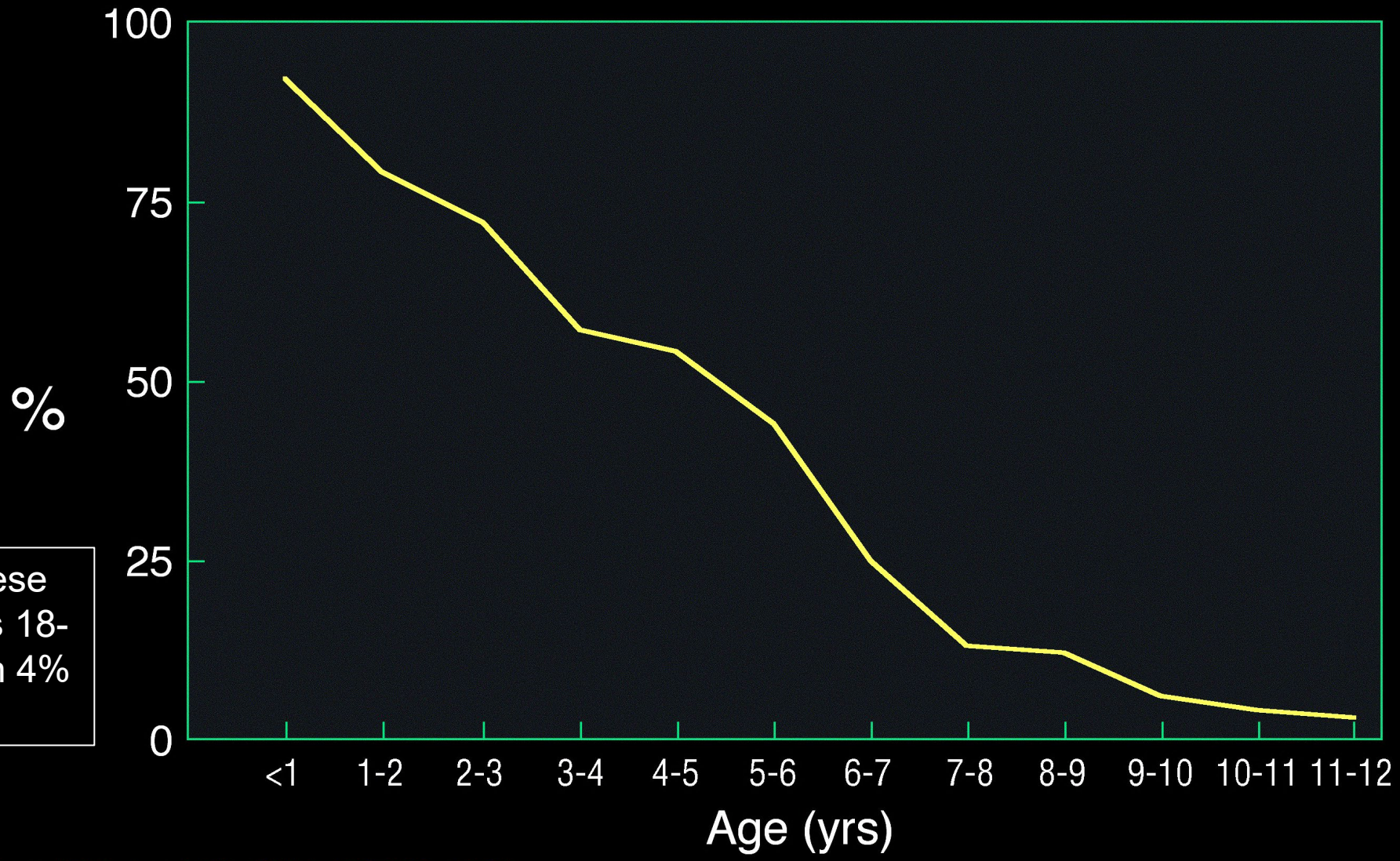
0396052n

Congenital (Circumscribed) Dermal Melanocytosis



Asian > Black > White individuals

Prevalence of Circumscribed Dermal Melanocytosis in 3,230 Chinese Children



Of 9996 Japanese policemen ages 18-26, persistent in 4% (Hidano, 1971)

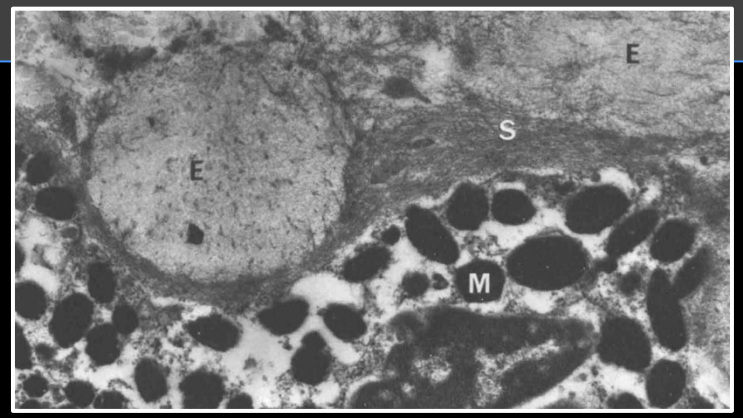
Lau JRK. Am J Dis Child 136:863, 1982

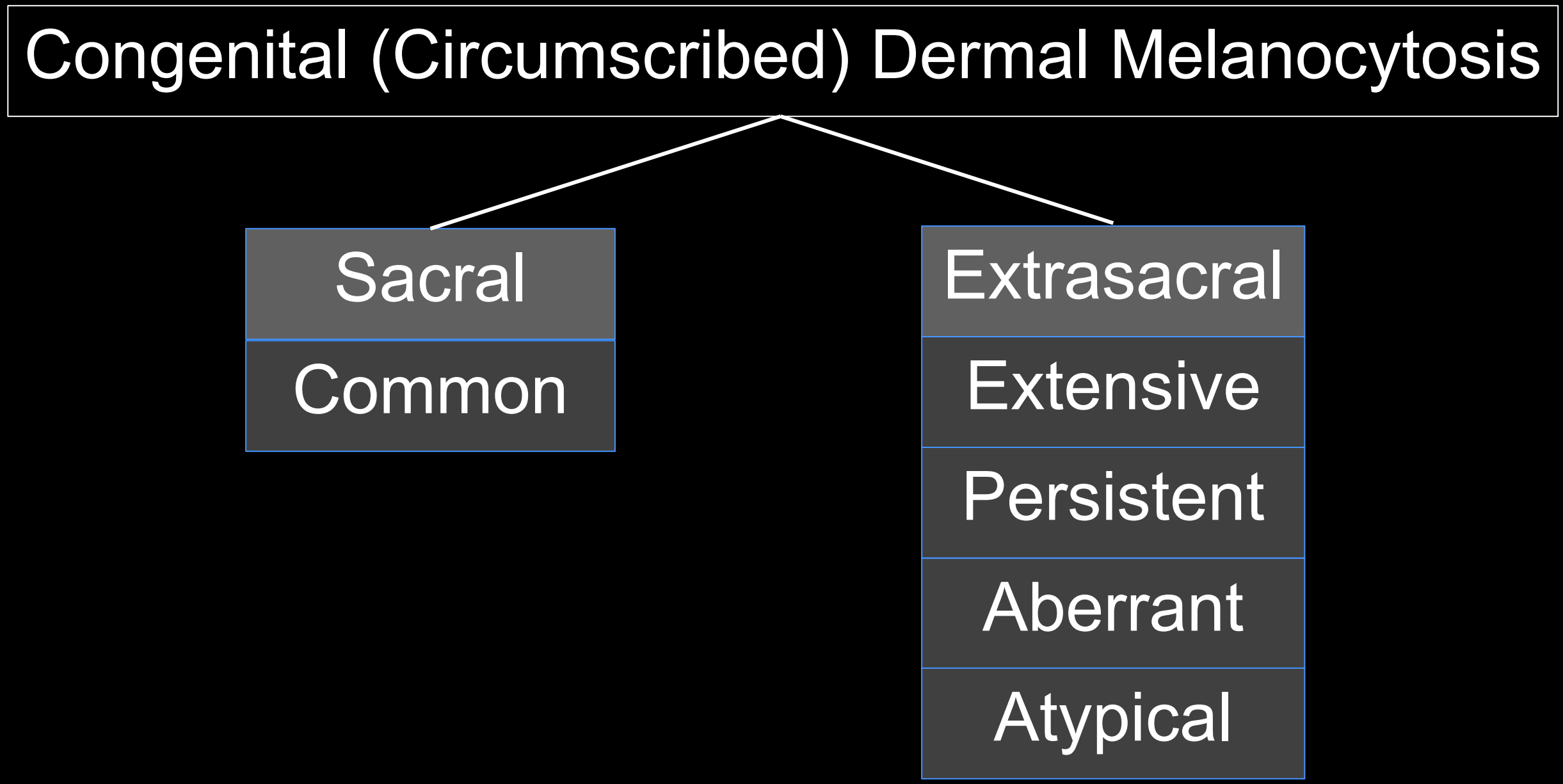
0197016n

What is the explanation for persistent CDM?

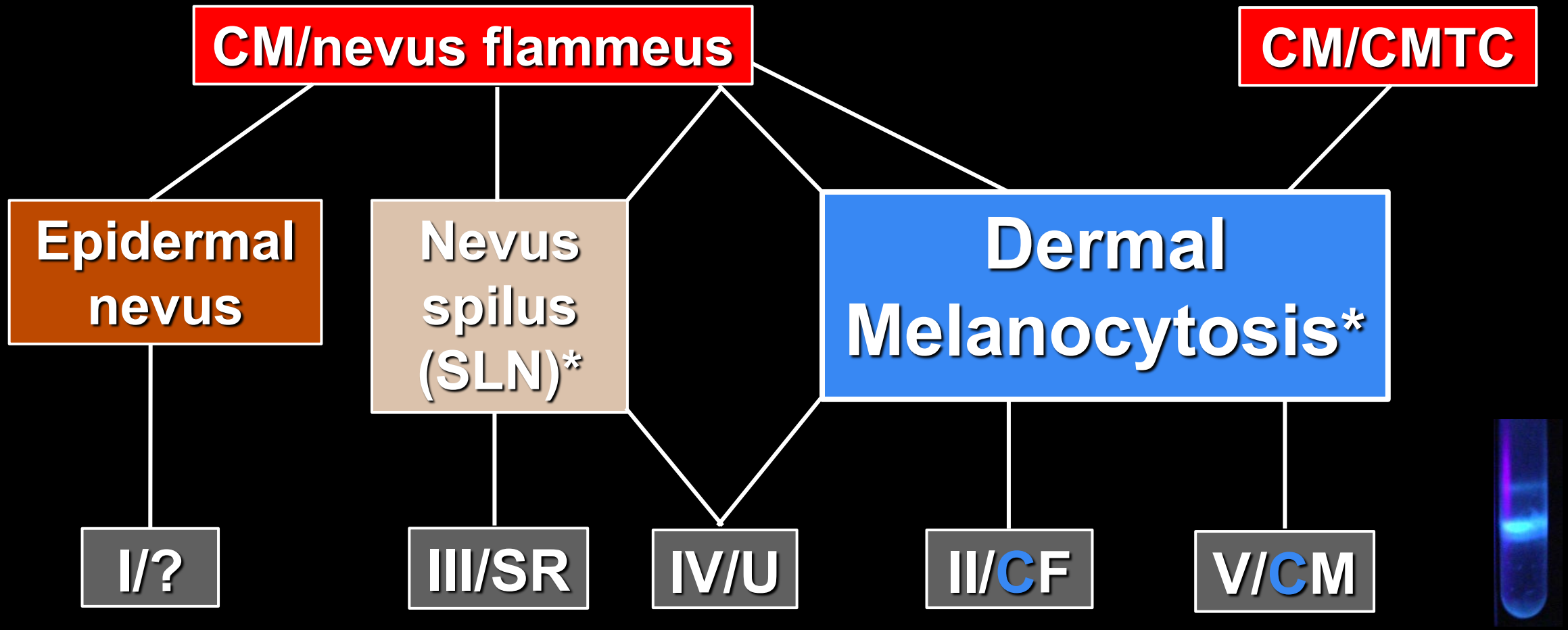
- Persistence of the extracellular sheath that encloses dermal melanocytes
- Hypothesized that lost of this extracellular sheath (S) is followed by ”disintegration” of the dermal melanocyte
- Unclear how this is related to mosaic activating mutations in *GNAQ* in patients with extensive dermal melanocytosis

Inoue S. *Nippon Hifuku* 1967;77:291.
Okawa Y. *JID* 1979;73:224.
Thomas AC. *JID* 2016;136:770.




Congenital (Circumscribed) Dermal Melanocytosis
Sacral
Common
Extrasacral
Extensive
Persistent
Aberrant
Atypical

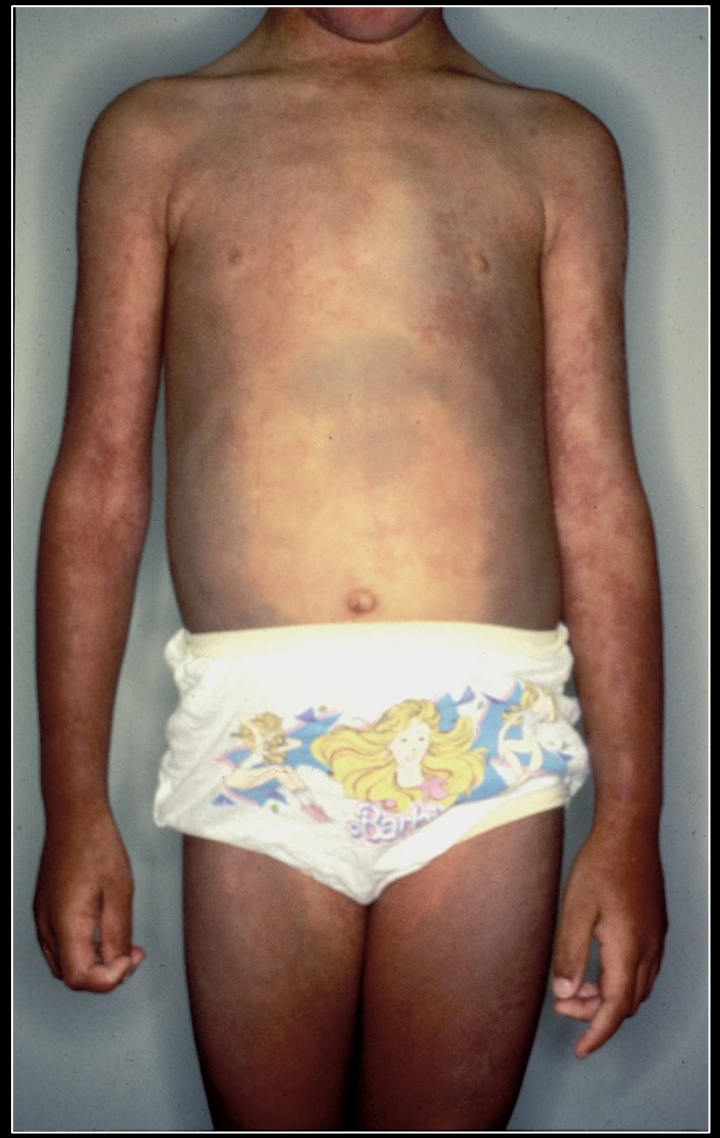
Phakomatosis Pigmentovascularis (Ota, 1947)



*+/- nevus anemicus
**flag-like hypermelanosis

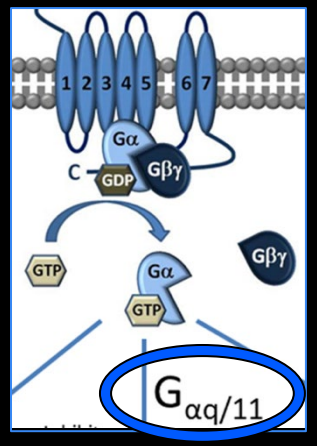
CF, cesioflammea; CM, cesiomarmorata; CMTC, cutis marmorata telangiectatica congenita; MR, melanorosea; SR, spilorosea; SLN, speckled lentiginous nevus; U, unclassified

Mosaic activating mutations in *GNA11* or *GNAQ** – paralogous genes



Capillary malformations
- Sturge-Weber syndrome
- Klippel-Trenaunay syndrome

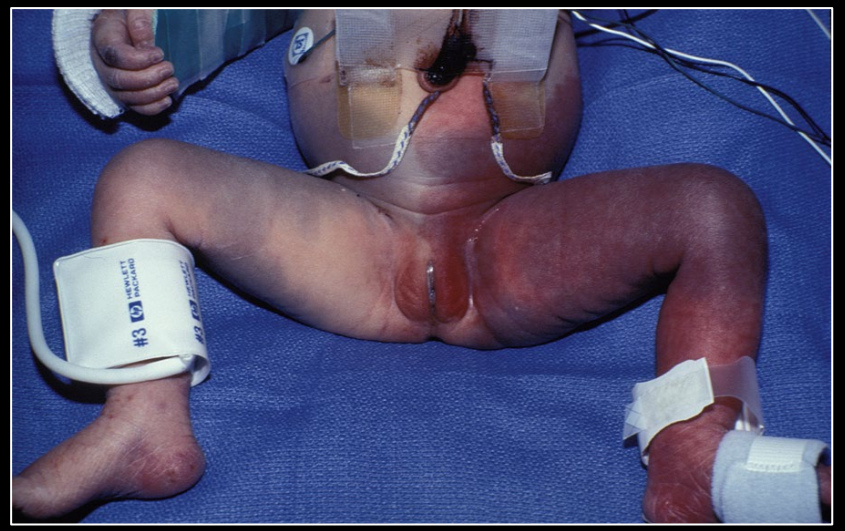
Dermal melanocytosis
- Oculodermal melanocytosis



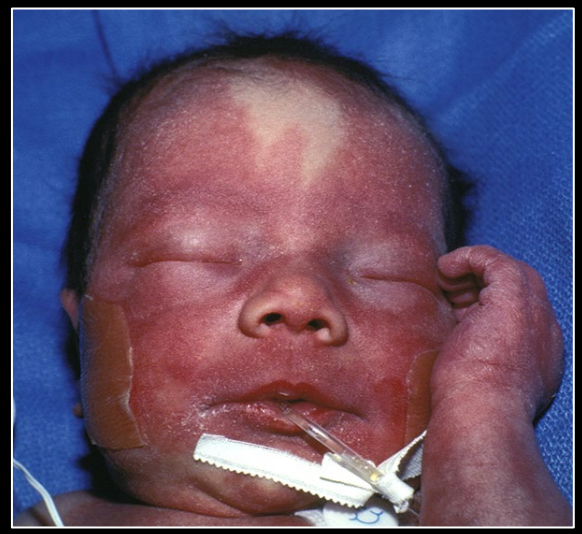
PLC: PIP_2 --> DAG (diacylglycerol) + IP_3 (inositol triphos-phate)

Ca^{2+}

PPV3/SR (lacks dermal melanocytosis) - *PTPN11*



Courtesy, Elaine Siegfried, MD

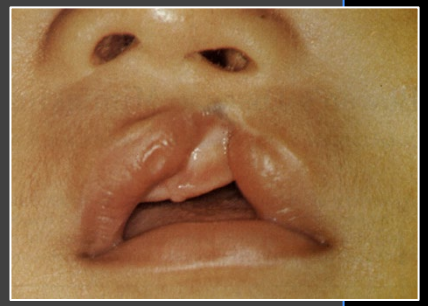


*Primarily R183C (*GNA11*) and R183Q (*GNAQ*)

Thomas AC et al. *JID* 2016;136:770.
Polubothu S, et al. *JID* 2023;143:1042.

Disorders associated with CDM

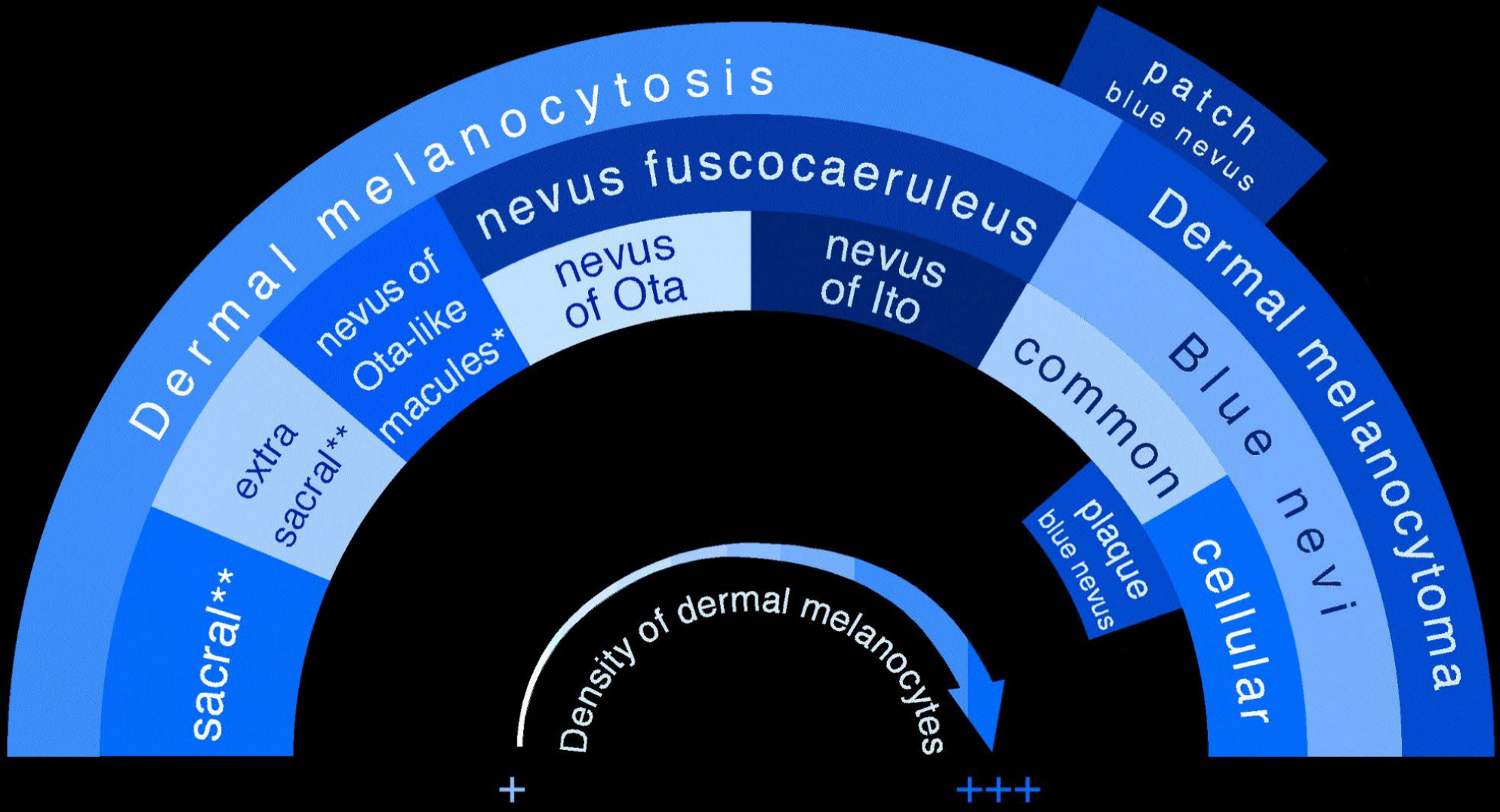
- **Localized** – co-localizes with a unilateral cleft lip/palate; in 1 series of 66 patients, observed in 50%



- **Persistent and/or extensive**
  - phakomatosis pigmentovascularis II/SR, IV/U, V/CM
  - lysosomal storage diseases – primarily Hurler's syndrome (MPS 1) and GM_1 gangliosidosis type I*; does binding of accumulated metabolites to Trk, a receptor for nerve growth factor (NGF), lead to increased NGF activity?

*less often, MPS II, MPS VI, mucolipidosis II, α-mannosidosis, Sandhoff disease, MPS IIIC (carrier), ?Niemann-Pick disease, ?Krabbe disease

Inoue S. *Arch Dermatol* 1982;118:443.
Igawa HH. *JAAD* 1994;30:566.
Hanson M. *Arch Dermatol* 2003;139:916.

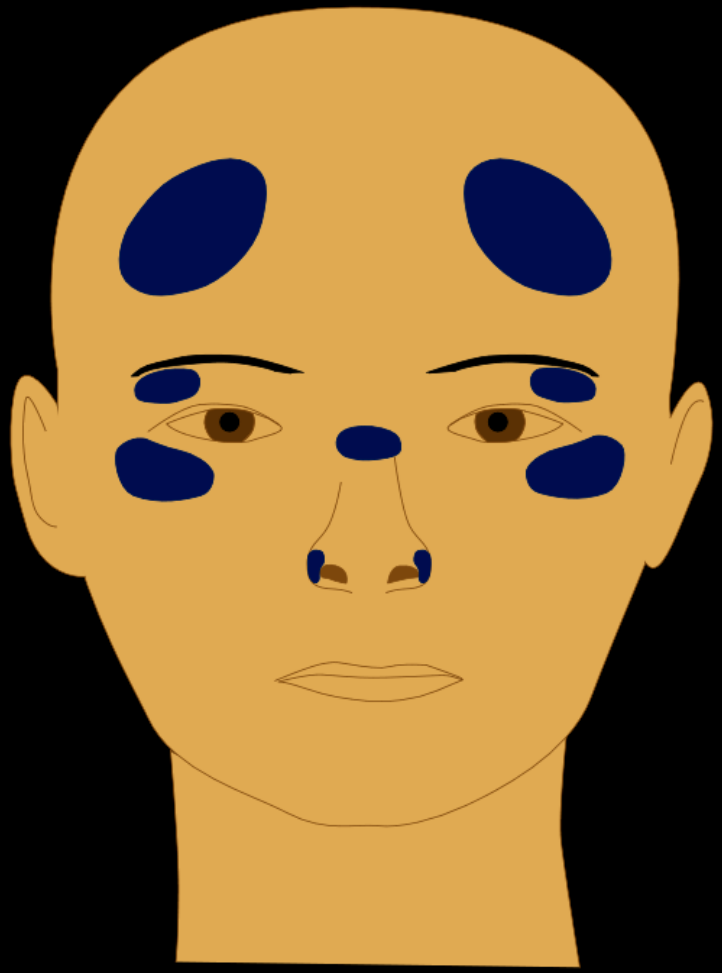


*acquired **congenital dermal melanocytosis

Nevus of Ota-like Macules

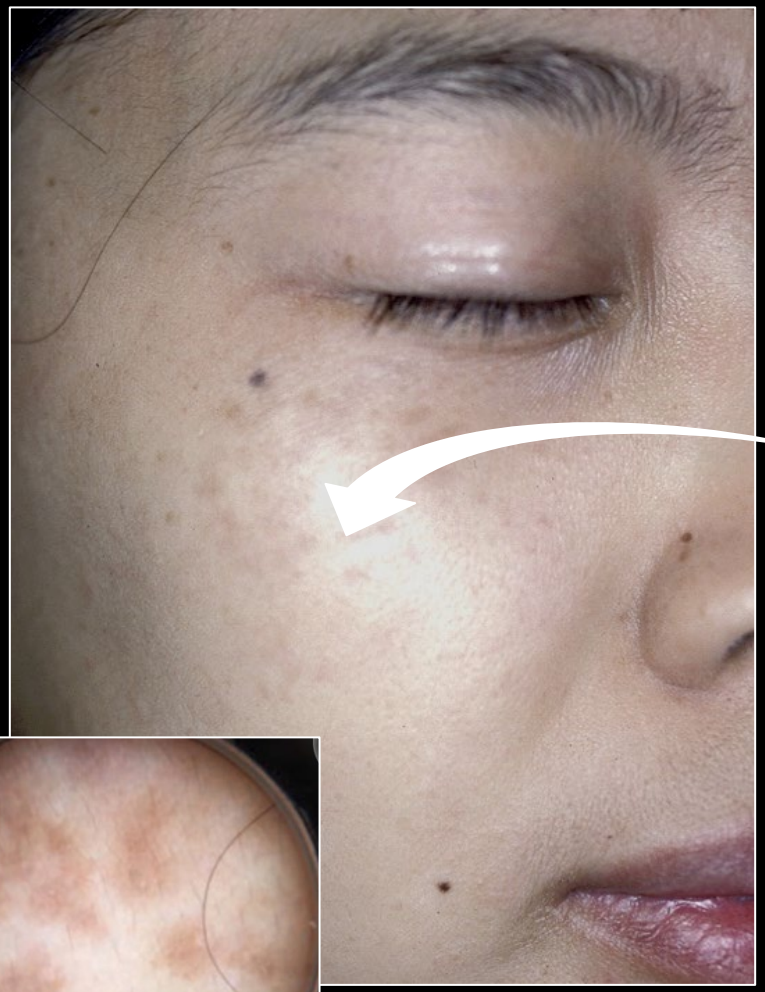
Favors females
V1 & V2

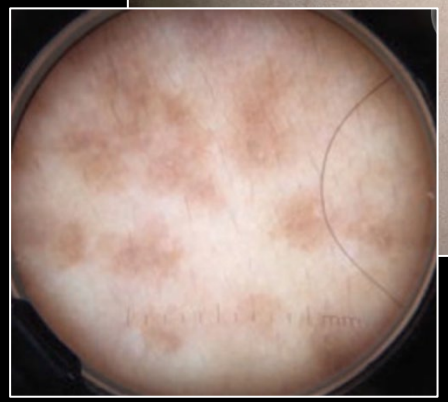
Acquired (adults)
Bilateral (9:1 odds)
Absence of ocular involvement (8-9:1 odds when bilateral)

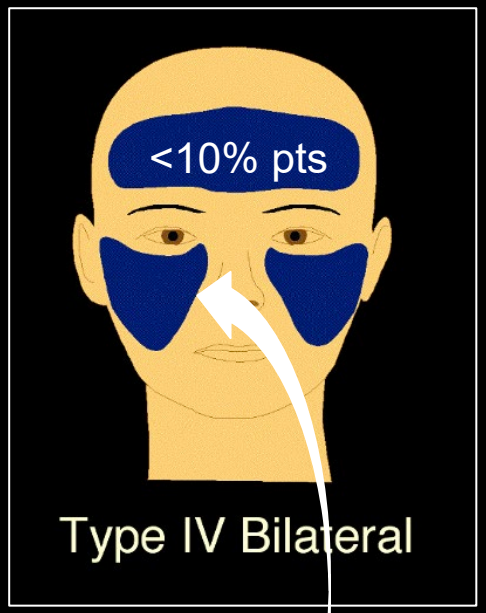


1. Lateral sites of the forehead
2. Upper eyelids
3. Malar area
4. Root of the nose
5. Alae of the nose

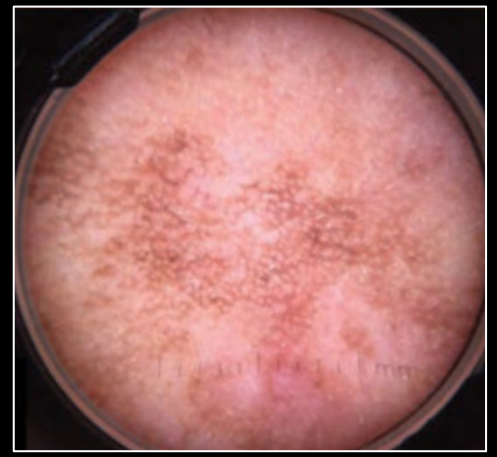
Hori Y et al., J Am Acad Dermatol 10:961-964, 1984







755 nm picosecond alexandrite laser



Rattananukrom T. *J Clin Aesthet Dermatol* 2022;15:16.

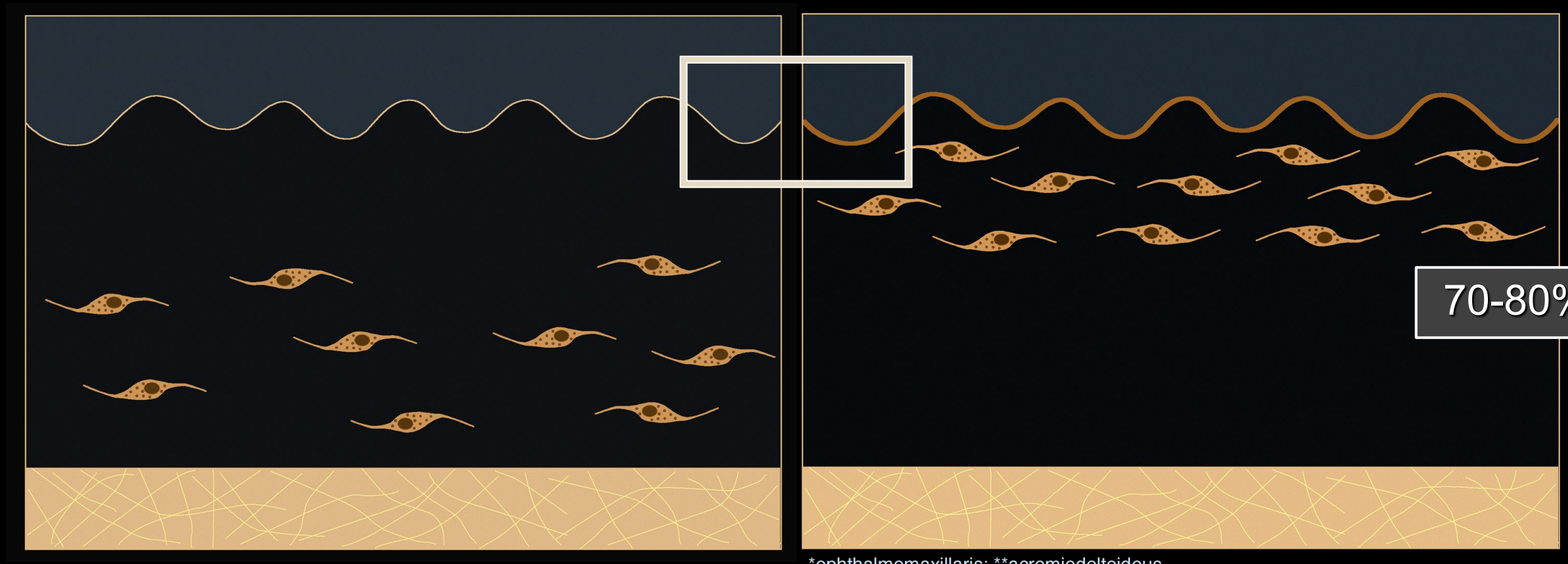
fusco-caeruleus

- *fusco*-, from fuscus = dark, tawny (brownish)
- *c(a)eruleus* = sky blue

Inoue S. *Nippon Hifuku* 1967;77:291.
Okawa Y. *JID* 1979;73:224.

Congenital Dermal Melanocytosis

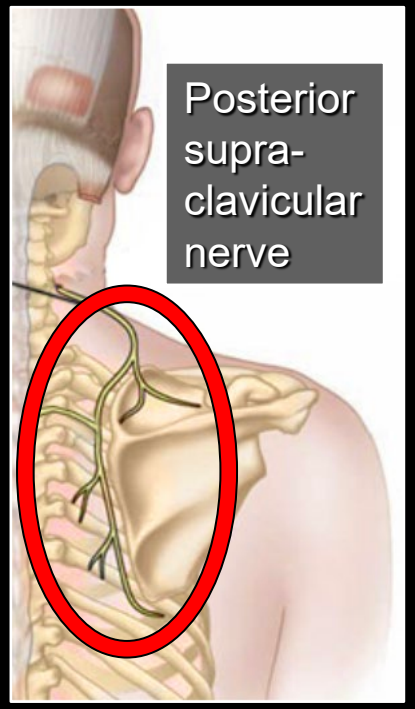
Nevus of Ota* and Nevus of Ito**
(Nevus fuscocaeruleus)

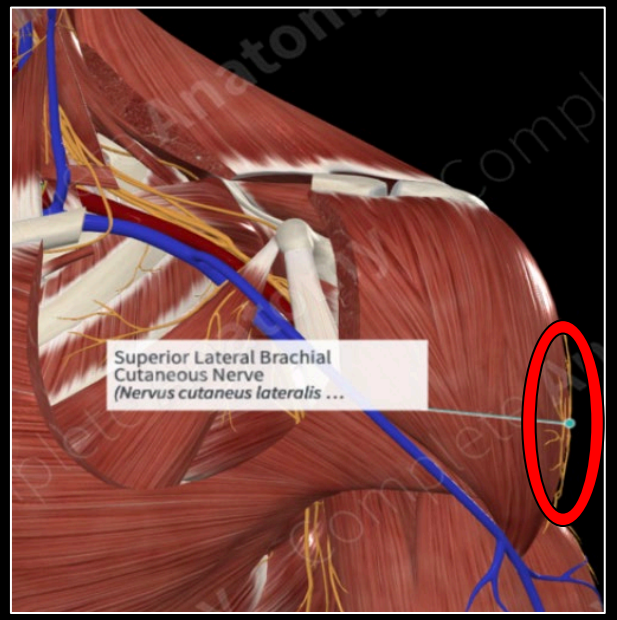


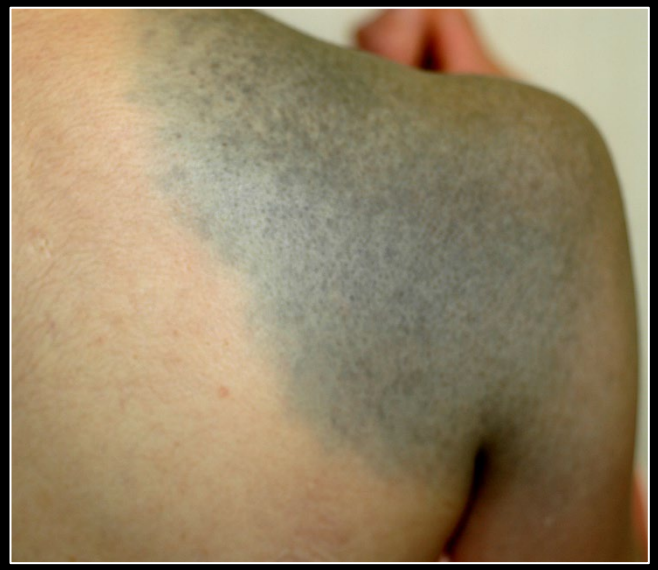
*ophthalmomaxillaris; **acromiodeltoideus

Nevus of Ito (nevus fusco-ceruleus acromio-deltoideus)

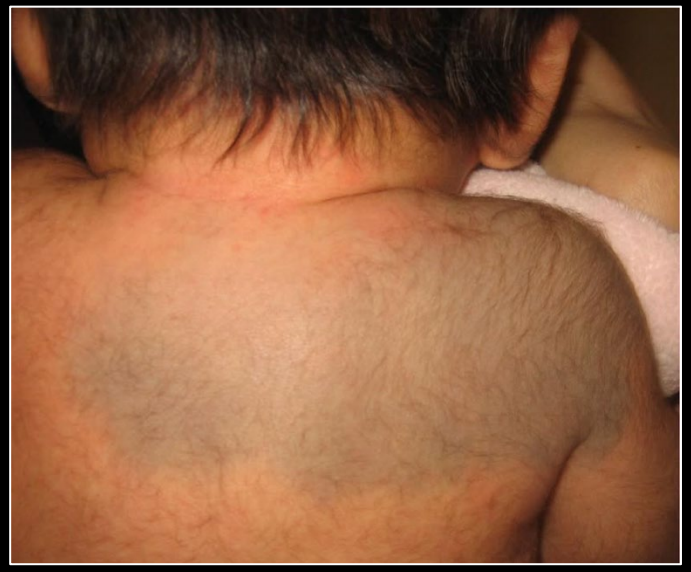
Dermal melanocytosis in the distribution of the supraclaviculares posteriores and cutaneous brachii lateralis nerves







Courtesy, Luis Requena, MD



Courtesy, Liliana Castro Vinces, MD

Studies on Melanin

XXII. Nevus Fusco-caeruleus Acromio-deltoideus

By

Minor Itô

From the Department of Dermatology, Tohoku University, Sendai; Director: Prof. M. Itô

(Received for publication, May 25, 1954)

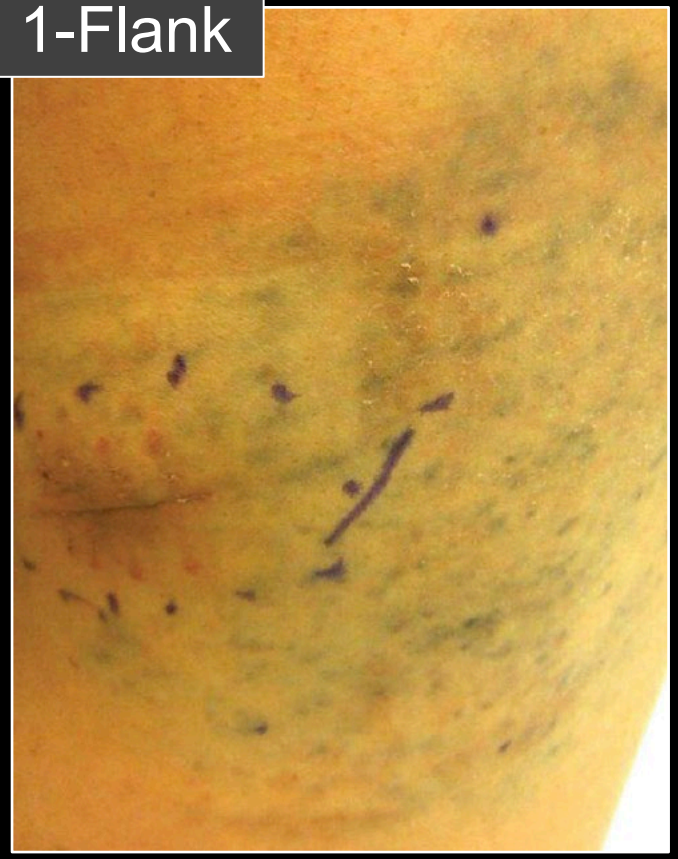
1954

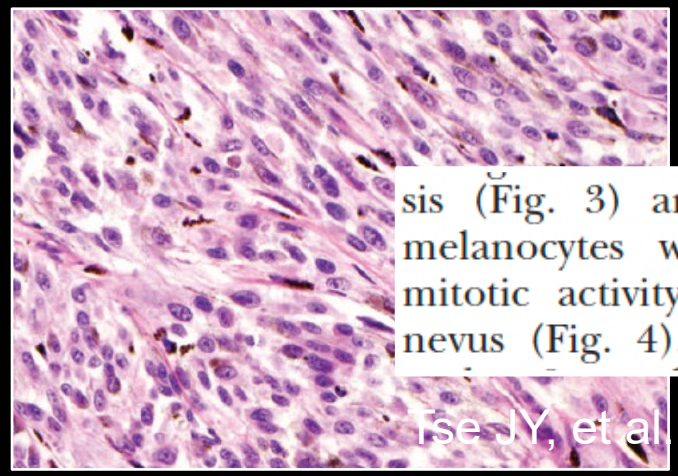
Nevus of Ito (nevus fusco-ceruleus acromio-deltoideus)

Associations:
- true/true related: nevus of Ota
- true but related to co-existing nevus of Ota: glaucoma, leptomeningeal melanocytosis (neurocutaneous melanosis), ocular melanoma
- most likely true/true unrelated: Bednar tumor (pigmented DFSP)*, reticulate acropigmentation of Kitamura*, nevus spilus*
- debatable – cutaneous melanoma – 4 case reports

*single case report
DFSP, dermatofibrosarcoma protuberans

1-Flank

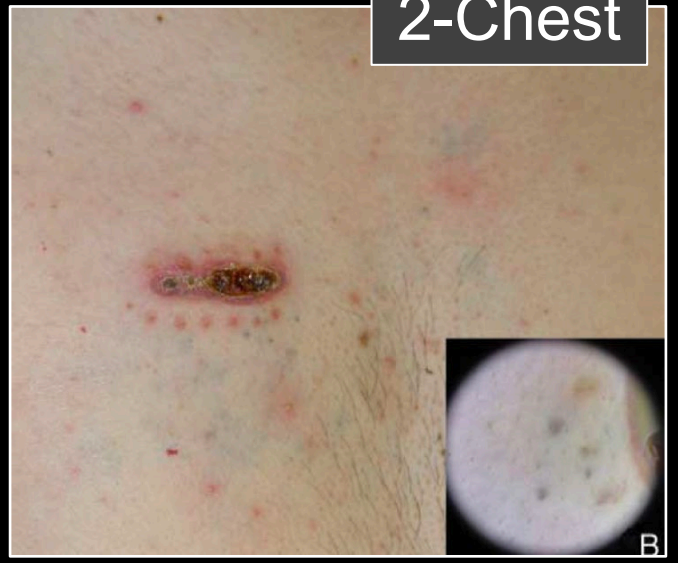




sis (Fig. 3) and nodules of bland spindled melanocytes without necrosis or significant mitotic activity, consistent with cellular blue nevus (Fig. 4). One of three sentinel lymph

Tse JY, et al. *J Cutan Pathol* 2016;43:57.

2-Chest

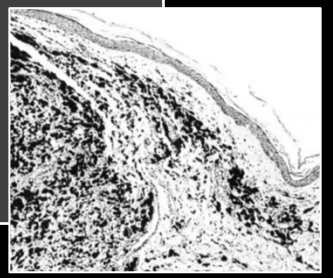


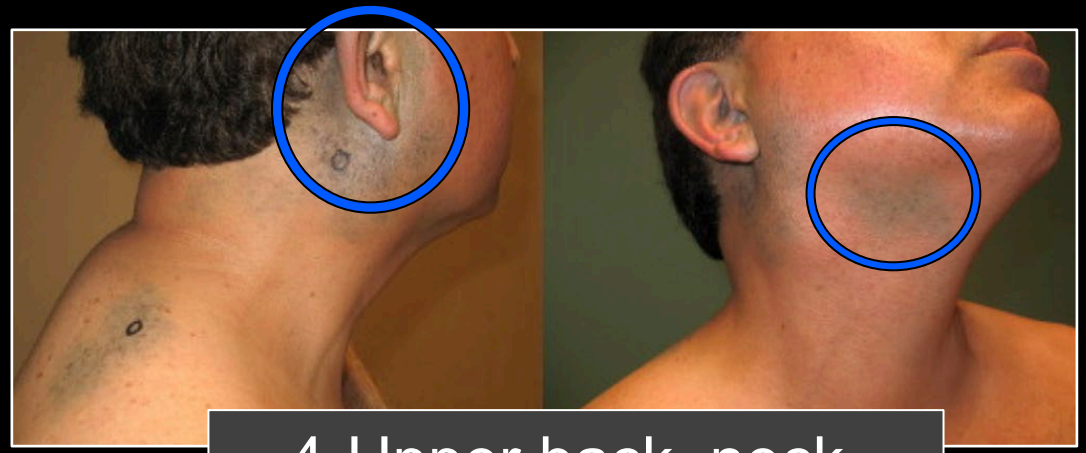
Diffuse proliferation in reticular dermis
Martínez-Peñuela A, et al.
Actas Dermo-Sifiliográficas
2011;102:817.

3-Upper arm

No clinical photograph but lesion described as only 2.5-3 cm in diameter

Van Krieken JH.
Histopathology
1988;12:100.





4-Upper back, neck, ear, periauricular

Wise SR, et al. *JAAD* 2010;62:869

Dr. Masao Ota

Ota M. *Jap J Dermatol* 1939;46:369.

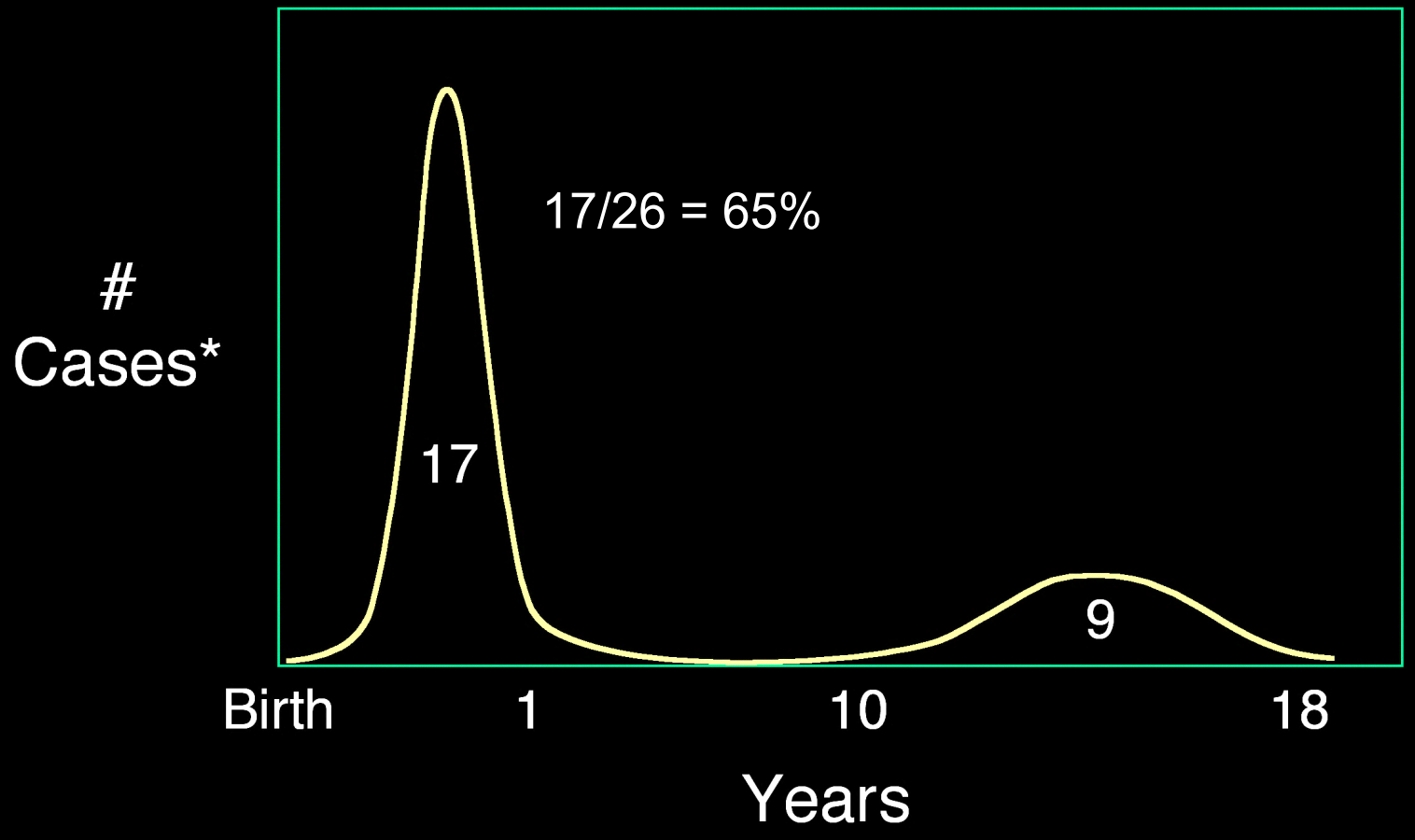
nevus of Ota

=

nevus fuscocaeruleus ophthalmomaxillaris

Additional names – oculodermal melanocytosis, oculodermal melanosis, melanosis oculi, congenital melanosis oculi

Appearance of Nevus of Ota



*total = 26

Tanino H. Jap J Dermatol 46:435, 1939.

Nevus of Ota - Clinical Characteristics

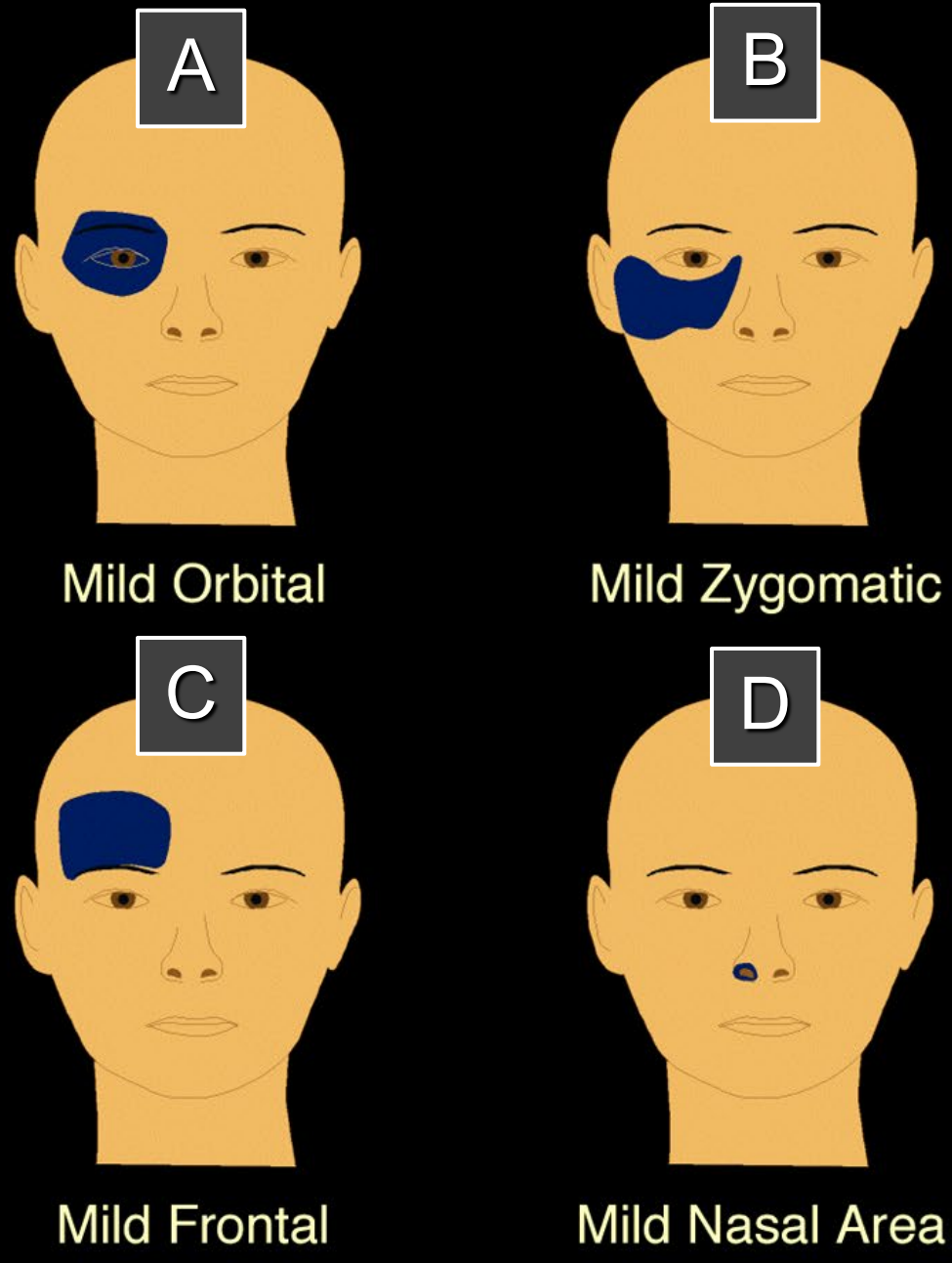
- Age of onset (n=358) – early, 62%
  delayed, 38%
- Sex (n=383) – female, 80%
  male, 20%
- Distribution (n=257) – V1, 13%
  V2, 30%
  V1&2, 57%

Inoue S. Jap J Dermatol 77:130, 1967

Nevus of Ota

Type I *

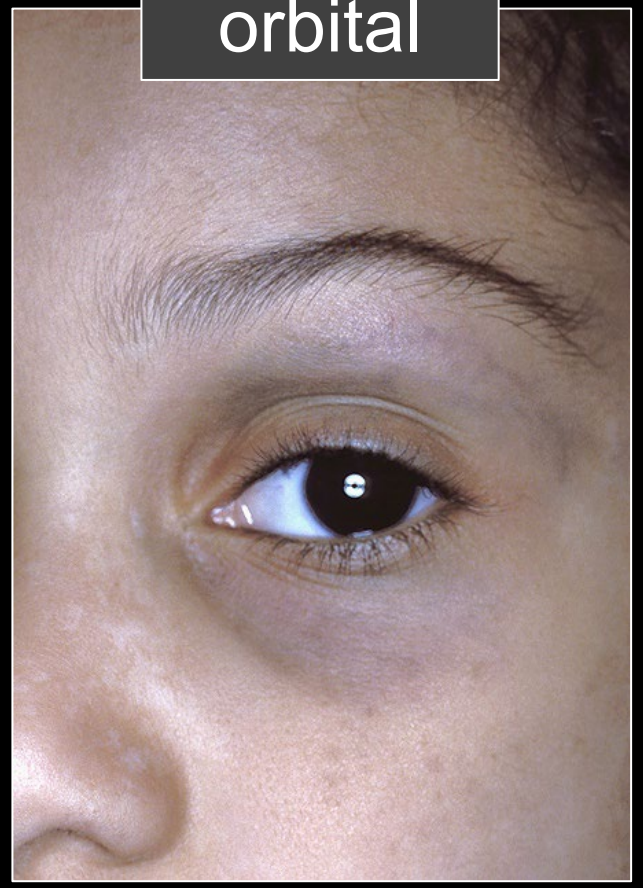
50% of patients



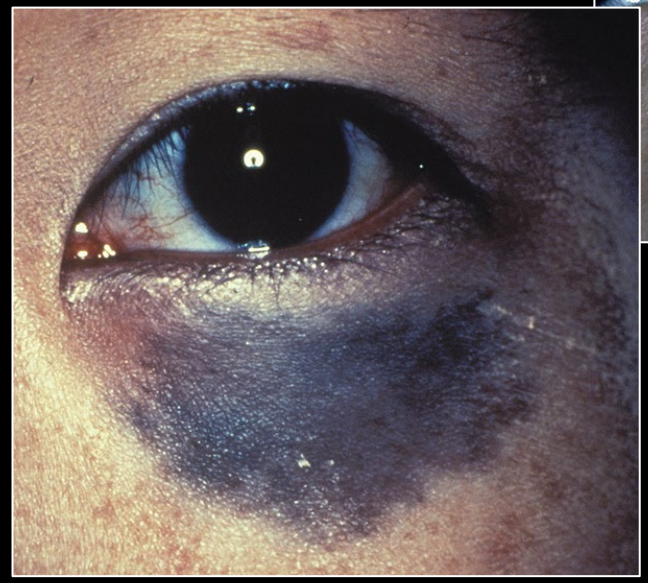
*Tanino 1939 classification

0195047n

Mild orbital



Mild zygomatic



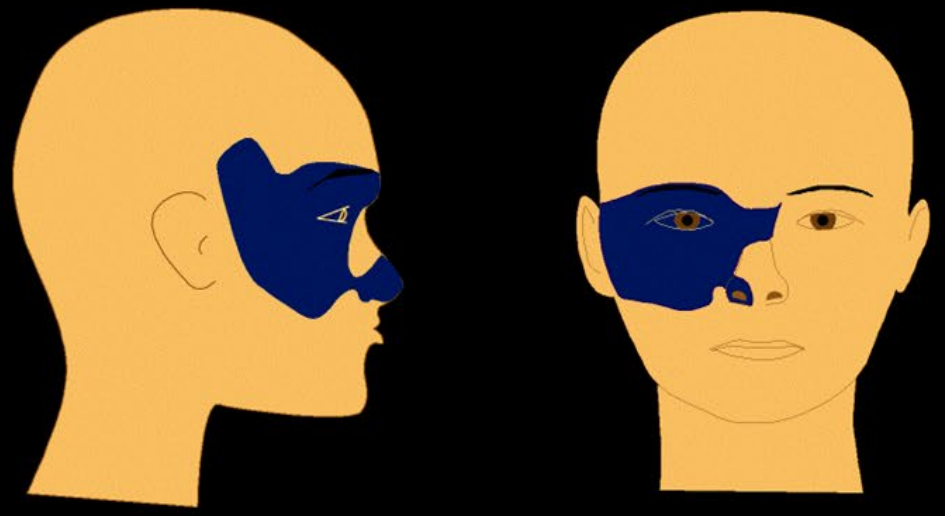
Courtesy, K Urabe, MD

Asian > Black > White individuals

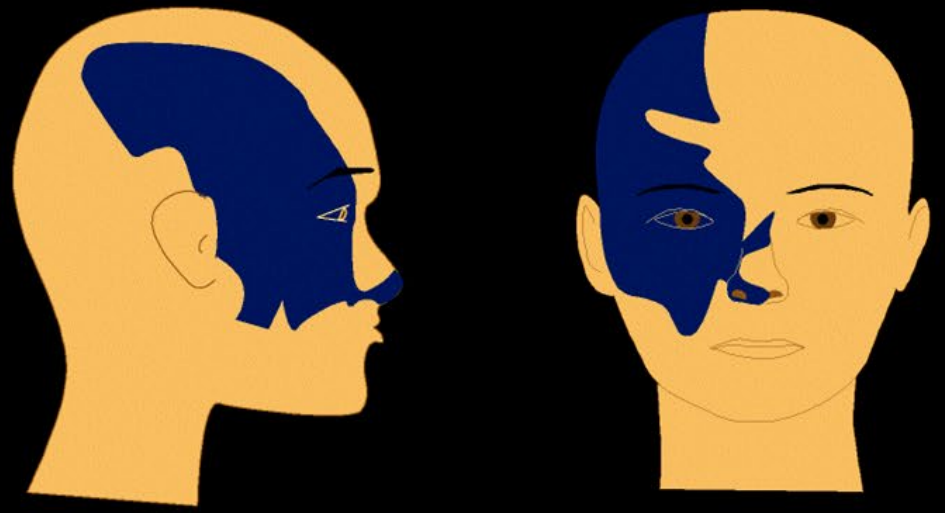
In one series of 14 patients with nevus of Ota, 1 had a *GNAQ* Q209 mutation

Van Raamsdonk CD, et al. *Nature* 2008;457:599.

Nevus of Ota

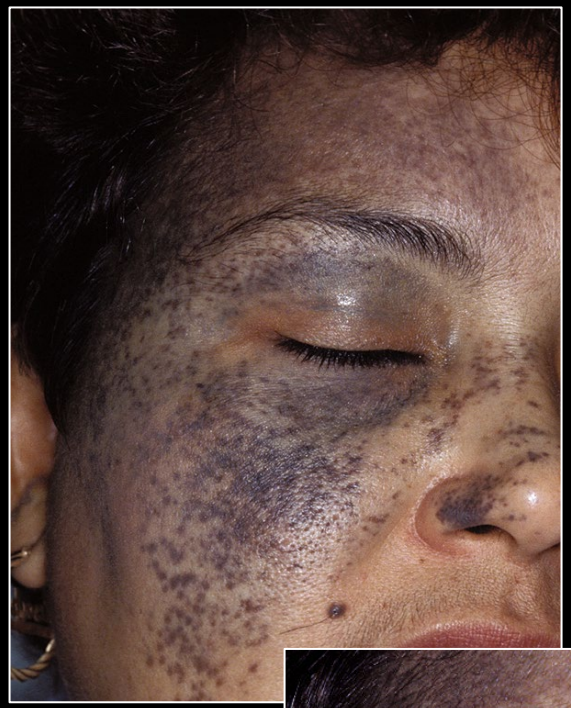


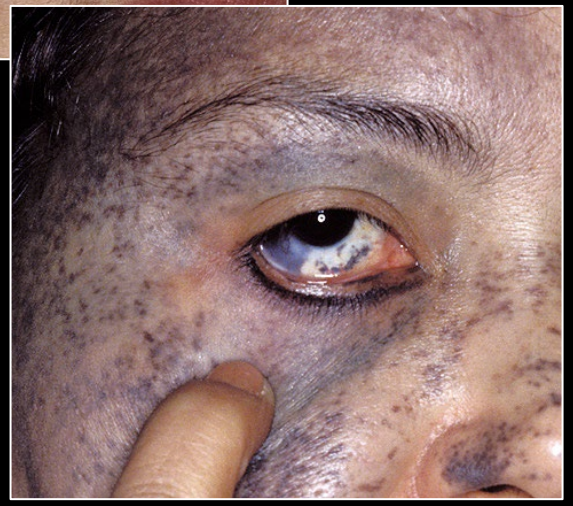
Type II Moderate



Type III Intensive

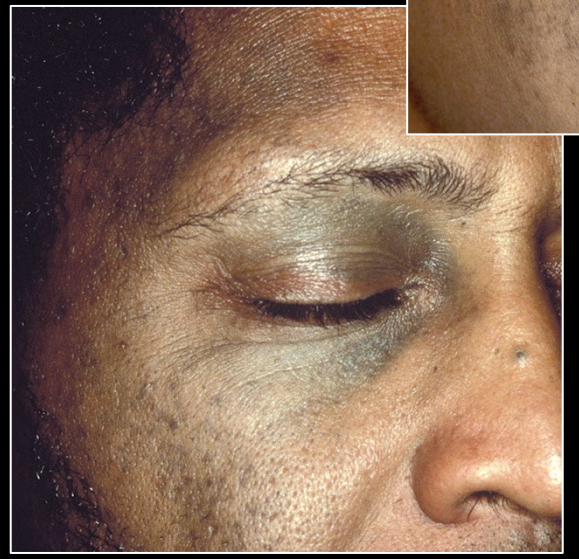
Type IV Bilateral

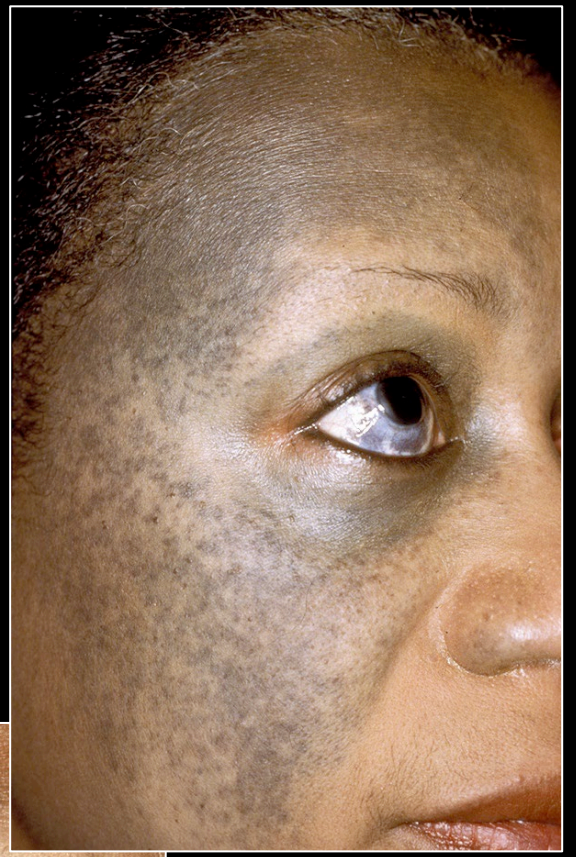




Type III

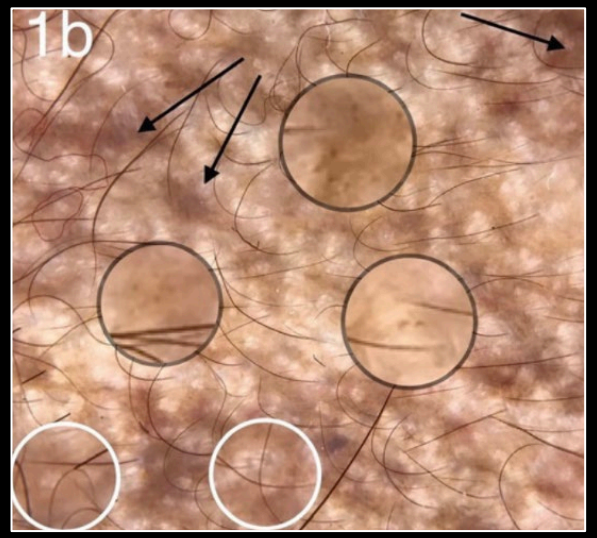
Type IV





Type III

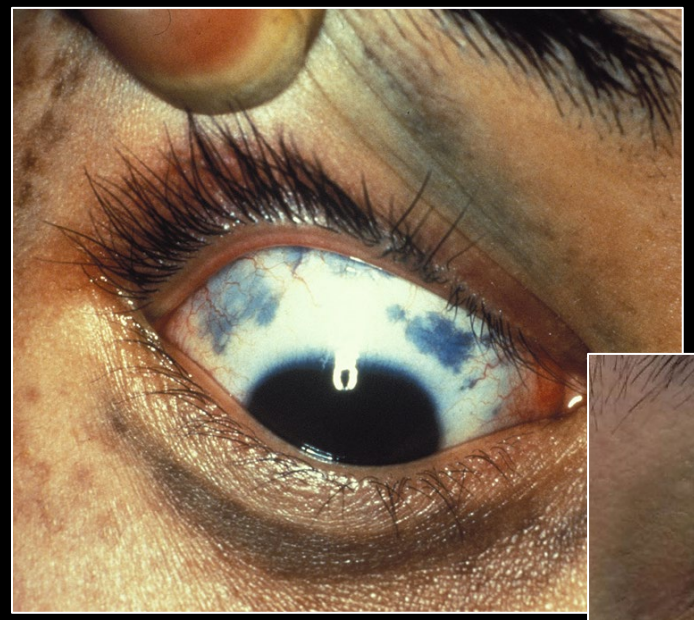
Nevus of Ota - Clinical Characteristics

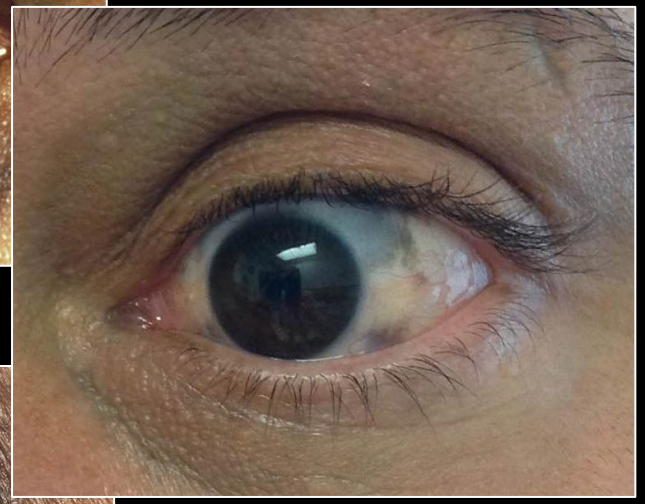


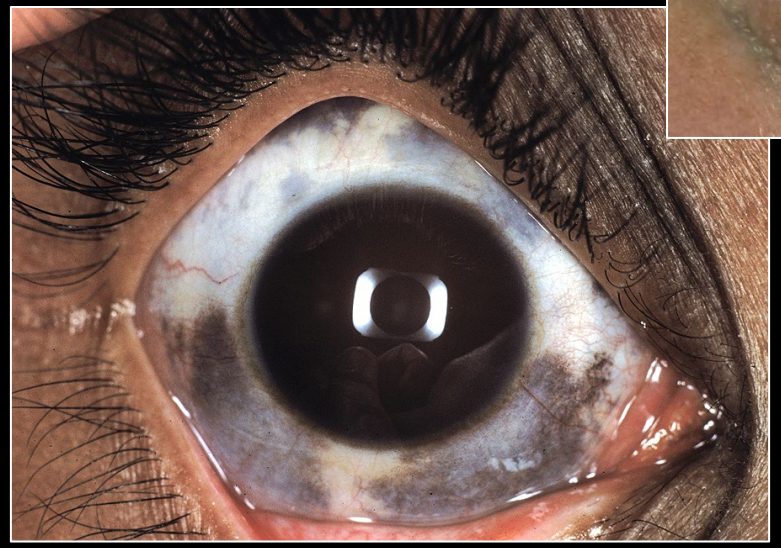
patchy distribution
structureless gray & brown areas
brown dots
Elmas OF. *BMJ* 2020;37:116.

- Grade of Involvement (n=415)
  - mild, 50%
  - moderate, 25%
  - intensive, 14%
  - bilateral, 8%
- Percent with melanosis oculi (n=292)
  - mild, 54%
  - moderate, 79%
  - intensive, 100%
  - bilateral, 85%

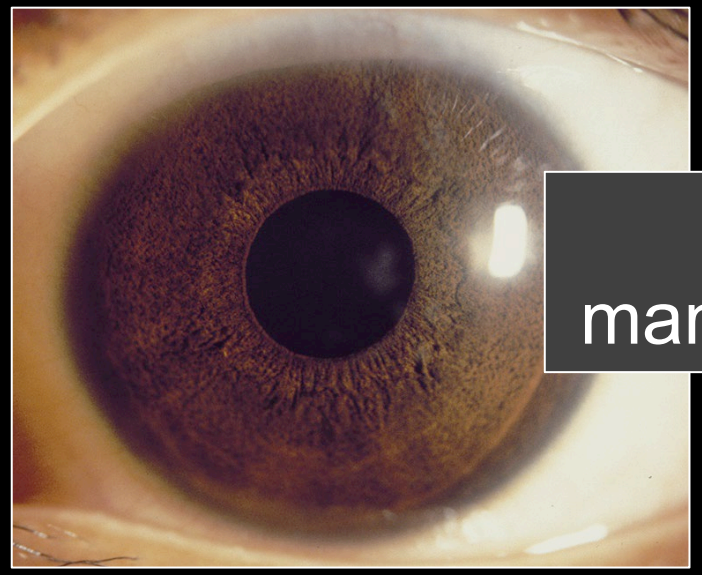
Inoue S. Jap J Dermatol 77:130, 1967



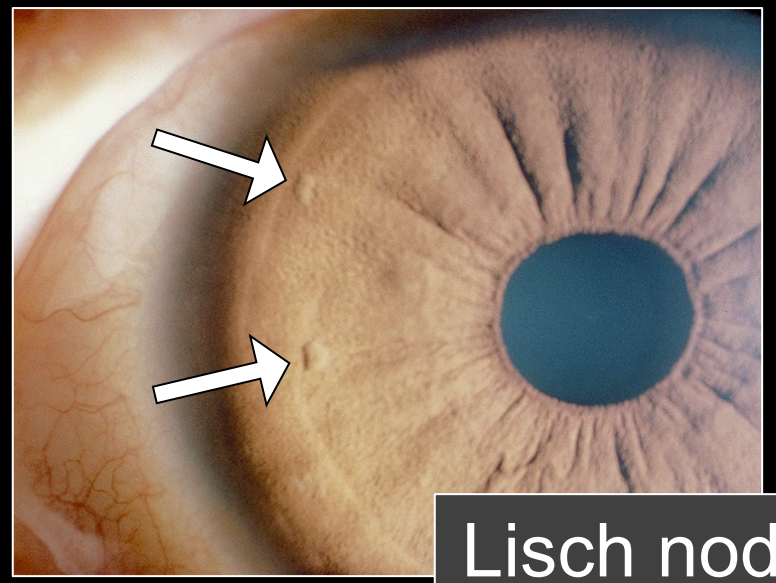




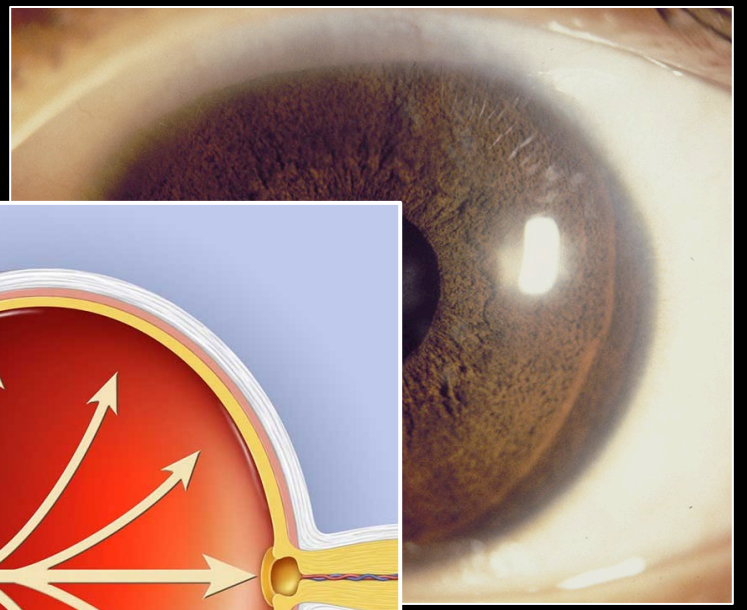
Melanosis oculi

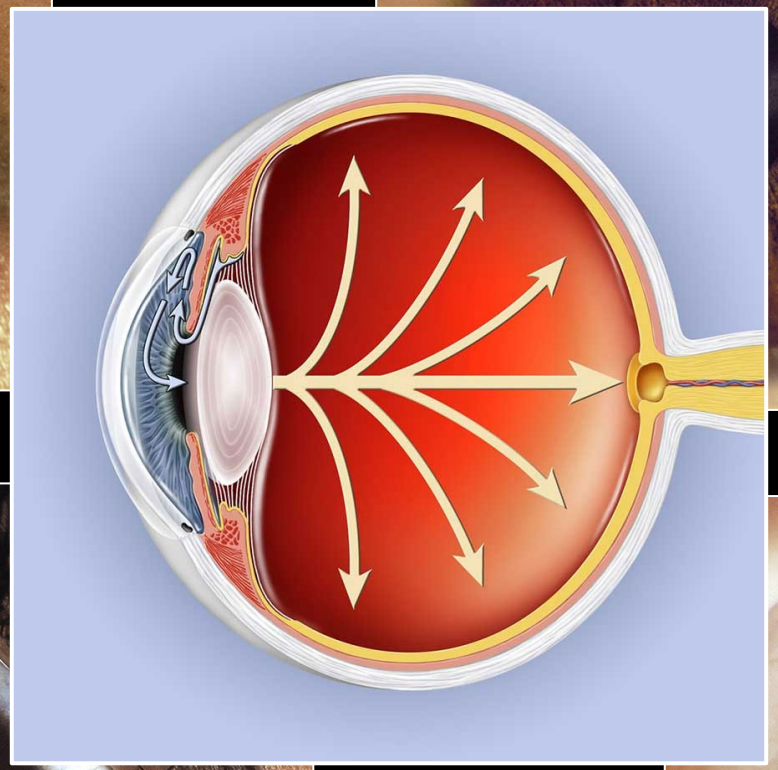


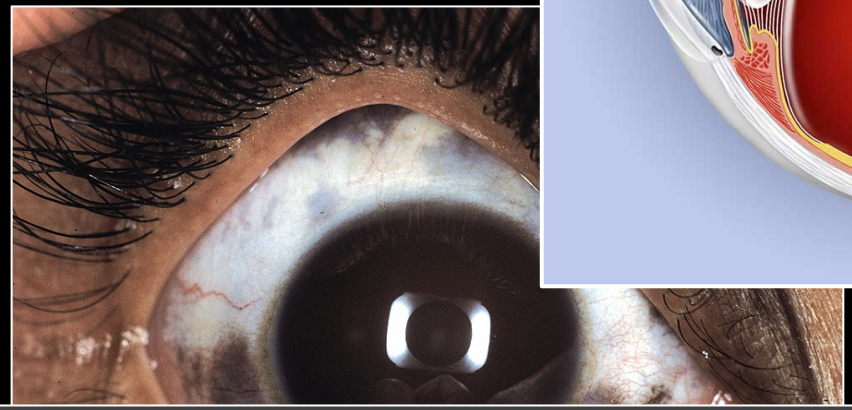
Iris mammillations

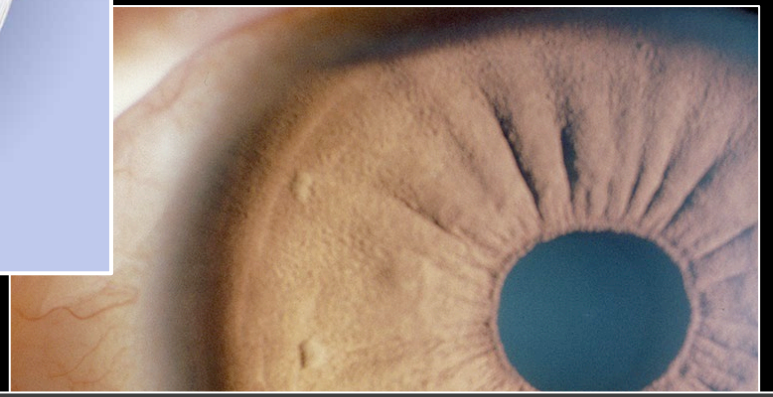


Lisch nodules







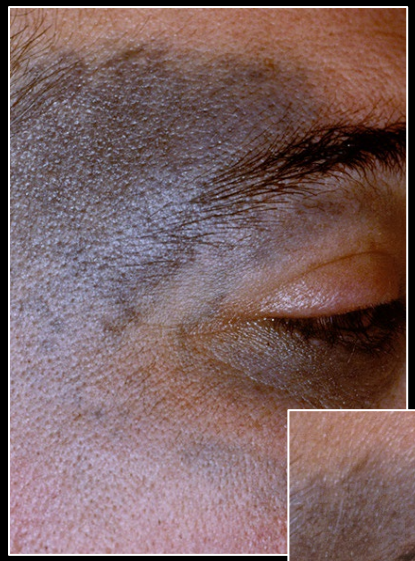


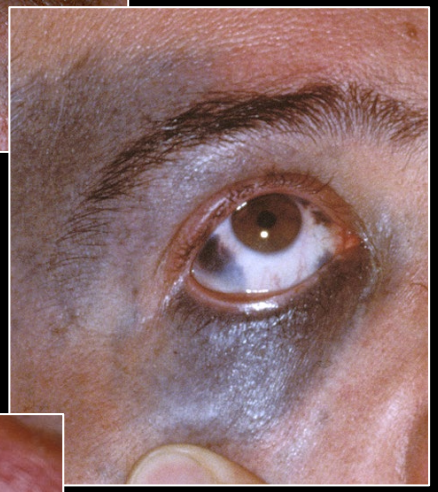
estimated 10% have elevated intraocular pressure - due to melanocytes blocking drainage of aqueous

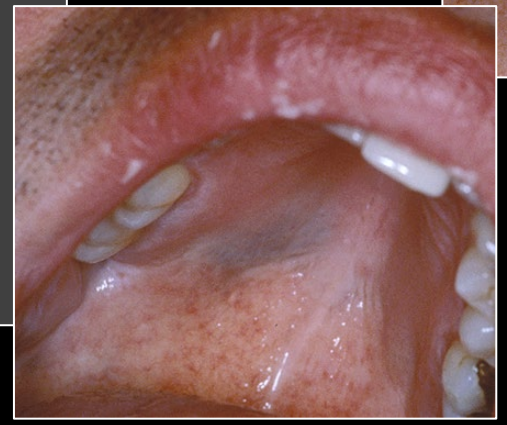
Nevus of Ota

Additional mucosal sites of involvement:

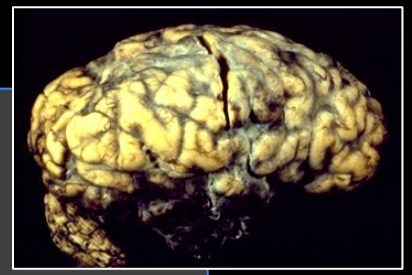
- Tympanum [eardrum] (55%)
- Nasal mucosa (28%)
- Pharynx (24%)
- Palate (18%)







Nevus of Ota-associated primary CNS melanoma



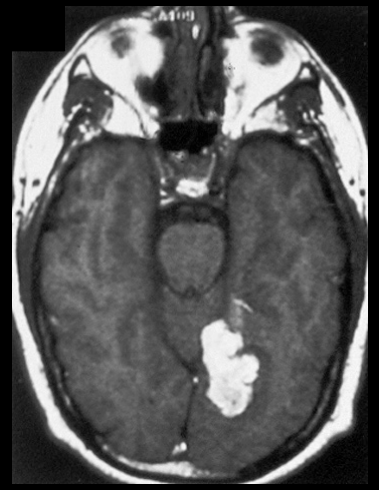
- Additional site of involvement – central nervous system (CNS)
- Termed leptomeningeal melanocytosis and previously referred to as neurocutaneous melanosis*
- Patients can develop melanocytomas and primary CNS melanomas

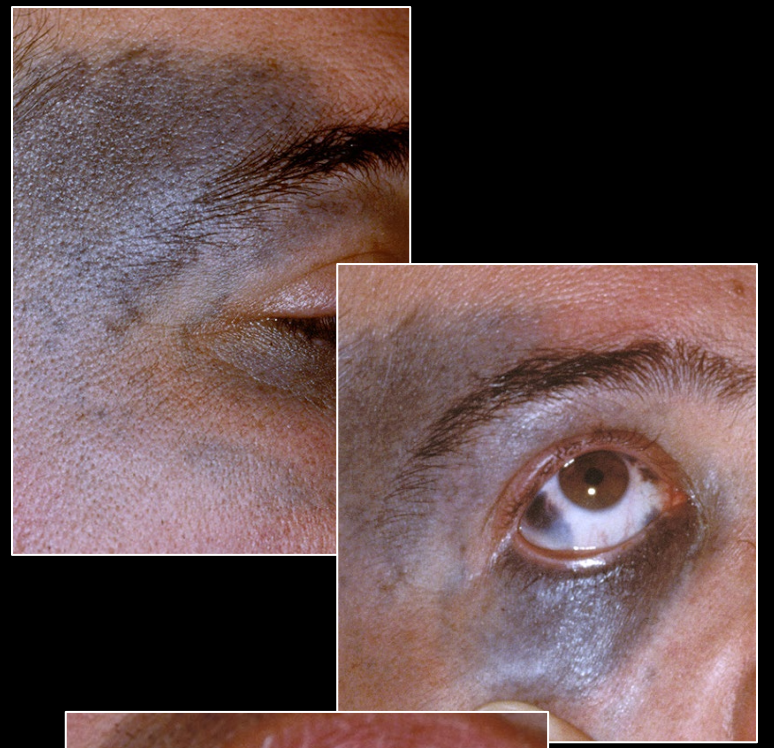
*also in patients with multiple medium-sized congenital nevi; giant congenital nevus, often with satellites; phakomatosis pigmentovascularis types II, IV, and ?V; plaque-type blue nevus (5 case reports)

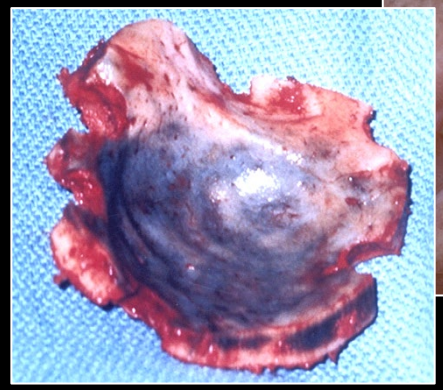
Nevus of Ota

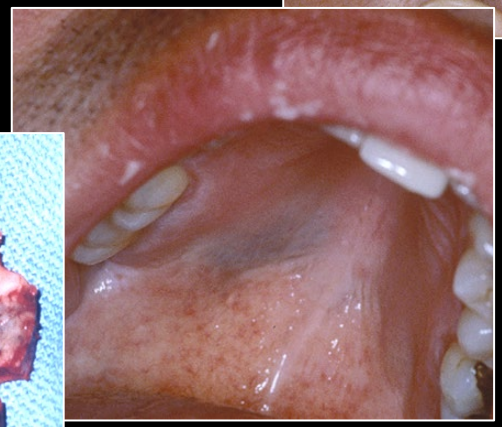
Additional sites of involvement:
- Tympanum (55%)
- Nasal mucosa (28%)
- Pharynx (24%)
- Palate (18%)

- CNS – leptomeningeal melanocytosis (neurocutaneous melanosis)* --> melanocytoma, primary CNS melanoma





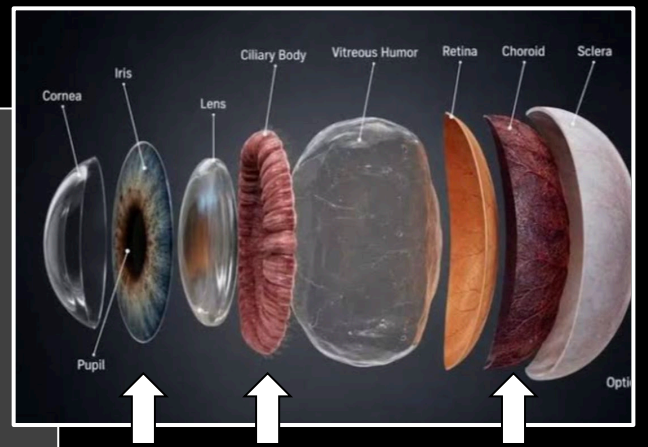


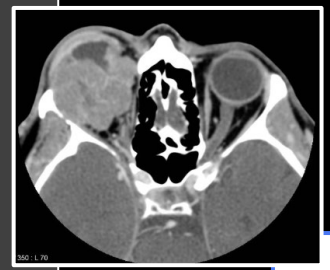


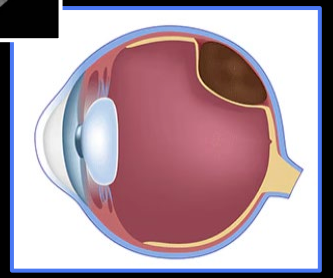
*also multiple medium-sized congenital nevi; giant congenital nevus, often with satellites; PPV II, IV, and ?V; plaque-type blue nevus (5 CRs MM or LMM)

Nevus of Ota-associated melanoma

- Most common site: uveal tract (choroid, ciliary body, and iris), in particular the choroid (44%)
- Estimated 35X risk of uveal tract melanoma compared to general population (estimated 1 in 400 in study of White individuals)
- Additional sites: CNS (23%), orbit (18%), skin (15%)
- Cutaneous melanomas can be dermal in origin







37 patients: Shaffer D. *Dermatology* 1992;185:146.
Singh AD. *Ophthalmol* 1998;105:195.

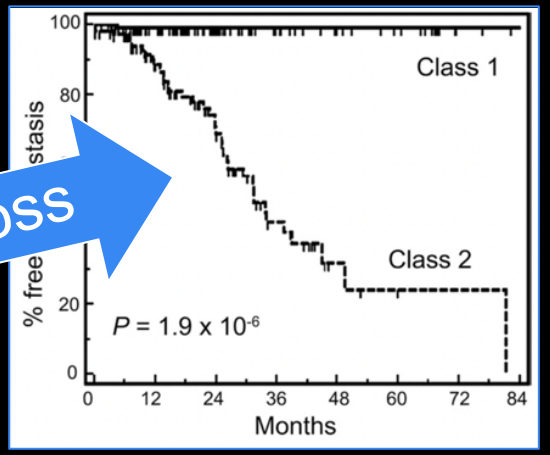
Nevus of Ota-associated melanoma

- 80-90% of ***isolated*** uveal melanomas have mutations in *GNAQ* or *GNA11* (Q209 [more oncogenic] >> R183)

early

second hit

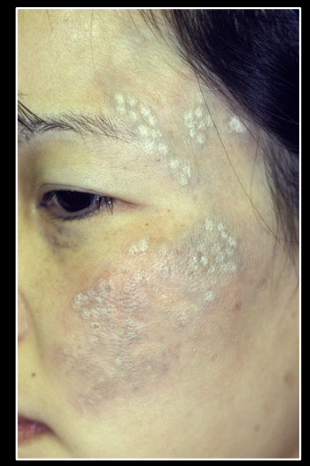
BAP1 loss



- Nevus of Ota-associated leptomeningeal melanomas: *GNAQ* Q209H, *GNAQ* R183Q + *BAP1* inactivating mutation (Goldman-Lévy, 2016)

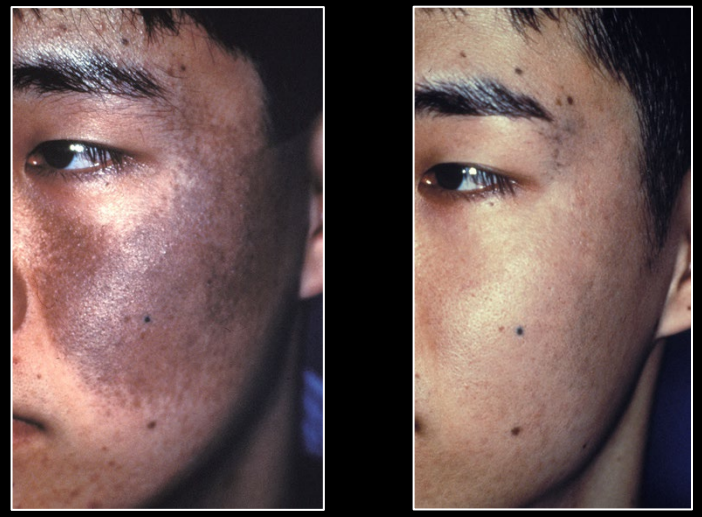
- Nevus of Ota-associated melanocytomas: *GNA11* Q209L + *BAP1* inactivation & *EIF1AX* (Zhou, 2022), GNAQ Q209P (Lv, 2024)

Nevus of Ota – Laser Therapy



- Q-switched Nd:YAG laser*
- Q-switched alexandrite laser*
- Q-switched ruby laser

- QS ruby: after 4-5 Rxs, 33/35 patients (94%) had excellent results (≥70% lightening)**

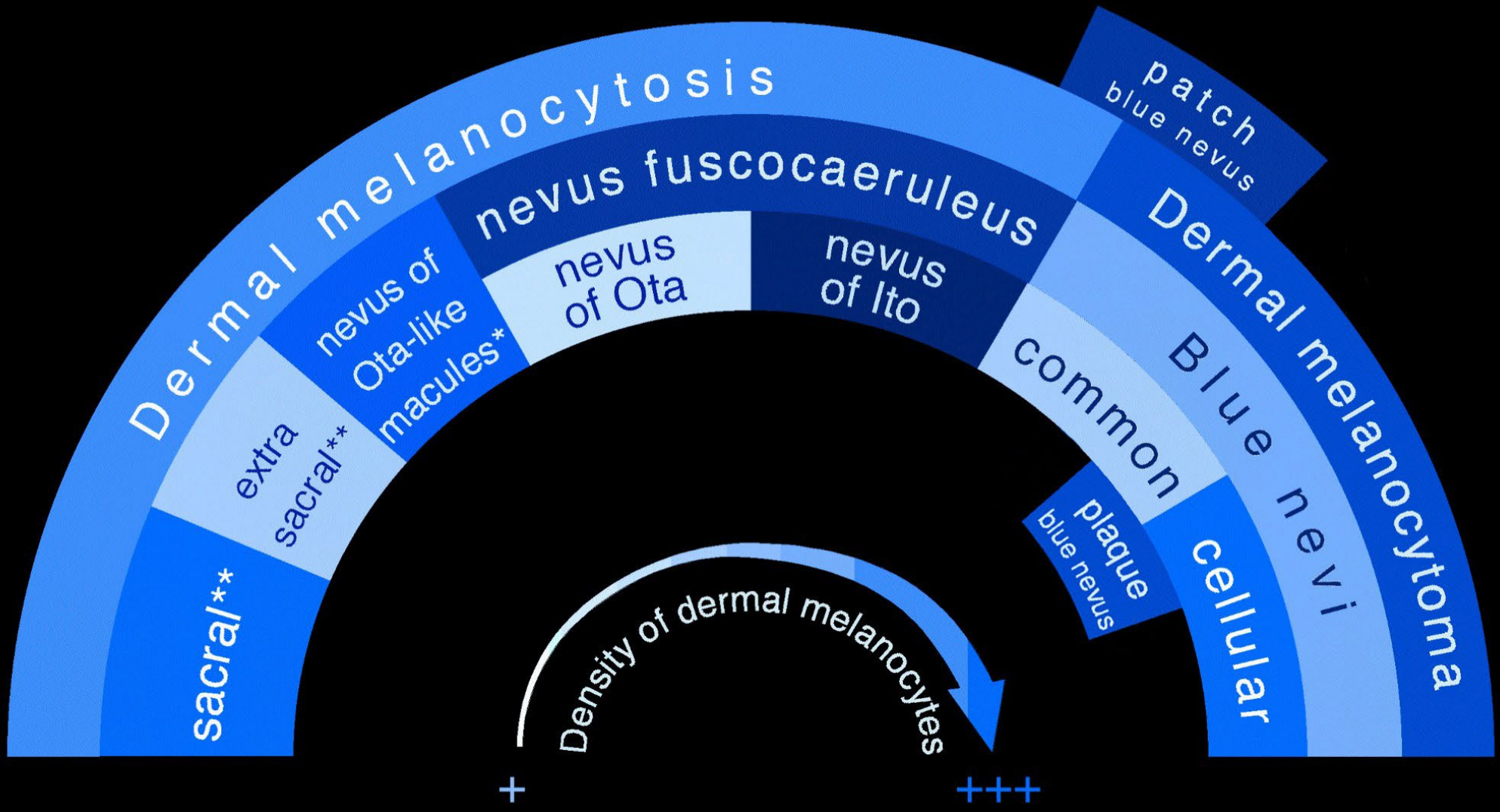


Courtesy, K Urabe, MD

- Recommendations: longitudinal ophthalmologic care
  monitor for cutaneous papules
  hardest discussion re: CNS

*Also picosecond; **6J/cm$^{2;}$ 30 nsec; 694.3 nm; q3-4 months

**Watanabe S. *NEJM* 1994;331:1745.



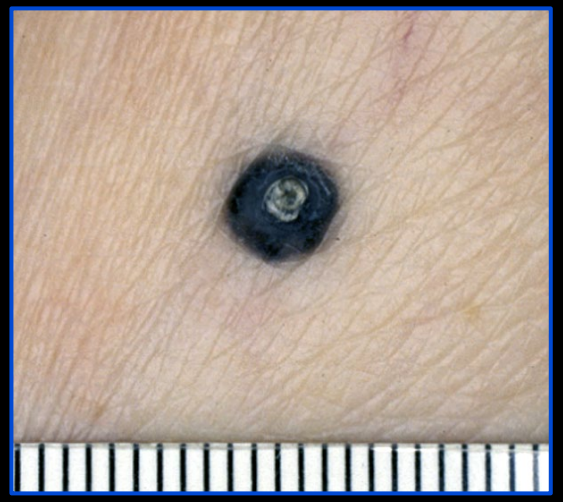
*acquired **congenital dermal melanocytosis

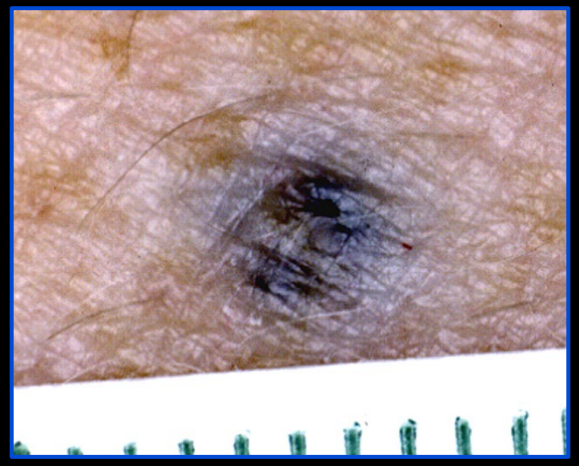
Blue nevi – clinical types

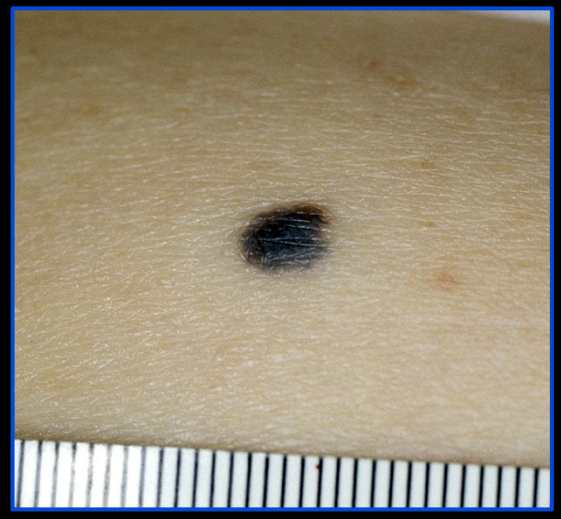
- Common*
- Combined**
- Cellular*
- Patch (-type)
- Plaque (-type)
- Within nevus spilus/ speckled lentiginous nevus
- “Giant” congenital/invasive
- Target
- Atypical**/bizarre

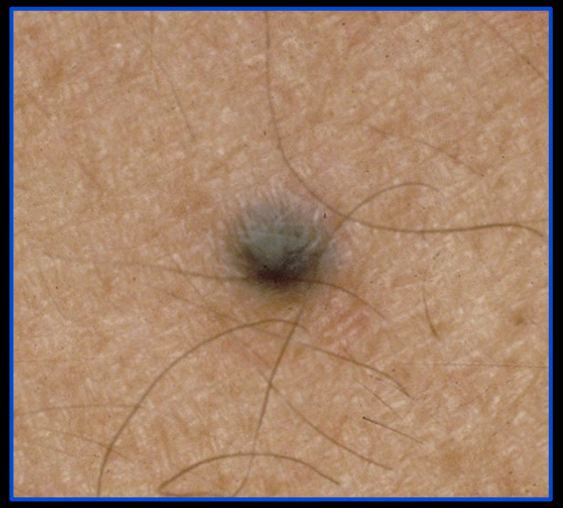
*4:1 common: cellular

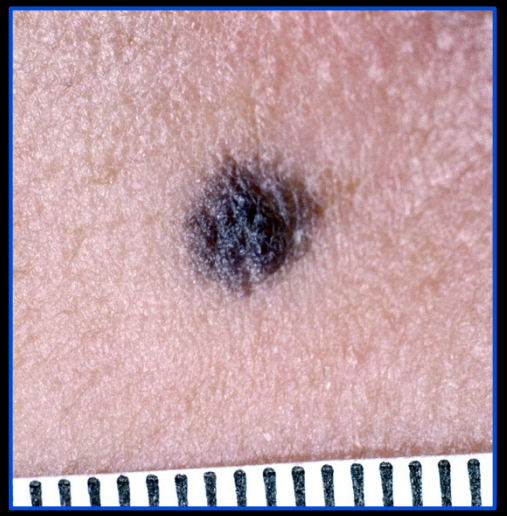
**Kitamura classification (1950): (1) combined compound and blue nevus; (2) within nevus spilus/speckled lentiginous nevus; (3) blue nevus plus fibromatous or myomatous (nonmelanocytic) change

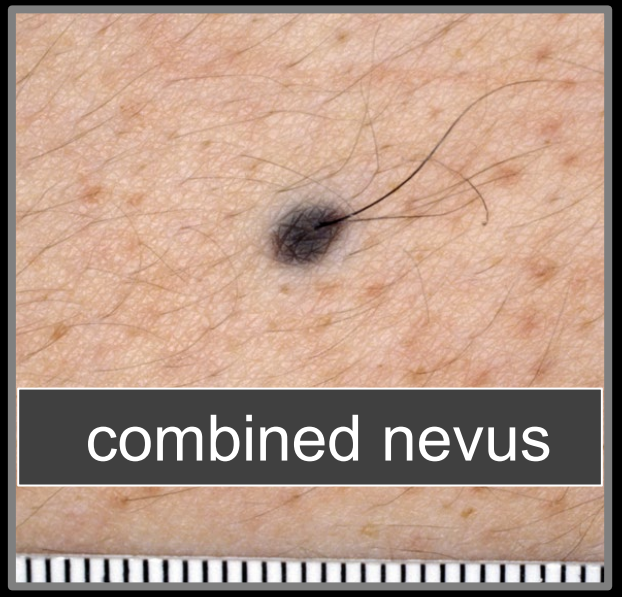








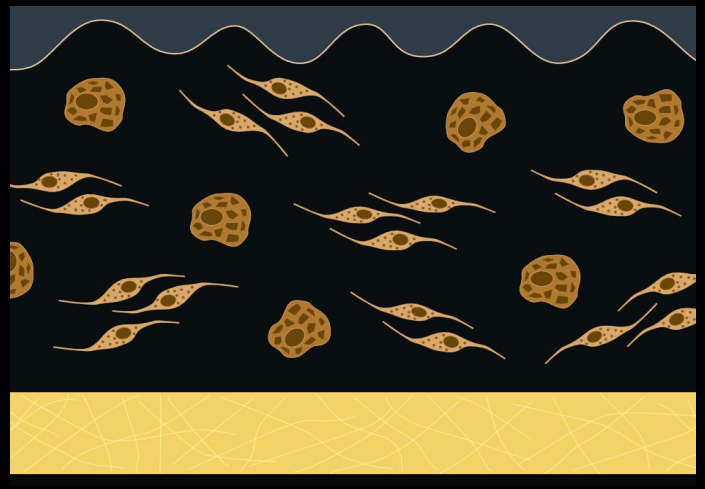


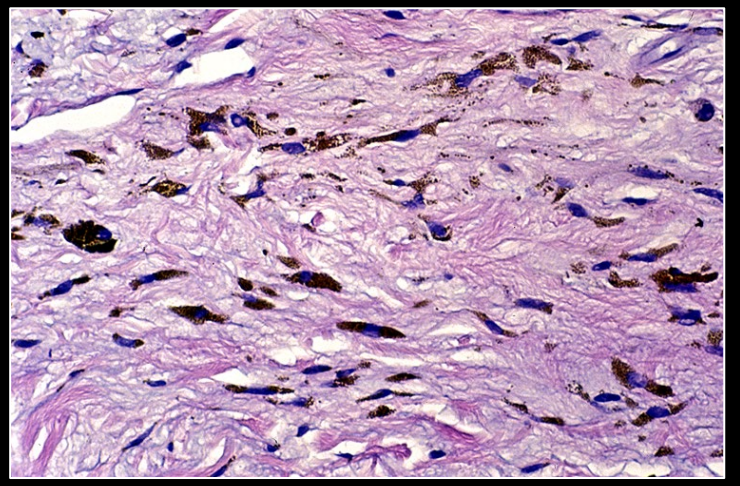


In 5 large series (n=756), ~15% of common blue nevi were congenital

Common blue nevus - histopathology

- Dorsal hands & feet, scalp, and face (can be multiple in Asians)
- Pigmented dendritic melanocytes in the dermis, usually the lower two-thirds
- Melanophages containing course granules
- Can see fibrosis and osteoma cutis
- Benign biology, with the exception of conjunctival lesions





Histologic Classification and Size of 142 Blue Nevi

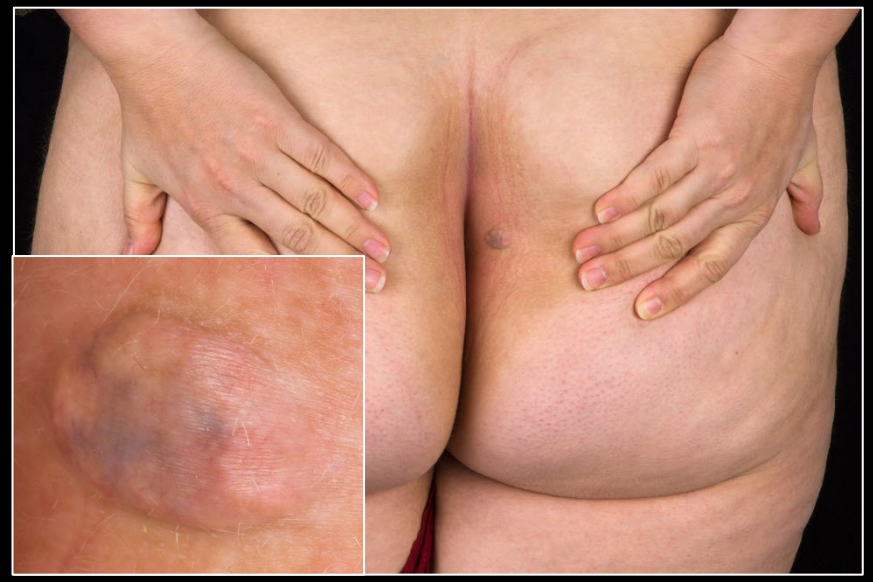
Diameter (mm)	Common Blue Nevus	Cellular Blue Nevus
2–5	60	3
6–10	38	2
11–20	12	11
21–30	3	8
31–35	2	1
Greater than 60	0	2 (plaque type)
Total	115	27

85% < 1 cm

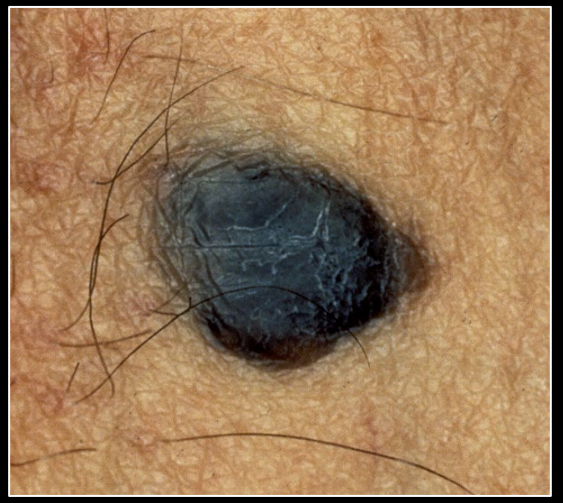
81% > 1 cm

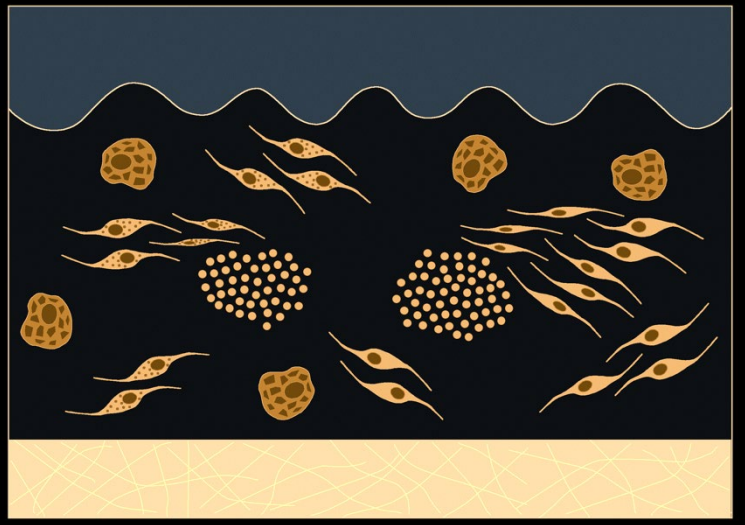
Dorsey CS and H Montgomery, J Invest Dermatol 22:226, 1954

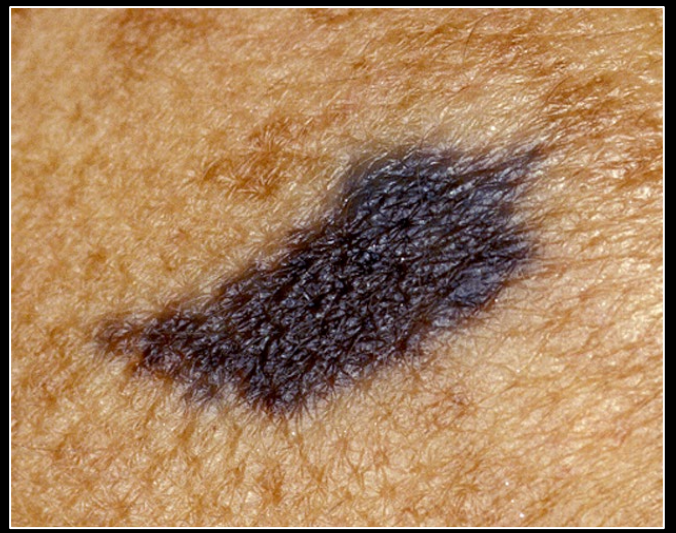
0797063n

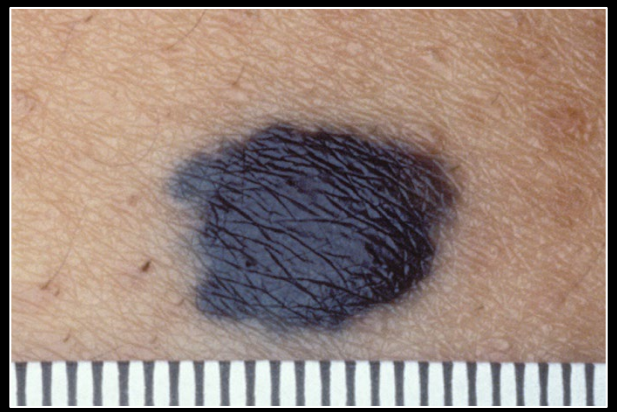


Courtesy, University of Graz

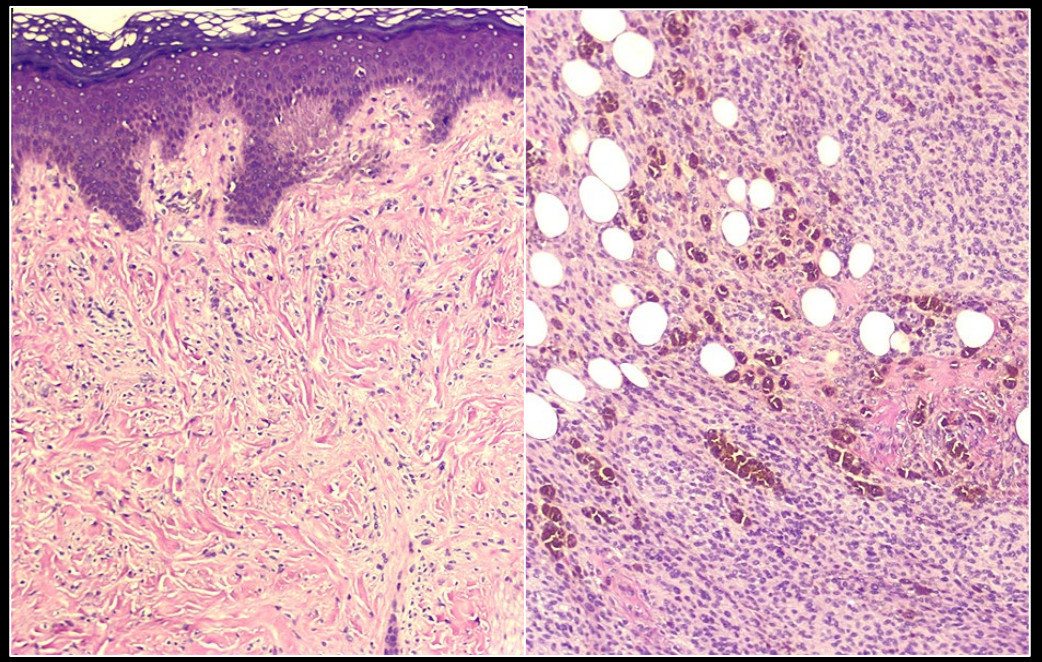








~30% congenital



Cellular blue nevi (melanocytomas)

- satellitosis
- “benign” lymph node involvement
- risk of *melanoma arising in a blue nevus* (WHO, 2023; previously referred to as malignant blue nevus), which most commonly develops on the **scalp**

Especially when on the scalp, consider prophylactic excision versus observation because ….

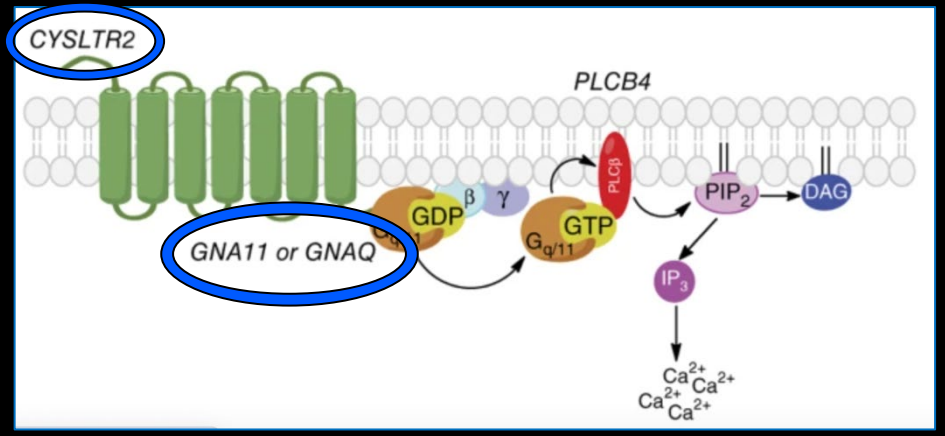
both clinical assessment and histopathologic distinction can be challenging

Blue nevi – genetic analysis

Mutually Exclusive

- *Genetic analysis of 103 blue nevi^*,
- 61 (59%) *GNAQ* mutations (Q209L, Q209P* >> R183Q)
- 17 (16%) *GNA11* mutations (Q209L)
- 3 (3%) *CYSLTR2* mutations (L125Q)
- 3 (3%) *NRAS* mutations (Q61R, Q61K, G12R/V)*
- 1 (1%) *BRAF* mutations (V600E)*

^81 common vs 22 cellular blue nevi (p = 0.29)
*Could not exclude combined nevus in non-examined portions of nevus
*more common in plaque blue nevus



cysteinyl leukotriene receptor 2

D mutations P
β-catenin
+
MAPK
N

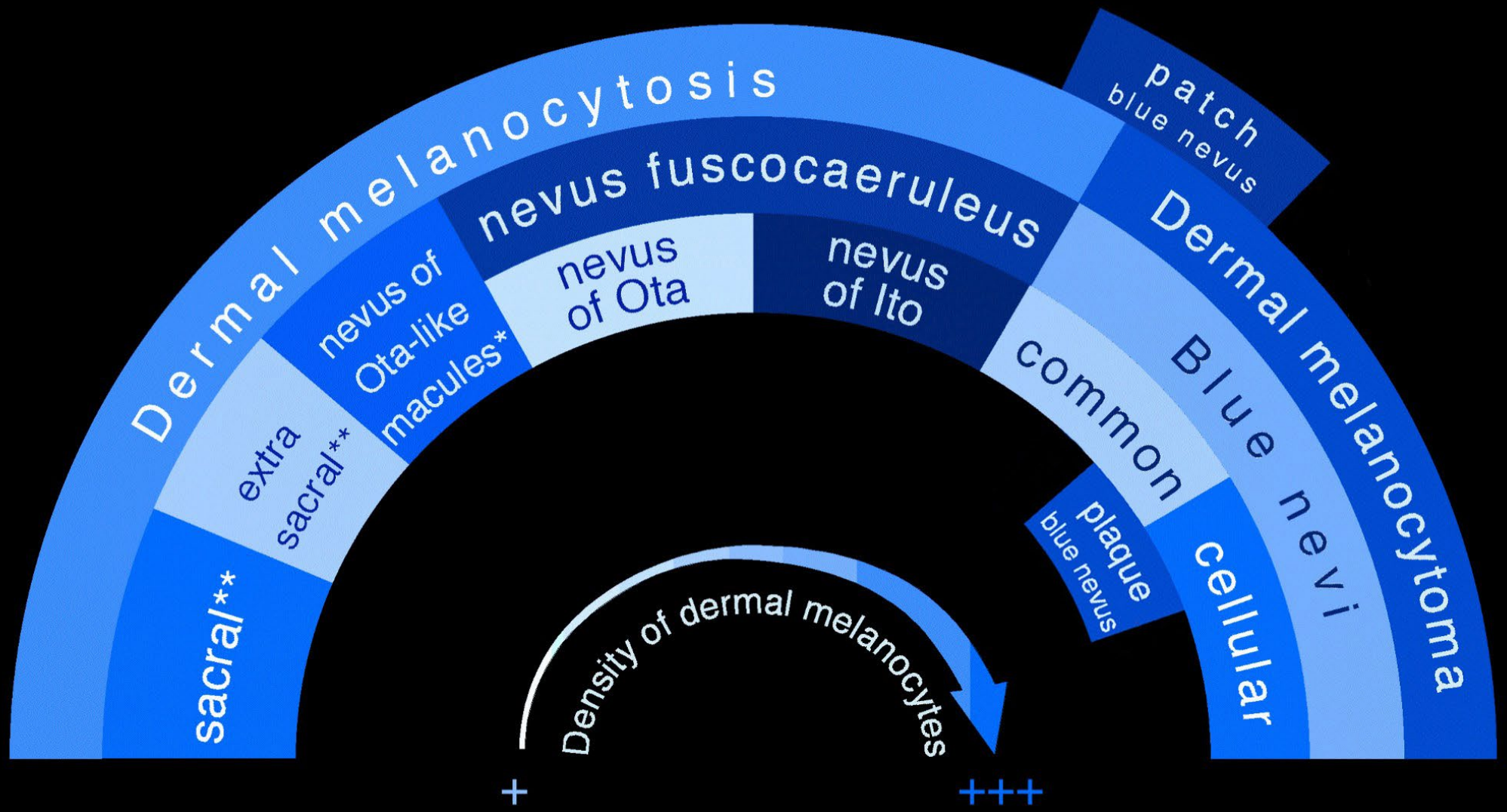
Möller I. *Mod Pathol* 2017;30:350.

Blue nevi – clinical types

- Common*
- Combined**
- Cellular*
- Patch (-type)
- Plaque (-type)
- Within nevus spilus/ speckled lentiginous nevus
- “Giant” congenital/invasive
- Target
- Atypical**/bizarre

*4:1 common: cellular

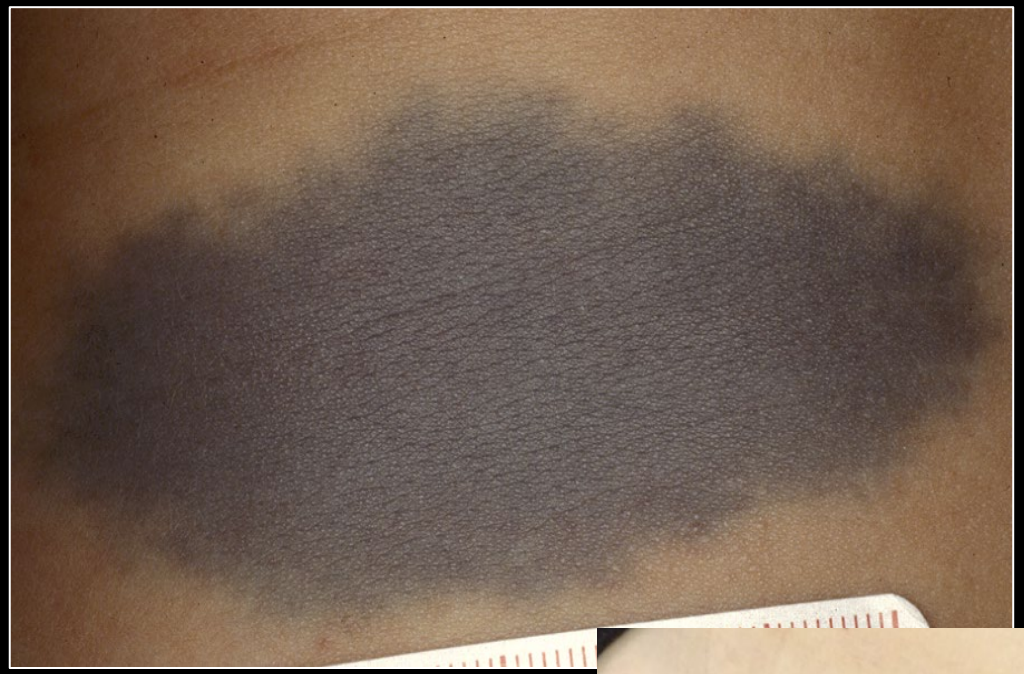
**Kitamura classification (1950): (1) combined compound and blue nevus; (2) within nevus spilus/speckled lentiginous nevus; (3) blue nevus plus fibromatous or myomatous (nonmelanocytic) change

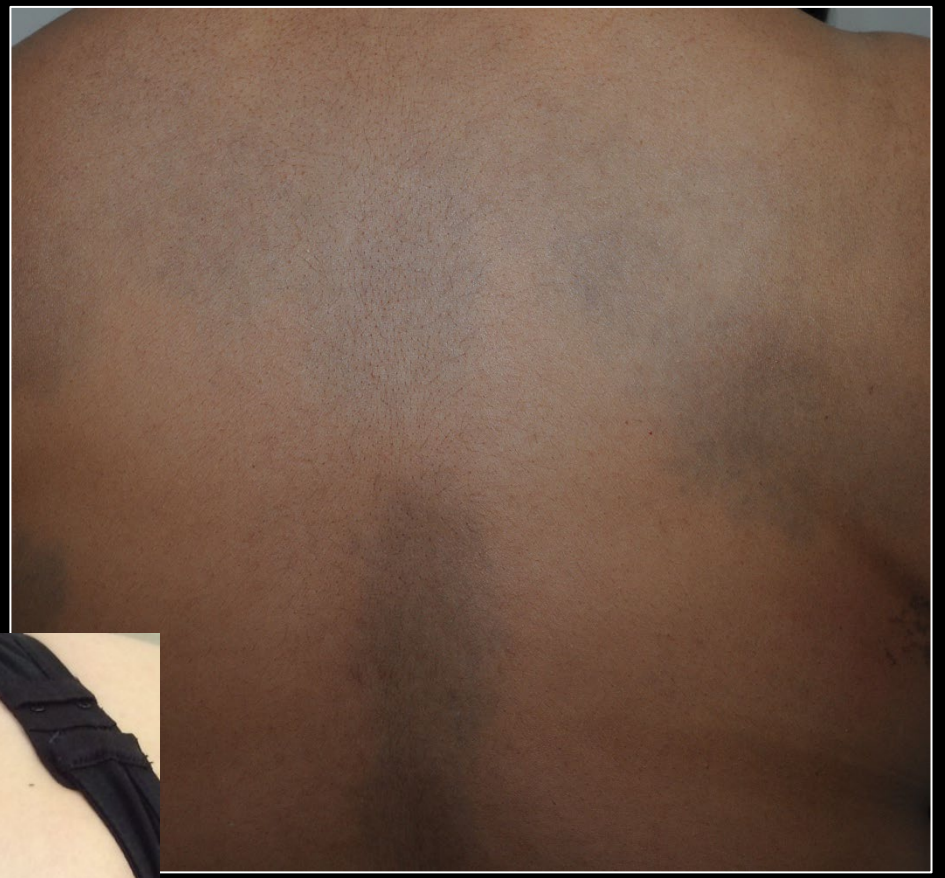


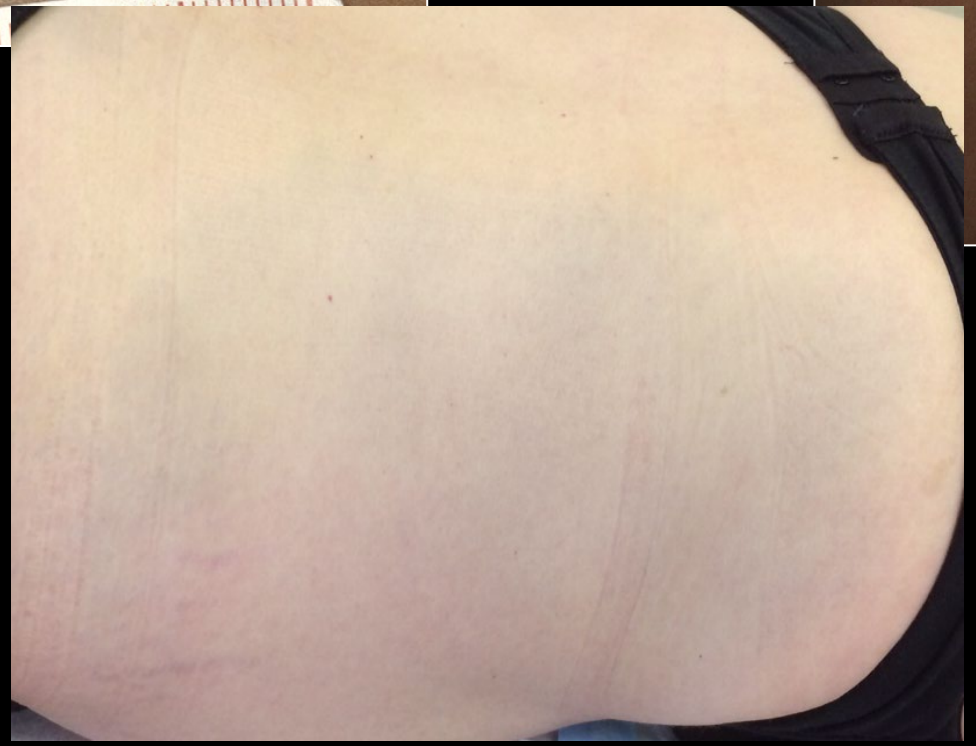
*acquired **congenital dermal melanocytosis

Patch (-type) blue nevus

- Area of ceruloderma without palpable infiltration
- Clinically, overlap with dermal melanocytosis
- Way too many names
- Histopathologic findings vary from scattered dermal melanocytes to occasional overlap with common blue nevus







Patch (-type) blue nevus – an umbrella term

- Congenital
  - Congenital segmental dermal melanocytosis
  - Dermal melanocyte hamartoma (also plaque-type)
- Acquired
  - Acquired dermal melanocytosis
  - Adult-onset Mongolian spot
  - Dermal melanocytosis of the macular type
  - Late-onset dermal melanocytosis
  - Late-onset Ito's nevus
  - Nevoid dermal melanocytosis

Abbott, 2009; Burkhart, 1981; Carmichael, 1993; Flores, 2018; Mataix, 2007; Mevorah, 1977; Özkesici, 2016; Vélez, 1992

Patch (-type) blue nevus – an umbrella term

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  - Acquir
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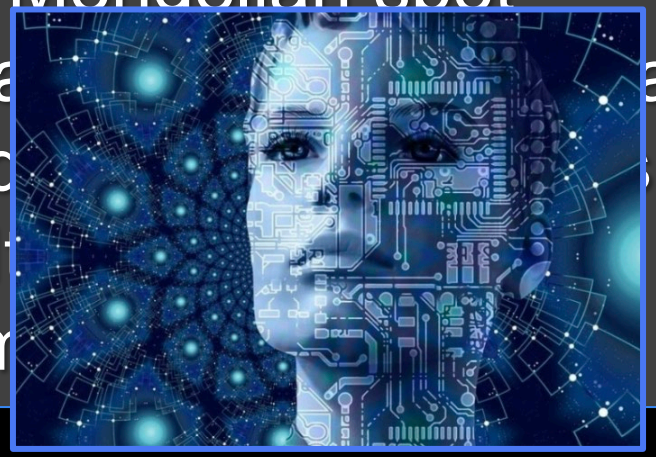
  - Late-onset c is
  - Late-onset I
  - Nevoid derm

The term "patch blue nevus" likely refers to the **plaque-type blue nevus**

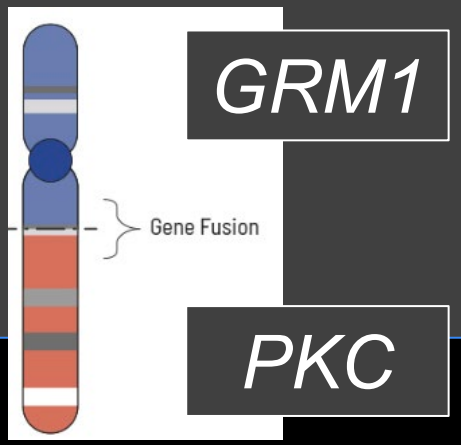
OpenEvidence®



Abbott, 2009; Burkhart, 1981; Carmichael, 1993; Flores, 2018; Mataix, 2007; Mevorah, 1977; Özkesici, 2016; Vélez, 1992

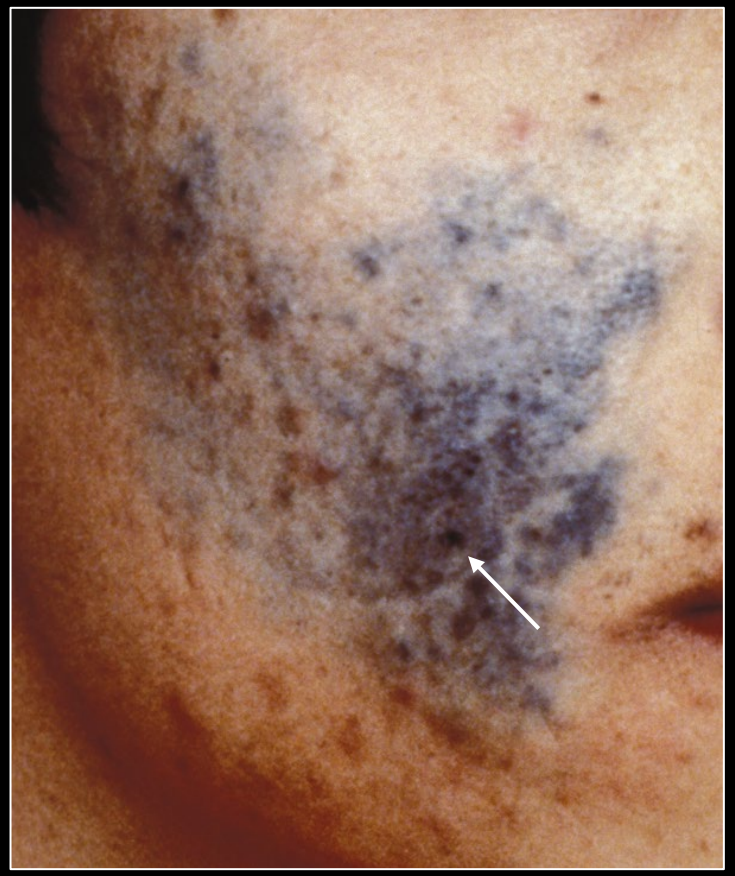
Plaque (-type) blue nevus

- Unusual – in a series of 142 blue nevi, 2 (1.4%)
- Diameter = ***1-8⁺ cm*** versus ***6⁺ cm***
- Varies clinically, from uniform plaque to patch with multiple papules +/or nodules
- Histopathologic features are those of a common or cellular blue nevus findings
- One variant – congenital with hypertrichosis (“hairy” plaque type)

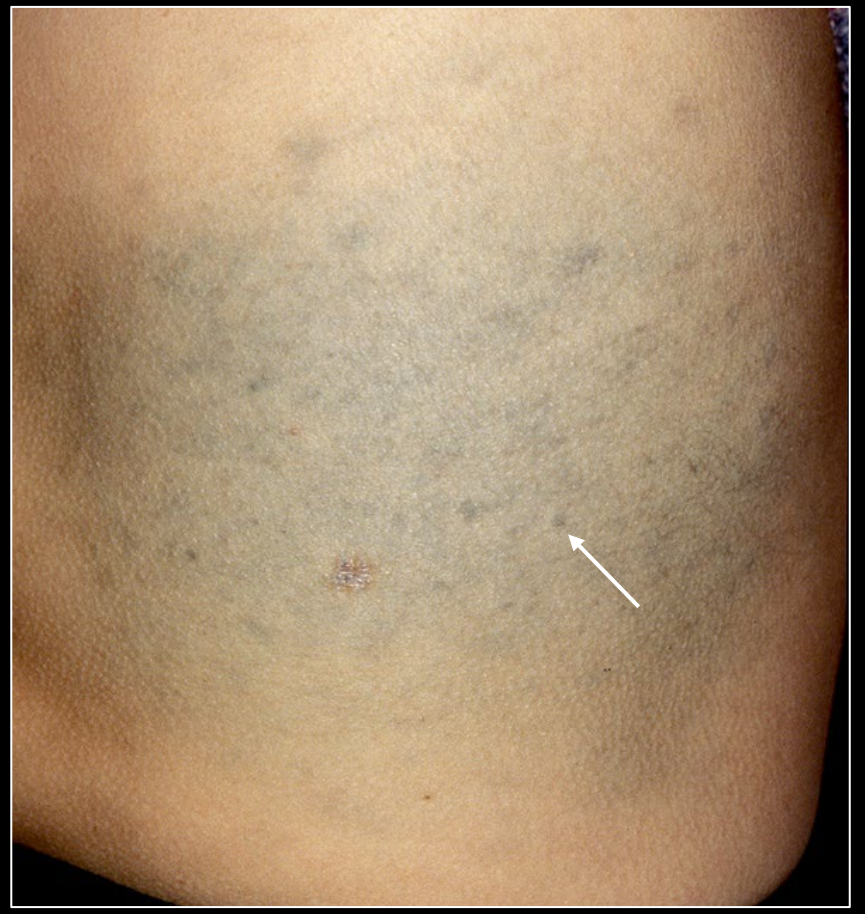


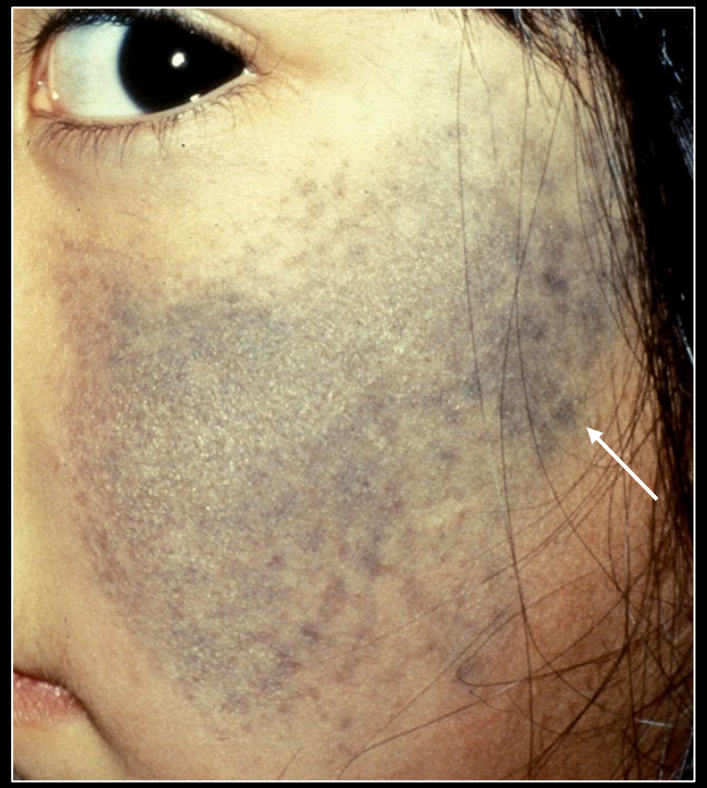
Dorsey CS. J Invest Dermatol 1954;22;225.
Ikeda S. Biology and Diseases of Dermal Pigmentation. 1981, pp.95-106.

Non-facial with common or cellular BN histology

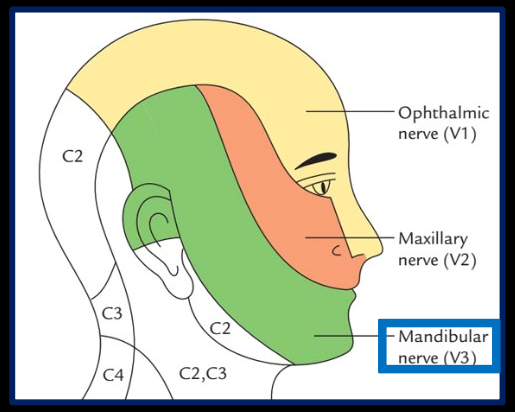


Hsiao G-H. *JAAD* 1994;30:849.





Courtesy, K Urabe, MD



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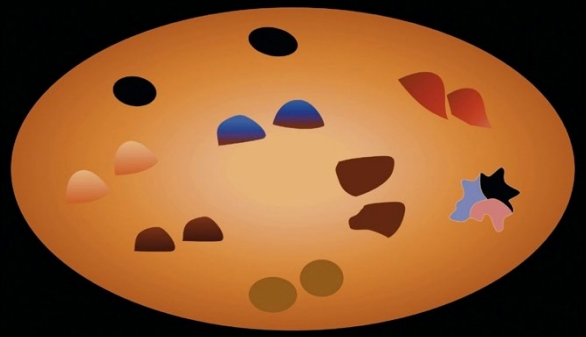
The “Spots”



Lentigines

Junctional Nevi

Compound Nevi

Atypical or Dysplastic Nevi

Small Congenital Nevi

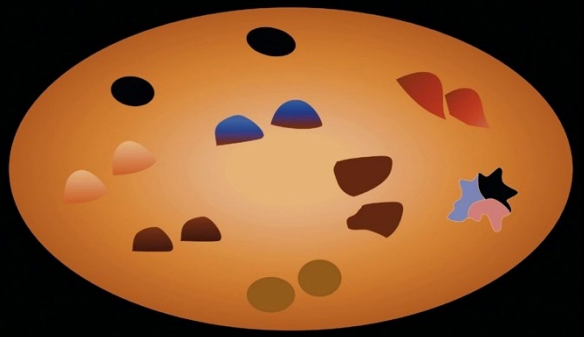
Dermal Nevi

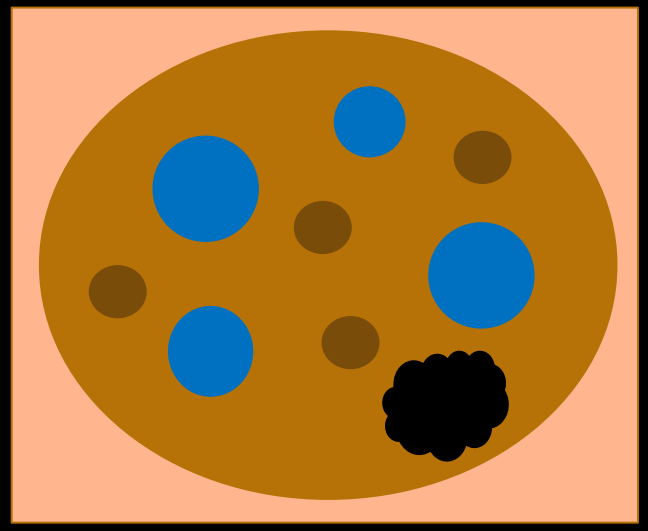
Blue Nevi

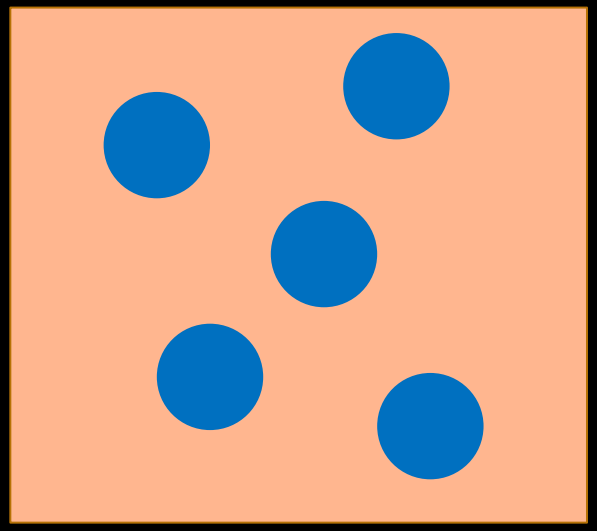
Spitz Nevi

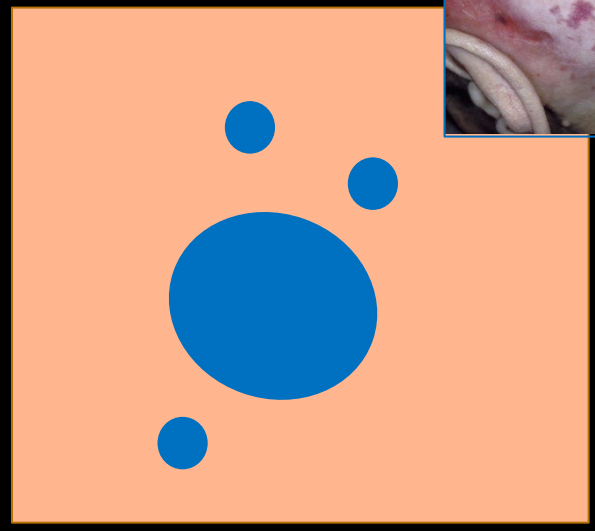
Melanoma

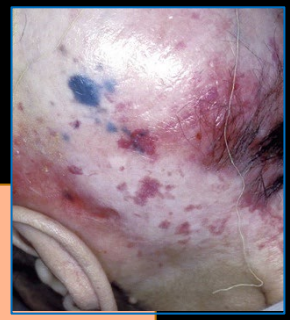
Medium-sized Congenital Nevi











Blue nevi within a nevus spilus/speckled lentiginous nevus

Agminated blue nevi
GNAQ Q209L

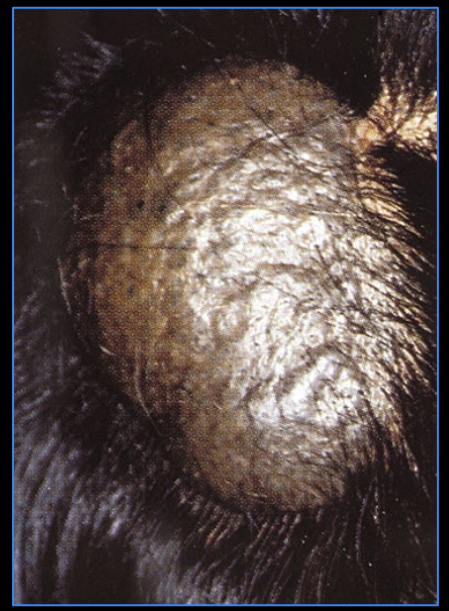
Cellular blue nevus with satellitosis

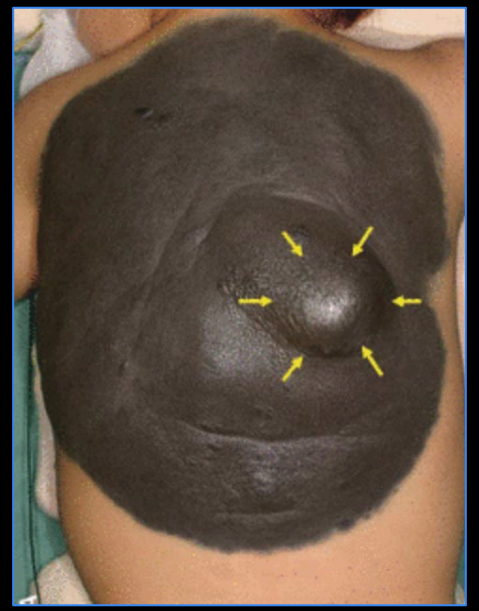
50% agminated misclassified

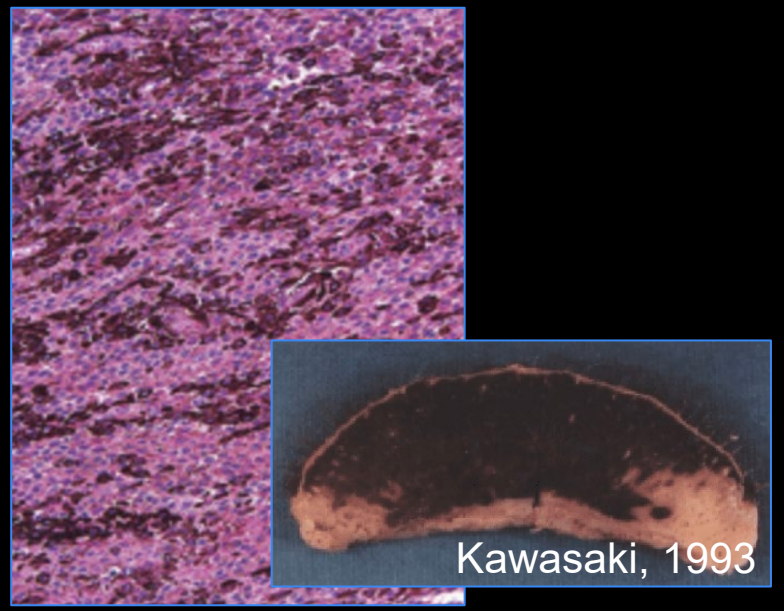
Eichenfield DZ. *J Cutan Pathol* 2019;46:93.

“Giant” congenital blue nevus

- Most commonly on scalp (>6 cm but <40 cm)
- Less commonly resembles classic giant congenital nevus
- On the scalp, can invade the cranium & CNS (invasive)



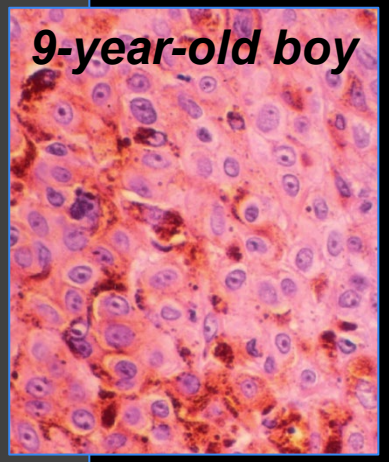


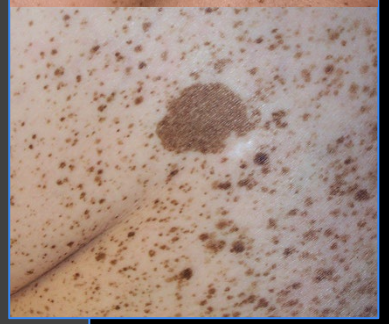


Nakamura Y. *Pediatr Dermatol 2012*;29:651.Cullom ME. *Ann Otol Rhinol Laryngol* 2021;130:1407.Acikilan M. *Turk Ekopatol* 2003;9:45.

Pigmented Epithelioid Melanocytoma

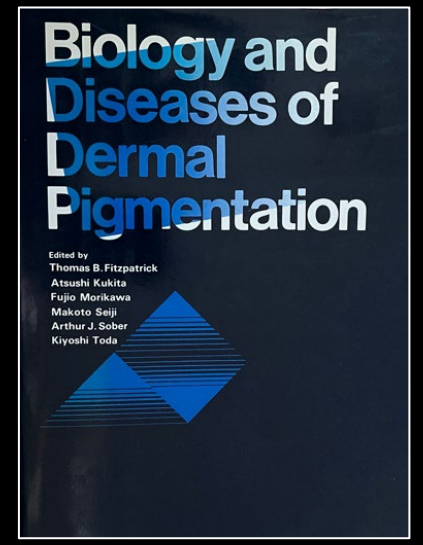
- Other names: epithelioid blue nevus, PRKAR1A-inactivated melanocytoma, “animal-type” melanoma
- Majority have loss of PRKARA1 immunoreactivity or inactivating mutations in *PRKAR1A* => activation of protein kinase A (PKA) catalytic subunits
- Usually combined with kinase fusions as observed in other types of nevi such as Spitz nevi
- Occur sporadically and in the setting of Carney complex
- Lymph node metastases in 30-50% of patients but rare distant metastases

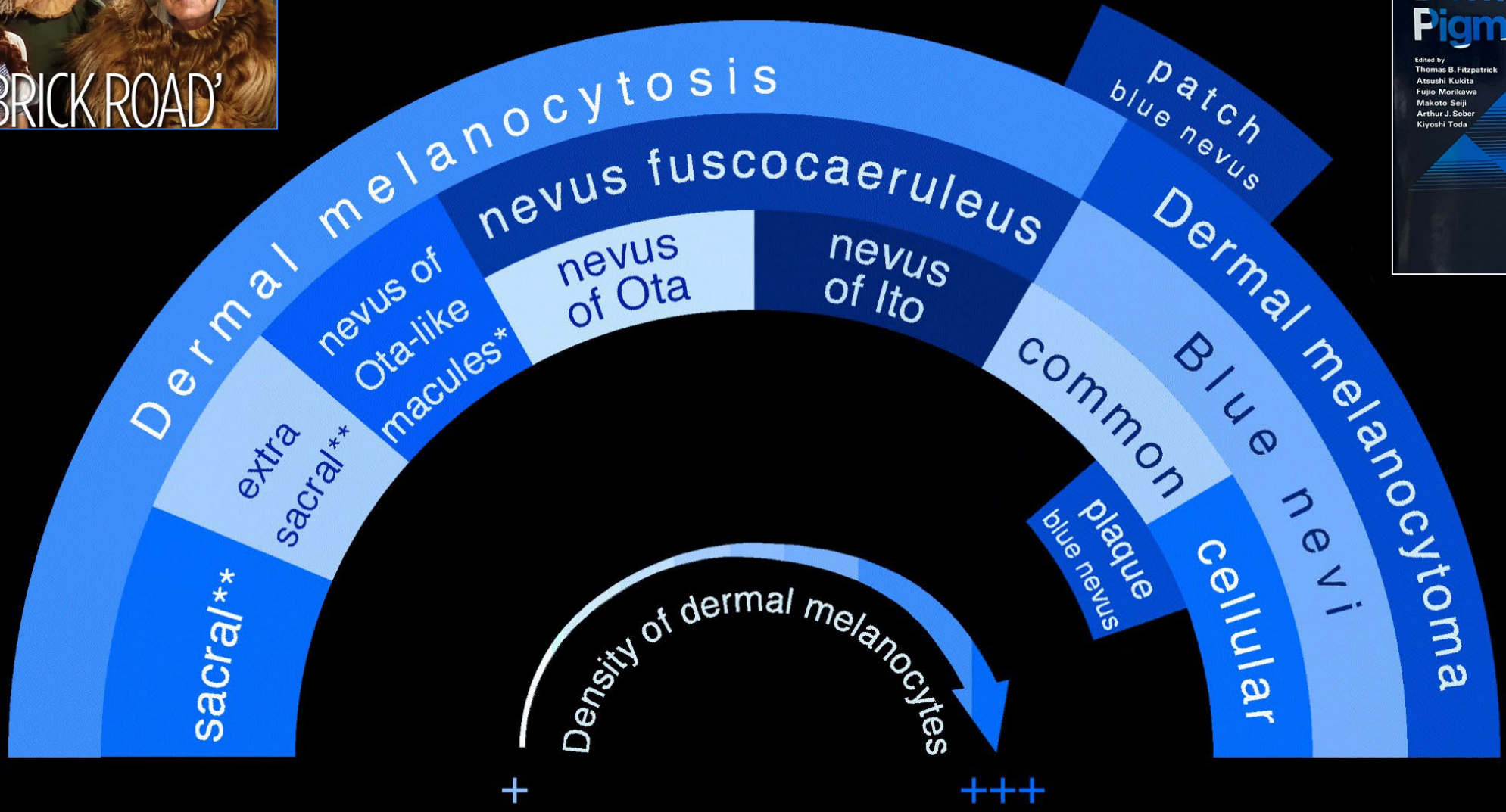




Zembowicz A. *Am J Surg Pathol* 2004;28:31.

BLUE





*acquired **congenital dermal melanocytosis


Bar
NEW YEAR RESOLUTION:
MAKE BETTER
BAD DECISIONS

Cellular blue nevus

- WHO classification of melanocytic tumors (classes I-IV)

Class II

  - Dysplastic nevi (high grade)
  - Spitz nevus
  - Cellular blue nevus
  - Deep penetrating nevus (plexiform)
  - Lentigo maligna
  - Melanoma in situ