

Freckle (Ephelis)

Pigment biology, morphology, and differential diagnosis

Dermatopathology teaching lecture

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Learning outcomes

- Recognize the clinical and microscopic phenotype of an ephelis.
- Distinguish altered melanin content from melanocytic hyperplasia.
- Explain the characteristic sunlight- and season-dependent appearance.
- Separate ephelis from lentigo, café-au-lait macule, and melanocytic nevus.

The diagnostic problem: Why is a macule brown?

A brown macule does not identify its cellular mechanism.

Pigment

More melanin in recipient cells

Cell number

More melanocytes in basal
layer

Architecture

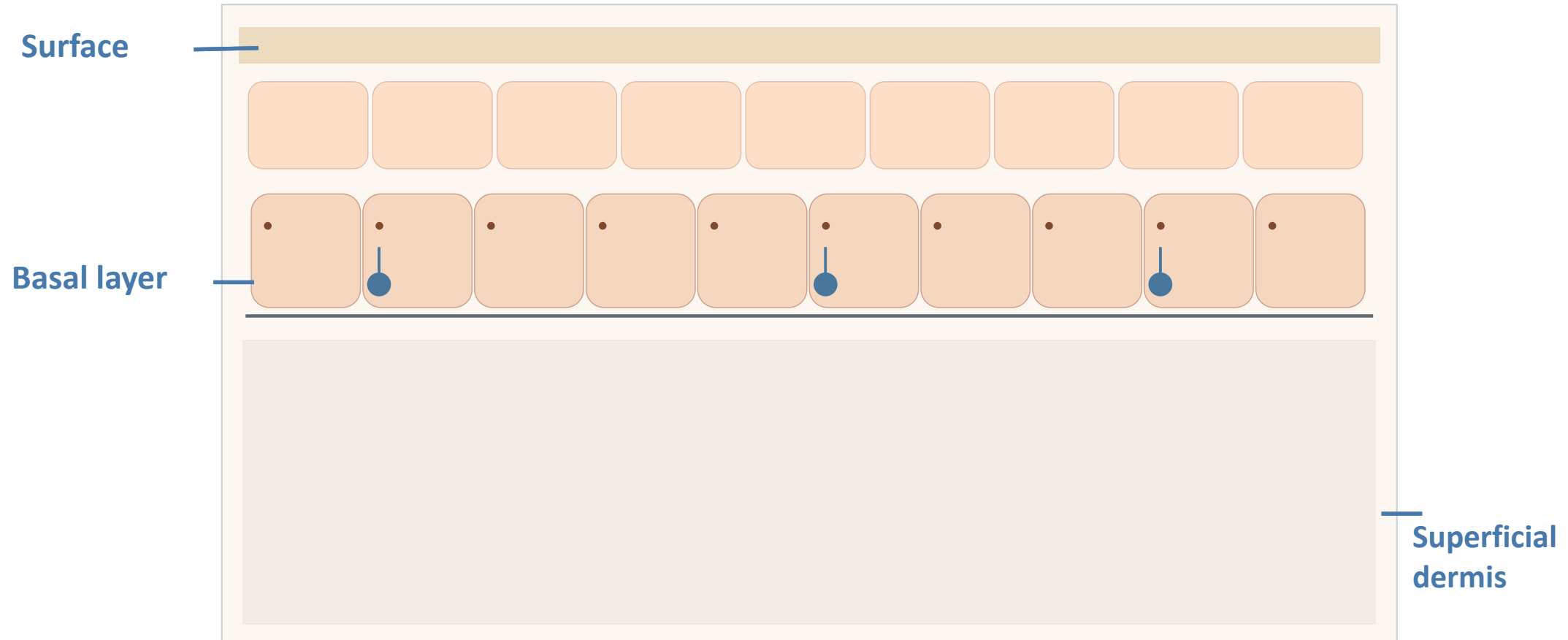
Nests or other growth pattern

Clinical appearance and histologic mechanism must be kept distinct.

Macule: A flat lesion distinguished by color

- A macule is circumscribed and flat: Its difference from adjacent skin is color.
- A macule is 10 mm or less in diameter; Larger flat lesions are patches.
- The term describes appearance—not whether the process is reactive, hyperplastic, or neoplastic.

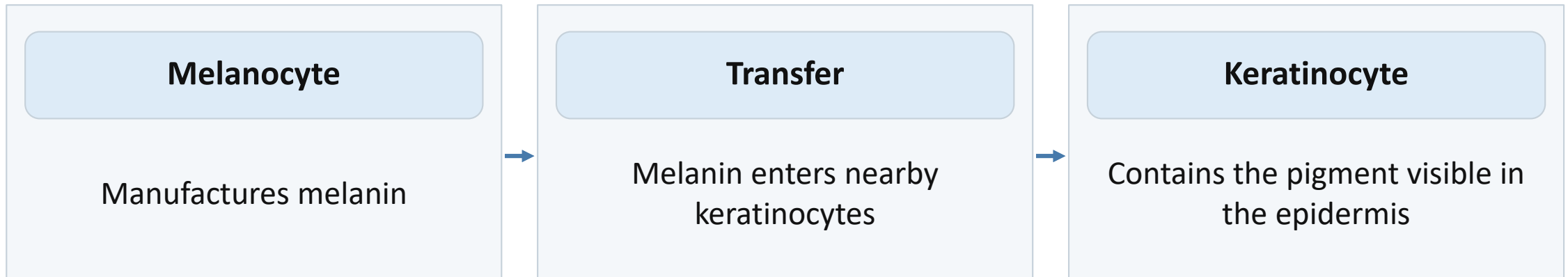
Skin architecture locates the pigmentation change



Schematic epidermis; Simplified relative geometry, not a tissue section.

Melanocytes synthesize pigment; Keratinocytes receive it

Different cells perform the production and storage roles.



Melanin provides a degree of UV protection

- Melanin as a brown pigment that absorbs ultraviolet radiation.
- Pigment synthesized in melanocytes is transferred to keratinocytes.
- The resulting distribution of melanin contributes to skin color.

Two questions should be asked of a pigmented lesion

Quantity of pigment

- Are basal keratinocytes more heavily pigmented?
- Does intensity vary with sun exposure?
- Is melanocyte density preserved?

Pattern of melanocytes

- Are basal melanocytes increased?
- Are cells arranged linearly?
- Do melanocytes form nests?

Ephelis: A common childhood pigmented lesion

The defining change is focal pigmentation without increased melanocyte density.

- Freckles are especially common in lightly pigmented children.
- They are small, flat, tan-red to light-brown lesions.
- They appear or become conspicuous after sunlight exposure.

Age and pigmentary background

Typical setting

- Common pigmented lesion in childhood
- Most often described in lightly pigmented individuals
- May present as numerous macules

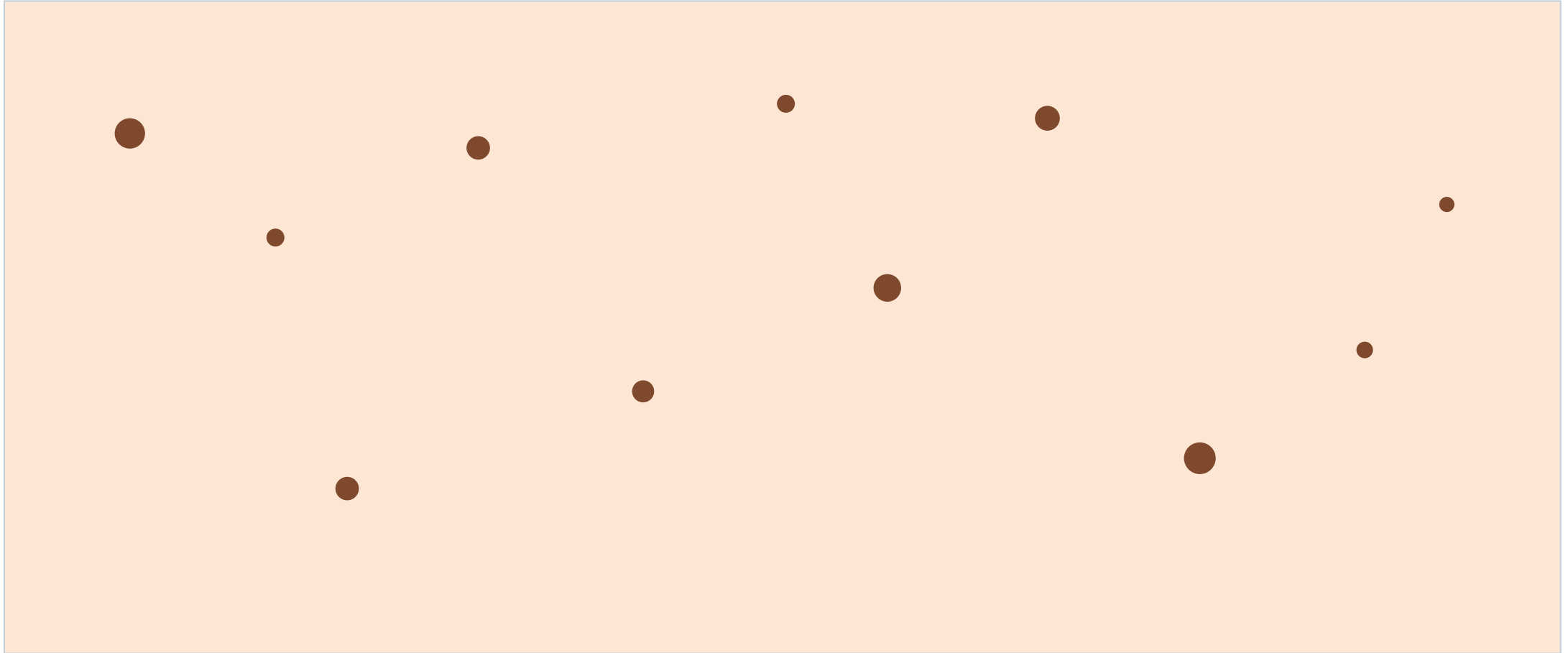
Interpretative limits

- Age and background alter pretest probability
- Neither feature alone is histologically diagnostic
- A pigmented macule still requires morphology-based assessment

Gross morphology of an ephelis

Feature	Robbins description
Lesion type	Macule (flat, color-defined)
Diameter	Usually 1 mm to several millimeters
Color	Tan-red or light brown
Trigger	Appears following sun exposure
Course	Fades in winter; darkens in summer

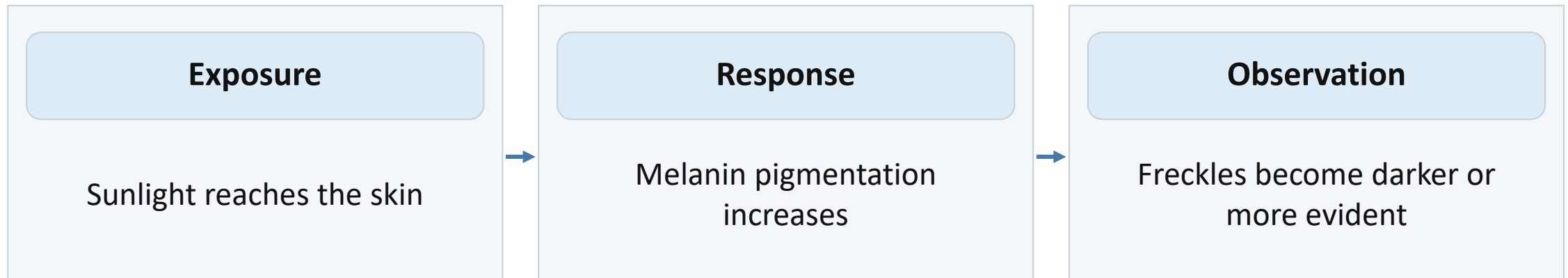
Visible macules: A schematic field



Multiple flat brown macules — conceptual appearance only

Sun exposure matters to the diagnosis

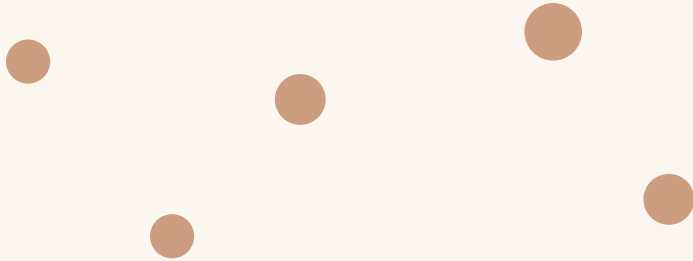
Sunlight changes the visibility of ephelides.



Robbins supports the sun-dependent clinical behavior; This is not a quantified dose-response.

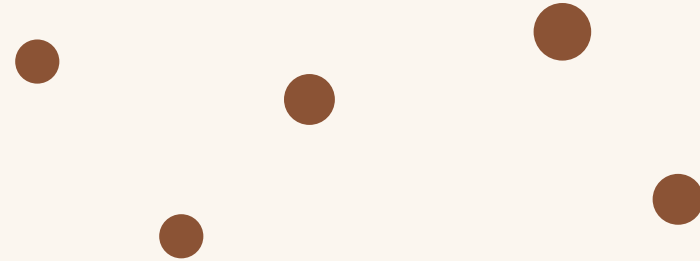
Ephelides change in a seasonal cycle

Winter



Lower visible pigment

Summer



Greater visible pigment

Same conceptual lesions; Pigmentation intensity changes with the season.

Seasonal darkening is not melanocyte expansion

What changes

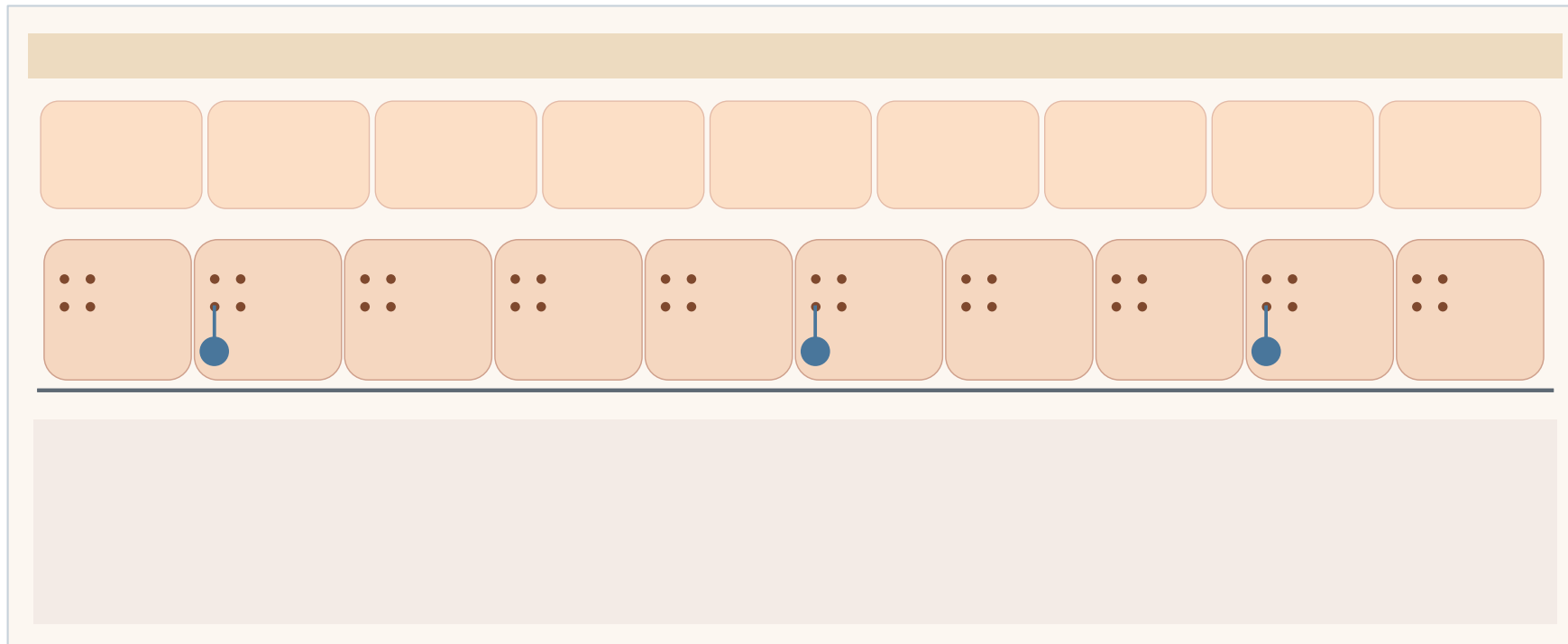
- Degree of epidermal pigmentation
- Clinical color intensity
- Visibility of existing freckles

What does not explain the cycle

- A seasonal increase in melanocyte density
- A proliferative melanocytic tumor
- Replacement of the basal cell population

Histologic hallmark: Pigmented basal keratinocytes

The excess brown pigment is localized principally within basal keratinocytes.



Schematic. Brown dots symbolize increased melanin; They do not represent an actual stain.

Melanocyte density remains normal in ephelis

Melanocytes

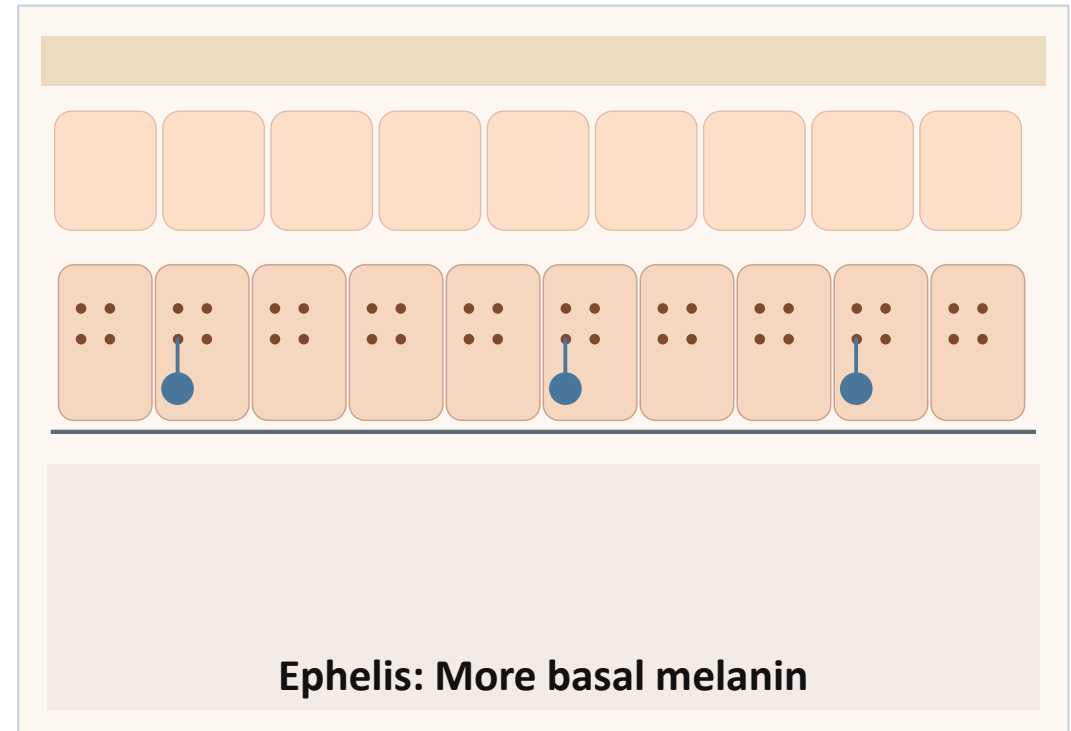
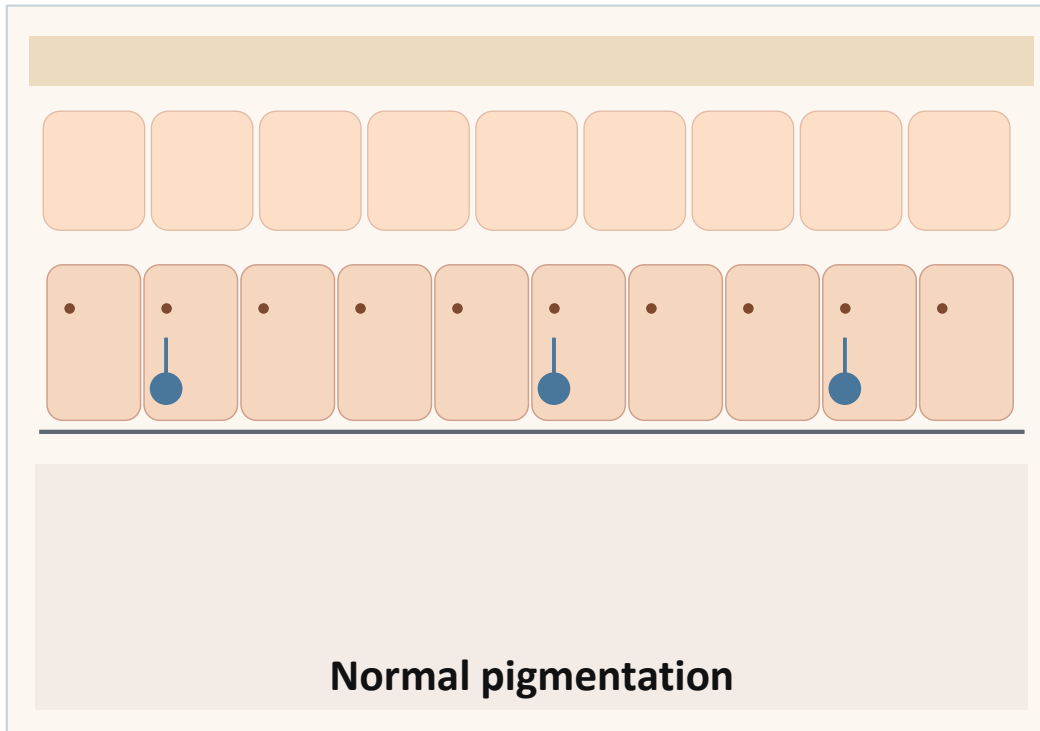
- Numbers remain normal
- Individual cells may be slightly enlarged
- No basal hyperplasia is required

Basal keratinocytes

- Show increased melanin pigment
- Explain the visible dark macule
- Drive seasonal fluctuations in lesion color

Pigment increase is not cell proliferation

A dark epidermis can have an unchanged number of melanocytes.



Schematic relative representation: Equal melanocyte density; Differing pigment content.

Slight melanocyte enlargement: A qualified finding

- Ephelis-associated melanocytes may be slightly enlarged.
- The qualifying word “may” is important: Enlargement is not obligatory.
- Normal melanocyte density, rather than cell dimensions alone, is the central distinction from lentigo.

Mechanism: Uncertainty

The source does not establish one exclusive cellular mechanism.

Option 1

Localized altered melanin
production

Option 2

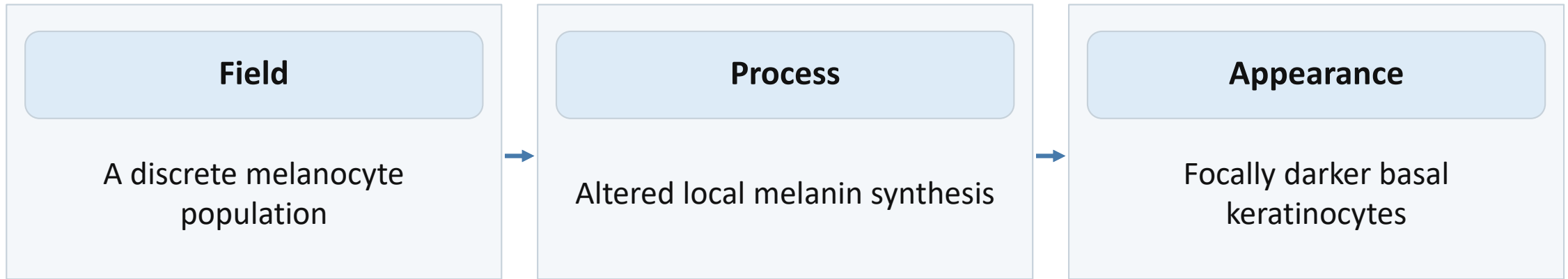
Enhanced transfer to basal
keratinocytes

Both

A contribution from both
mechanisms

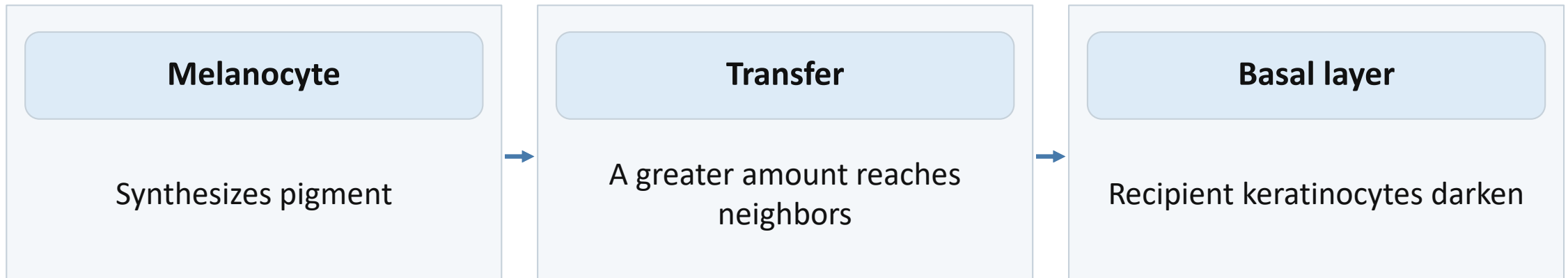
These are hypotheses explicitly presented by Robbins—not three established sequential events.

Hypothesis 1: A local pigment-production field



- The source presents this as a possible explanation, not a demonstrated exclusive cause.

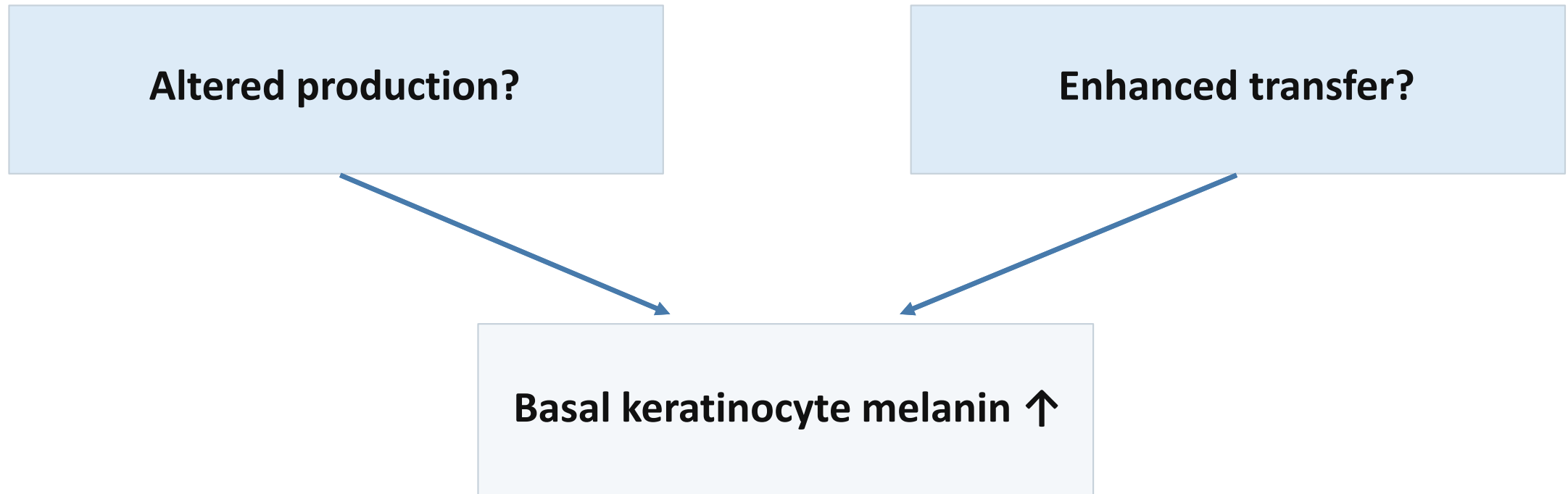
Hypothesis 2: Enhanced melanin transfer



- Robbins explicitly leaves the role of altered transfer unresolved.

The two mechanisms are not mutually exclusive

Increased pigment production and enhanced transfer can both raise basal keratinocyte melanin.

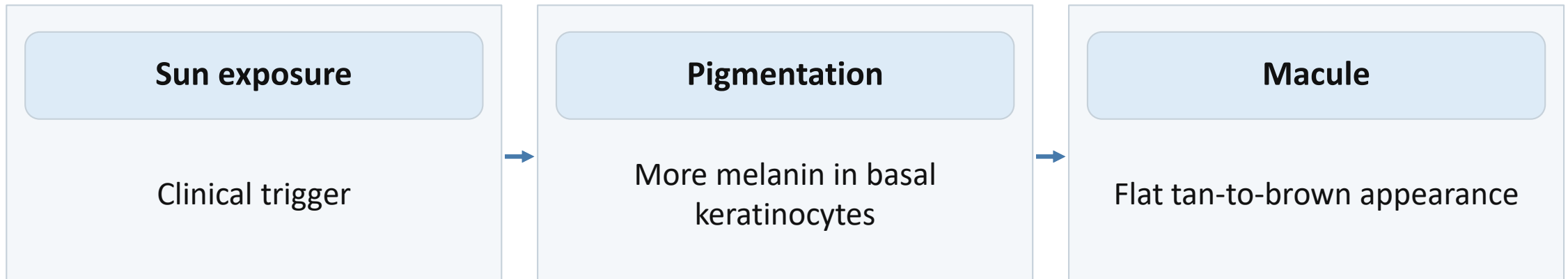


Question marks deliberately represent unresolved mechanistic alternatives.

Mechanism and morphology: Separate the evidence

Observation	Interpretation status
Basal keratinocyte hyperpigmentation	Established morphologic finding
Normal melanocyte density	Established morphologic finding
Localized pigment-production abnormality	Possible mechanism
Enhanced pigment transfer	Possible mechanism
Combination of production and transfer	Possible mechanism

A clinicopathologic chain for ephelis



This sequence summarizes observed associations; It does not resolve the upstream mechanism.

Why a skin section can be misleading

- The microscopic darkening may look similar to other pigmented macules.
- Pigment quantity and melanocyte pattern need separate assessment.
- An isolated histologic field may not reveal seasonal behavior or exposure history.
- Correlation with lesion size, distribution, and temporal course strengthens classification.

How to describe an ephelis in a teaching report

Clinical descriptor

- Small flat tan or light-brown macule
- Often noticed after sunlight exposure
- Winter fading and summer darkening

Histologic descriptor

- Increased melanin within basal keratinocytes
- Melanocyte density remains normal
- Associated melanocytes may be slightly enlarged

Population predisposition: Supporting clinical context

- Ephelides commonly occur in people with fair skin and may cluster in families.
- DermNet describes associations with variants in the melanocortin-1 receptor (MC1R) gene.
- Genetic association should not be confused with a required diagnostic molecular test.

Clinical distribution: Exposure is relevant

- Freckles are particularly conspicuous on sun-exposed sites.
- The nose and cheeks are common examples in clinical dermatology references.
- Distribution is useful context; It is not by itself a diagnosis.

Clinical recognition usually precedes biopsy

Classic ephelides are generally recognized clinically.

- History of appearance after sun exposure supports the impression.
- Morphology and course are more informative than color alone.
- A diagnostically uncertain pigmented lesion should not be dismissed merely as a freckle.

Ephelis has no required lesion-directed treatment

- For typical benign ephelides, routine lesion-directed treatment is unnecessary.
- Sun protection is relevant because ultraviolet exposure accentuates pigmentation.
- These counseling points are supportive clinical information, not histologic diagnostic criteria.

Sun protection modifies expression—not cell identity

Predisposition

A tendency to develop freckles

UV exposure

Modulates visible pigmentation

Protection

May reduce darkening

The relationship is qualitative; No sunscreen efficacy percentage is asserted.

Café-au-lait macules: A related pigmentary pattern

Café-au-lait spots as a comparator because they resemble freckles histologically.

- They are described in the setting of neurofibromatosis type 1.
- Their larger size and independence from sun exposure help distinguish them.
- The comparison tests why pigment distribution alone may be insufficient.

Café-au-lait spots differ in size and light response

Ephelis

- Usually 1 mm to several millimeters
- Appears after sunlight exposure
- Intensity varies with season

Café-au-lait spot

- Larger than an ephelis
- Arises independently of sun exposure
- Histology can resemble that of ephelis

Macromelanosomes: An ultrastructural clue

- In neurofibromatosis type 1—associated café-au-lait spots, aggregated melanosomes.
- These “macromelanosomes” can be seen within melanocyte cytoplasm by electron microscopy.
- This is an ultrastructural statement—not a claim that macromelanosomes are routinely proven on H&E.

H&E and electron microscopy answer different questions

Routine light microscopy

- Can assess epidermal pigment distribution
- Can compare melanocyte patterns
- Cannot resolve every subcellular melanosome aggregate

Electron microscopy

- Can visualize cytoplasmic melanosome ultrastructure
- May reveal aggregated macromelanosomes
- Not the standard first step for an ordinary freckle

Ephelis versus café-au-lait macule

Feature	Ephelis	Café-au-lait macule
Typical size	Small, 1 mm to several mm	Larger
Exposure relationship	Sun-associated	Independent of sunlight
Microscopic resemblance	Basal pigment	Can resemble ephelis
Special finding	Not specified	Macromelanosomes in NF1-associated lesions

Lentigo is a benign melanocytic hyperplasia

Unlike ephelis, lentigo involves more melanocytes.

- Lentigo (plural: Lentigines) is a common benign localized melanocyte hyperplasia.
- The cells are arranged linearly and individually, rather than as nests.
- The basal cell layer is additionally hyperpigmented.

Lentigines occur across sexes and skin pigmentations

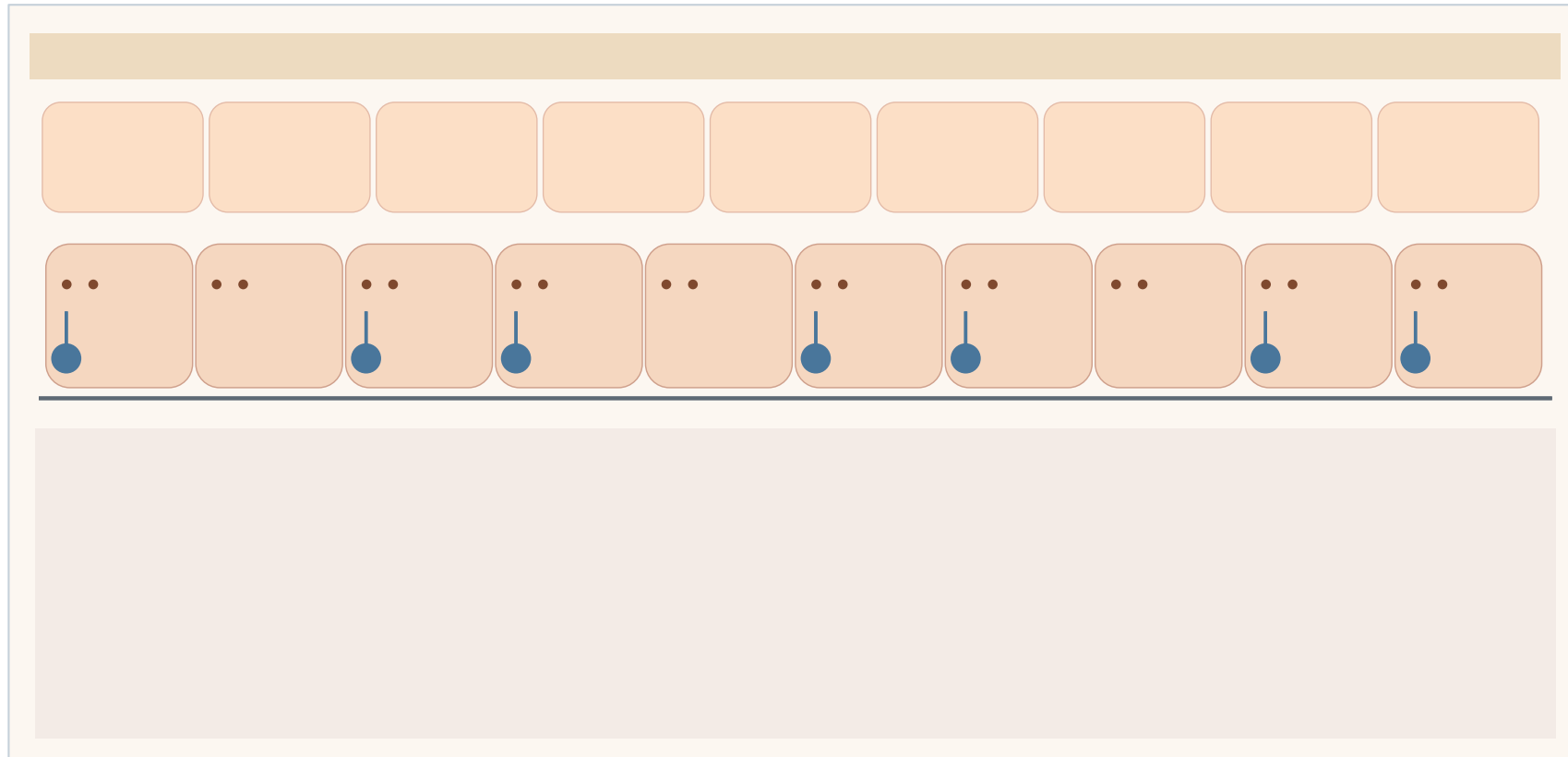
- Lentigines as equally common in males and females.
- They occur in people with lightly and darkly pigmented skin.
- They can develop at any age and are commonly encountered in infants and children.
- These population features overlap with ephelides and do not settle the diagnosis alone.

Gross appearance and sites of lentigines

Feature	Description
Shape	Small oval macules or patches
Color	Tan-brown
Size	Usually 5–10 mm across
Location	Skin and mucous membranes
Seasonality	Do not darken with sun exposure (Robbins simple lentigo)

Lentigo: A basal linear proliferation

More melanocytes align along the basement membrane.



Schematic: Increased basal melanocytes, without nesting or defined numerical density.

“Lentiginous” describes an architectural pattern

- The term refers to an increased linear distribution of individual melanocytes.
- These melanocytes in the layer immediately above the basement membrane.
- A lentiginous pattern differs from a nest-based arrangement of nevus cells.

Lentigo lacks the seasonal darkening of ephelis

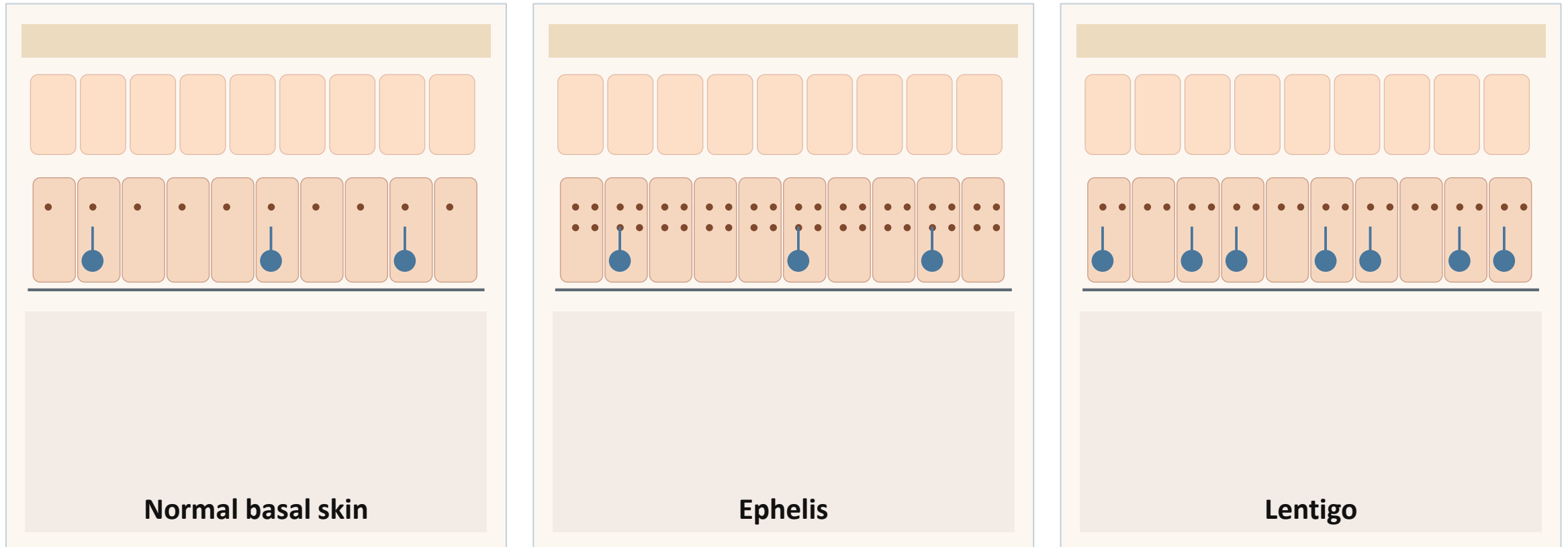
Ephelis

- Light-dependent prominence
- Summer darkening and winter fading
- Melanocyte density stays normal

Lentigo

- Does not darken in sunlight according to the grouped source
- Benign proliferation of basal melanocytes
- Distinction depends also on cell pattern

Normal skin, ephelis, and lentigo: One model



Schematic contrast: Pigment quantity differs from melanocyte density.

Compare ephelis and lentigo: Clinical clues

Clinical clue	Ephelis	Lentigo
Size	1 mm to several mm	5–10 mm
Surface	Flat macule	Flat macule or patch
Pigmentation	Tan-red to light brown	Tan-brown
Sunlight response	Darkens after exposure	Does not darken with sunlight
Site	Sun-exposed context	Skin or mucosal surface

Compare ephelis and lentigo: Histologic clues

Pathology feature	Ephelis	Lentigo
Basal melanin	Increased	Increased
Melanocyte number	Normal density	Increased (hyperplasia)
Architectural pattern	No described linear hyperplasia	Linear, nonnested proliferation
Primary explanation	Pigment excess	Melanocyte hyperplasia with basal pigmentation

Melanocytic nevus occupies a separate category

A nevus is a benign melanocytic neoplasm, not merely increased epidermal pigment.

- Acquired nevi as frequently harboring activated RAS pathway components.
- Junctional nevi contain nests of melanocytes at the dermoepidermal junction.
- Nesting is a different architectural question from the linear basal hyperplasia of lentigo.

Linear proliferation versus nests

Lentigo

- Single melanocytes increase along the basal layer
- Linear pattern
- Nonnested melanocytic hyperplasia

Junctional nevus

- Melanocytes form aggregates or nests
- Nests are located at dermoepidermal junction
- A benign neoplasm rather than a simple freckle

Three distinct tissue-level explanations

Ephelis

Increased basal melanin; Normal melanocyte density

Lentigo

Linear basal melanocyte hyperplasia

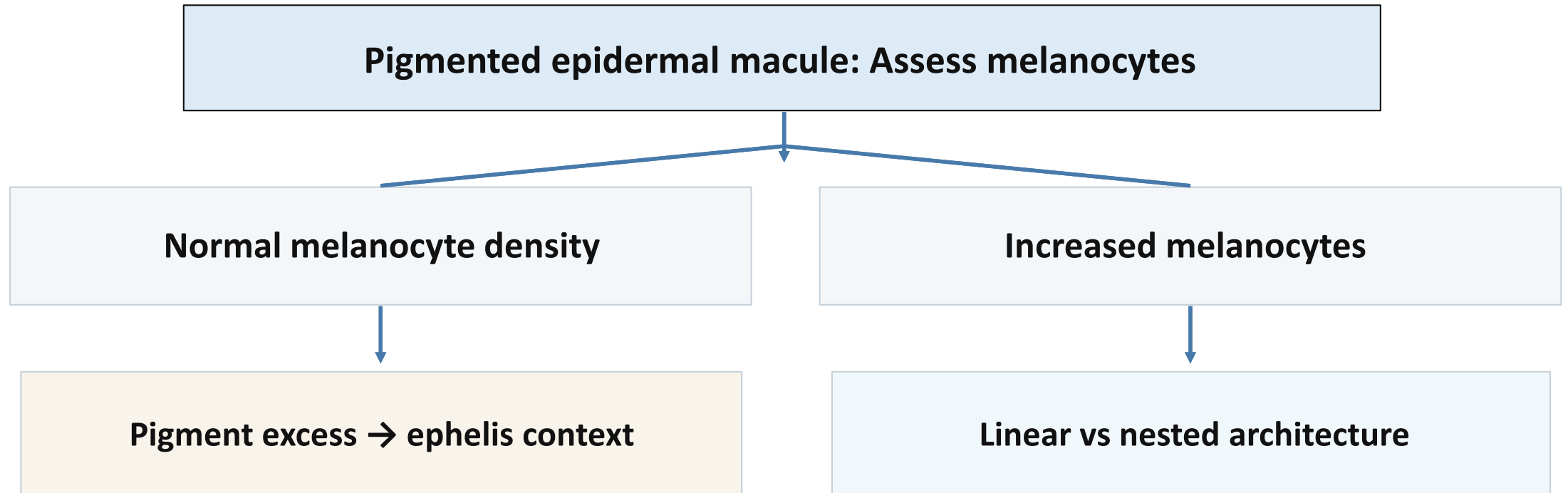
Junctional nevus

Nested melanocytes at the dermoepidermal junction

Do not substitute one histologic mechanism for another because all appear brown.

A practical tissue interpretation pathway

First distinguish pigment accumulation from melanocytic proliferation.



Simplified teaching decision aid; A full pigmented-lesion workup has wider differentials.

Clinical morphology cannot replace tissue context

- Flatness and brown color describe a lesion but do not prove the histologic mechanism.
- Sun exposure and seasonal behavior particularly support ephelis.
- Persistent macules may require differentiation from lentigines and other lesions.
- Changing or atypical lesions require an independent clinical assessment.

Clinical scenario A: Seasonal childhood macules

Clinical scenario

A lightly pigmented child develops multiple tiny tan macules after summer outdoor activity. The macules become much less visible during winter.

Which cellular feature would best fit the leading diagnosis?

Scenario A: Interpret the cells, not just the color

Most consistent with ephelides.

- Expect increased melanin in basal keratinocytes.
- Melanocyte density should remain normal.
- Seasonal modulation reflects pigment intensity, not a changing melanocyte population.

Clinical scenario B: A nonseasonal brown macule

Clinical scenario

A 7-mm oval tan-brown macule remains similarly pigmented despite changes in seasonal sun exposure. Histology shows increased single melanocytes along the epidermal basal layer.

Which architecture identifies the lesion?

Scenario B: Linear hyperplasia points to lentigo

The histologic pattern is lentiginous.

- Increased basal melanocyte density supports a melanocytic hyperplasia.
- The cells form a linear, nonnested pattern.
- Persistence without sun-related darkening helps distinguish it from ephelis.

Clinical scenario C: A larger, sun-independent spot

Clinical scenario

A child has a larger, uniformly pigmented flat patch that does not fluctuate with sun exposure. The clinical assessment raises concern for an associated neurocutaneous disorder.

Which Robbins comparison is relevant, and what is the ultrastructural finding?

Scenario C: Café-au-lait macule correlation

The source highlights NF1-associated café-au-lait spots.

- Larger dimensions and sunlight independence separate the lesion from typical freckles.
- Macromelanosomes are described in melanocytes on electron microscopy.
- One pigmented patch alone does not establish neurofibromatosis type 1.

Microscopic challenge: Basal pigment only

Clinical scenario

A teaching micrograph is described as showing markedly pigmented basal keratinocytes, with no increase in melanocyte density.

What key inference is supported, and which process is not demonstrated?

Description is textual: No authentic photomicrograph is supplied.

Microscopic challenge: Answer

The microscopic finding supports pigment accumulation without hyperplasia.

- It is compatible with ephelis when clinical context fits.
- It does not demonstrate a lentiginous melanocytic proliferation.
- It cannot by itself establish whether production or transfer is the predominant cause.

Terminology check: Three questions

Question	Correct concept
What makes a macule?	Flat lesion distinguished by color
What is “lentiginous”?	Linear basal pattern of melanocyte proliferation
What creates an ephelis?	More basal keratinocyte melanin without more melanocytes
What is a junctional nevus?	Melanocytic nests at the junction

Avoid four diagnostic overstatements

- “Brown means melanocytic proliferation” — false: Melanin may increase without more cells.
- “Summer darkening means the melanocyte number rose” — false for ephelis.
- “Pigment microscopy identifies the sole biochemical mechanism” — unsupported.
- “All freckles are lentigines” — imprecise; Ephelis and lentigo differ structurally.

Integrated diagnostic distinctions

Entity	Principal clue	Histologic process
Ephelis	Sun/season responsive	Basal pigment increased; melanocyte count normal
Lentigo	Persistent; often 5–10 mm	Linear, nonnested basal melanocyte hyperplasia
Café-au-lait macule	Larger; sun independent	May resemble ephelis; NF1 macromelanosomes on EM
Junctional nevus	May be flat or raised	Melanocytic nests at junction

Teaching synthesis: The freckle phenotype

Four propositions resolve most essential distinctions.

- Clinical: Small tan-to-light-brown macule with sun-dependent pigmentation.
- Seasonal: Stronger pigmentation in summer; Fading during winter.
- Histologic: Increased melanin in basal keratinocytes, normal melanocyte density.
- Mechanistic: Altered pigment production, transfer, or both remain possible.

Source references and interpretation boundary

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 25: The Skin, pp. 1028–1031.
- DermNet: Ephelis (2016) — supplementary clinical distribution, inherited susceptibility, diagnosis and care.
- DermNet: Brown spots, lentigos and freckles (2018) — supplementary clinical comparison.
- All diagrams in this presentation are original editable schematics, not patient images or histologic photographs.