

Actinic Keratosis

Sun-damaged keratinocytes · dysplasia · progression risk

Clinicopathologic teaching lecture

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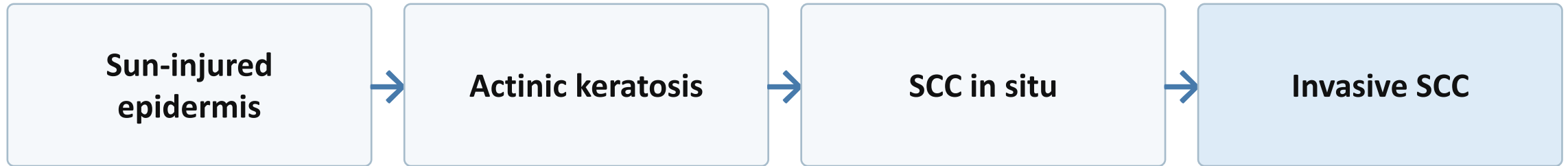
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Learning objectives

- Identify the clinical phenotype and distribution of actinic keratosis.
- Explain epidermal dysplasia, keratinization, and dermal solar elastosis.
- Relate ultraviolet injury to precursor lesions and squamous carcinoma.
- Distinguish a keratosis from in situ and invasive carcinoma.
- Explain the rationale and mechanisms of local lesion eradication.

Actinic keratosis in the epidermal tumor spectrum

A localized lesion is understood in relation to progressive squamous atypia.



- These are morphologic states, not an inevitable sequence for every lesion.
- The critical transitions are extent of atypia and basement-membrane breach.

Core definition: A dysplastic keratinocytic lesion

- An actinic keratosis arises most often in chronically sun-damaged skin.
- It is associated with surface hyperkeratosis and basal epidermal atypia.
- Progressively greater epithelial dysplasia may culminate in cutaneous SCC.

Interpretive anchor

Premalignant potential is a property of the lesion category—not a prediction for each plaque.

Why “actinic” and why “keratosis”?

Actinic — causal setting

- Sun exposure is the predominant association.
- UV injury links skin damage to keratinocyte mutation.
- Typical distribution favors exposed skin.

Keratosis — surface change

- Stratum corneum is abnormally thickened.
- Roughness can be more evident than color.
- Pronounced keratin may create a horn.

High-risk host phenotype

- Light pigmentation is associated with a particularly high incidence.
- The association is consistent with reduced protection against UV injury.
- Cumulative exposure and host susceptibility act together.

Do not overextend the textbook statement

The source does not provide an individual risk score or a precise lesion-transformation percentage.

Etiologic exposures linked to similar lesions

Ultraviolet exposure

- Principal association in sun-damaged skin.
- Typical exposure pattern involves uncovered sites.

Ionizing radiation

- May induce lesions resembling AK.
- Non-solar radiation is a separate exposure category.

Chemical carcinogens

- Industrial hydrocarbons may contribute.
- Arsenical exposure may induce similar lesions.

Anatomic distribution is an etiologic clue

OBSERVED FEATURES

- Face is a common involved site.
- Arms and dorsal hands are frequently affected.
- The lip can show an analogous actinic lesion.

WHY DISTRIBUTION MATTERS

A lesion's location supports interpretation when it matches the pattern of cumulative environmental injury.

Typical lesion size and clinical scale

- Most lesions are described as less than 1 cm across.
- Small size does not exclude biologically important dysplasia.
- The clinical surface may be more conspicuous than the lesion's elevation.

Size is descriptive, not a diagnostic cutoff

The source gives typical dimensions, not an absolute threshold or staging rule.

Clinical color does not have one fixed appearance

Tan–brown

- A pigmented lesion can retain the characteristic rough surface.
- Color alone is insufficient for identification.

Red

- Erythematous lesions are within the usual spectrum.
- Inspection must be combined with surface assessment.

Skin-colored

- Some lesions are subtle on visual inspection.
- The rough consistency is an important clue.

The characteristic tactile clue

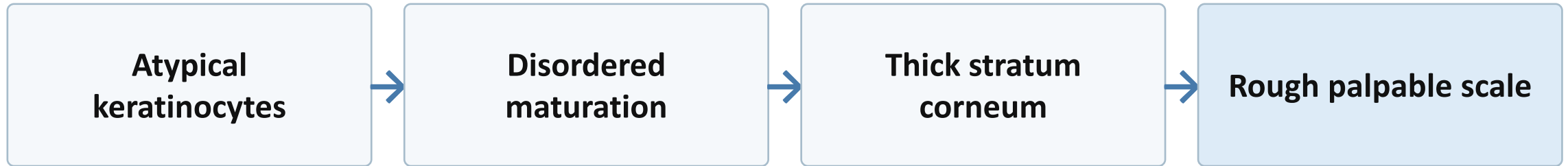
CLINICAL RECOGNITION

A rough, sandpaper-like surface is typical.

- The sensation is explained by abnormal keratin accumulation.
- “Scaly” is a structural observation, not a histologic diagnosis.

How excessive keratin produces surface scale

Clinical texture is a consequence of altered epidermal differentiation.



- This is a conceptual explanation of the source morphology, not a proven single molecular pathway.

Hyperkeratosis can dominate the gross appearance

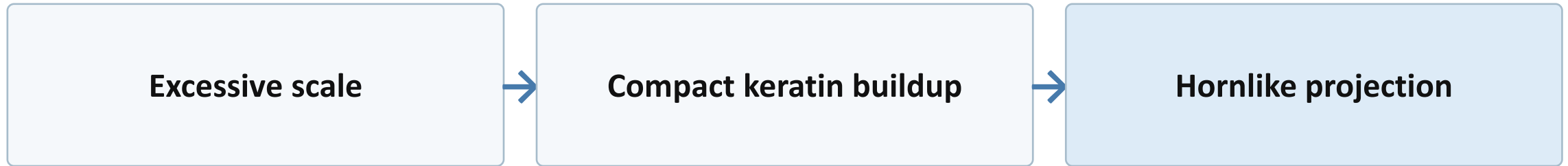
- The cornified surface may become markedly thickened.
- An exuberant keratin mass can obscure the underlying dysplastic focus.
- Gross keratin quantity does not alone define epithelial invasion.

Diagnostic separation

A horn describes keratin architecture; Histology is needed to establish the underlying lesion.

A cutaneous horn: Architecture versus etiology

“Cutaneous horn” names the keratin projection, not a unique disease.



- The horn phenotype as a possible manifestation of actinic keratosis.
- One must not equate a dramatic horn with confirmed invasive carcinoma.

Actinic cheilitis: The lip counterpart

- Sun-exposed lip epithelium may develop comparable actinic change.
- The name actinic cheilitis for this presentation.
- The shared pathologic theme is sunlight-associated squamous epithelial injury.

Vocabulary distinction

Cheilitis specifies the involved lip; Keratosis denotes the analogous cutaneous setting.

Reading a rough plaque clinically

OBSERVED FEATURES

- Record color as tan–brown, red, or skin-colored.
- Assess rough scale and the degree of keratin buildup.
- Consider whether the site matches chronic sun exposure.
- Interpret all features together—not any feature alone.

CLINICOPATHOLOGIC CORRELATION

A coherent clinical description guides the differential; The defining cellular changes are microscopic.

Transition from gross to microscopic anatomy

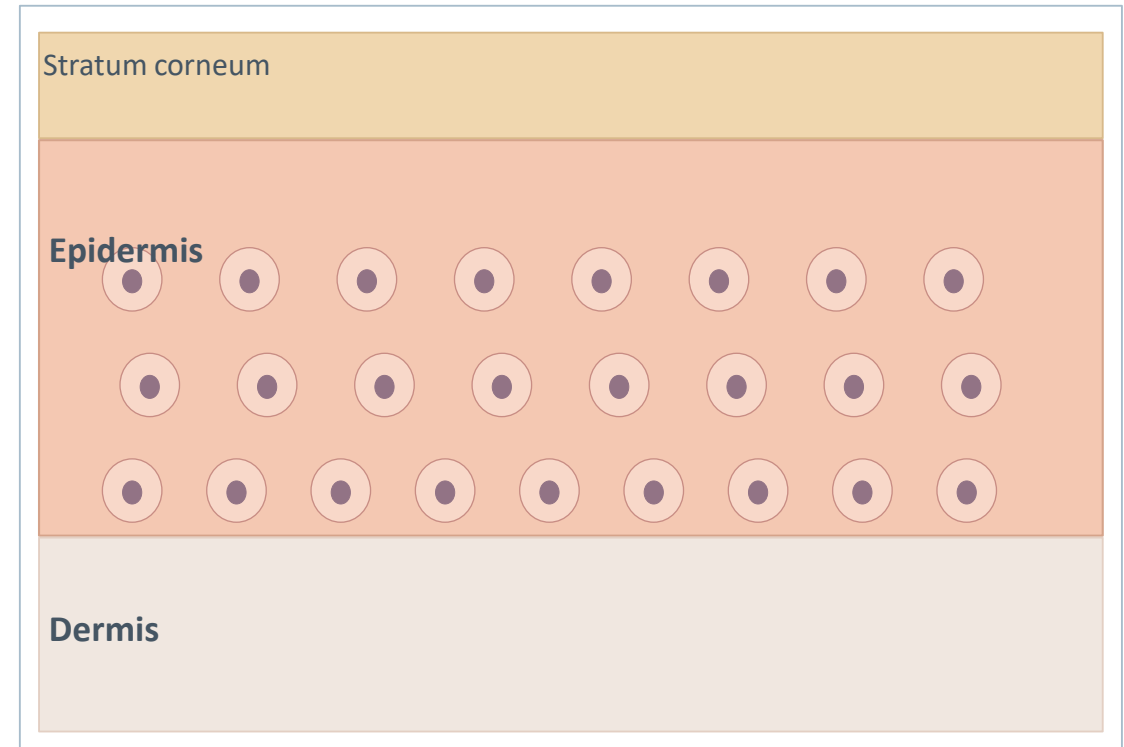
EPIDERMAL MICROSCOPY

The defining abnormality begins in epithelial cells—not in the visible scale alone.

- The basal portion of the epidermis is the key initial compartment.
- The stratum corneum and superficial dermis show associated injury patterns.

Epidermal reference: Surface, basal layer, dermis

- Keratinizing epithelium lies above the dermal connective tissue.
- The superficial stratum corneum reflects terminal differentiation.
- The basal compartment adjoins the epidermal–dermal junction.

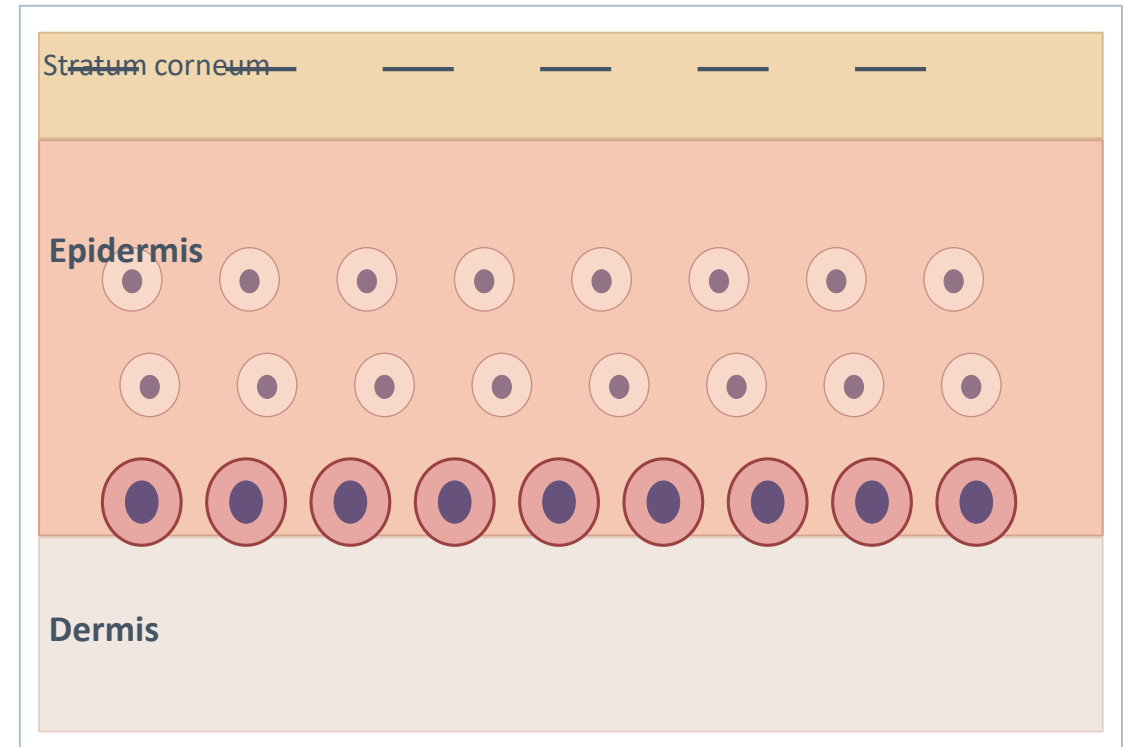


Schematic · not a histologic section

The schematic encodes compartments only; It is not an H&E photomicrograph.

The central microscopic feature is basal atypia

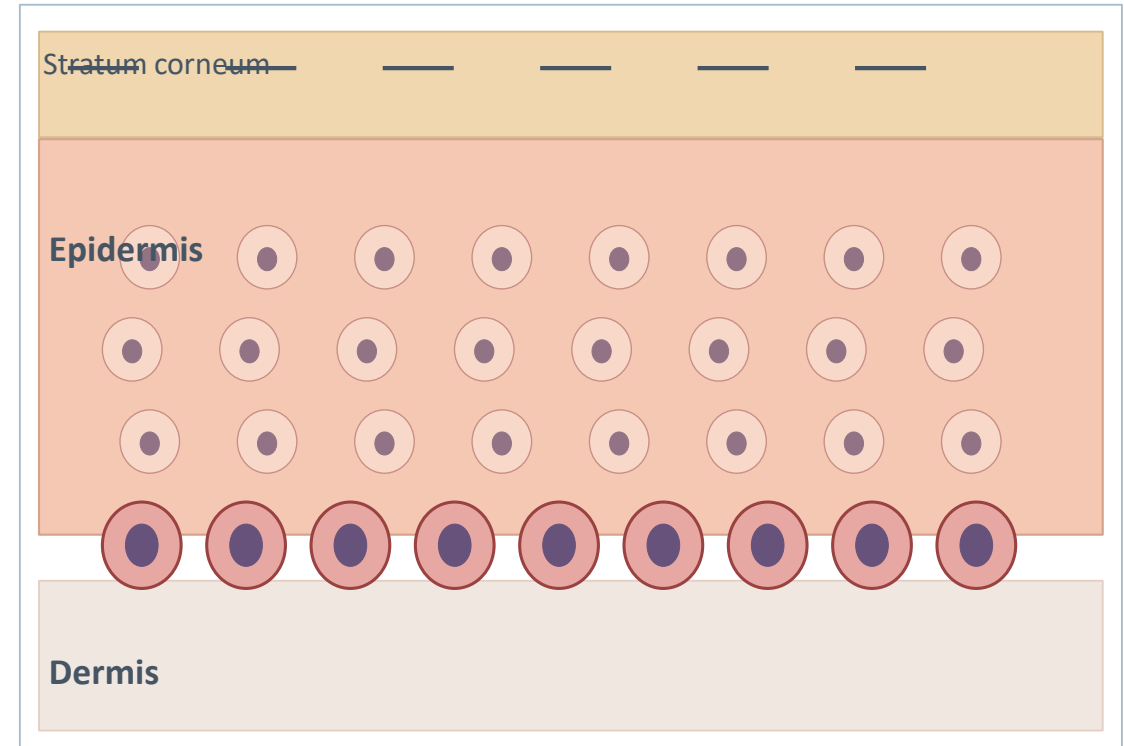
- Atypical keratinocytes populate low epidermal layers.
- Nuclear and cytoplasmic irregularity marks epithelial dysplasia.
- The upper epidermis may remain comparatively mature.



Schematic · not a histologic section

Basal hyperplasia can accompany dysplasia

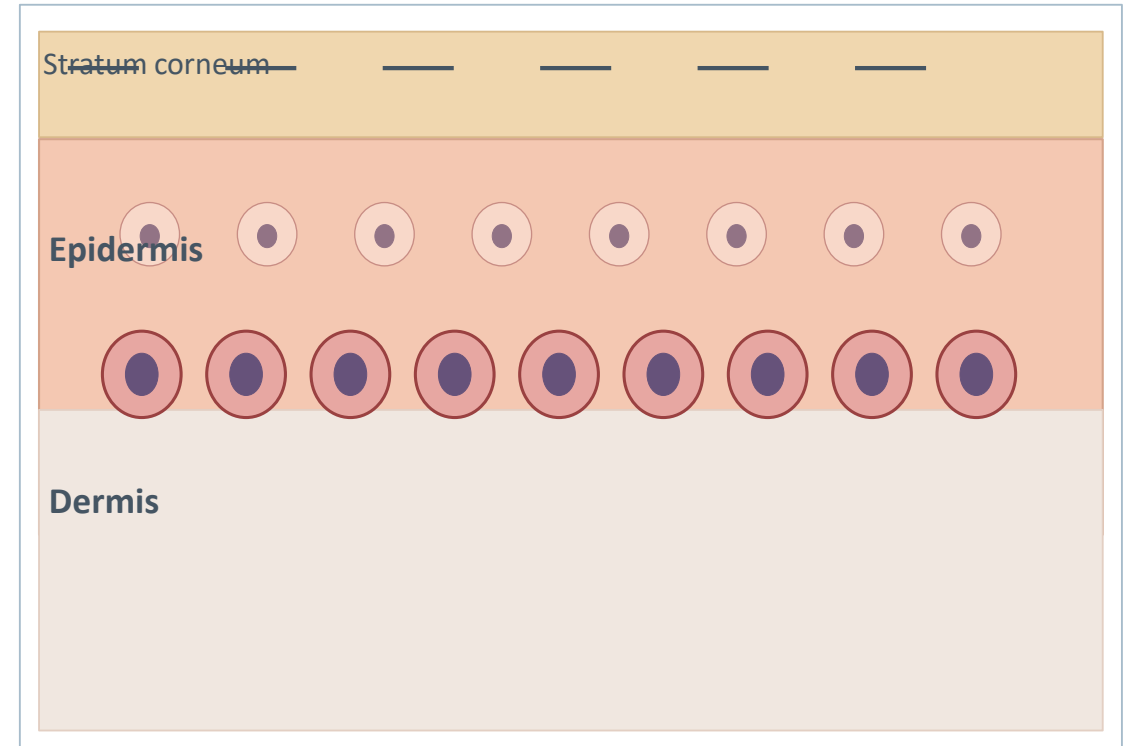
- The basal-cell population may be expanded.
- Increased epithelial cellularity coexists with basal atypia.
- This is one recognized architectural response in AK.



Schematic · not a histologic section

Epidermal atrophy is an alternative response

- Some actinic keratoses have a thinner epidermis rather than hyperplasia.
- Atypia cannot be ruled out because the epithelial compartment is attenuated.
- Architecture and cytology must be assessed separately.



Schematic · not a histologic section

Hyperplasia and atrophy are not contradictory

Hyperplastic pattern

- Basal-cell proliferation is increased.
- Epidermal thickness can be accentuated.
- Dysplasia remains the defining lesion.

Atrophic pattern

- Epidermal thickness is reduced.
- Atypical cells remain in basal layers.
- Thin epithelium does not imply a harmless lesion.

Dyskeratosis and eosinophilic cytoplasm

- Atypical basal keratinocytes often show pink or reddish cytoplasm.
- This appearance with dyskeratosis.
- The observation links aberrant cellular keratinization to atypical morphology.

Terminology

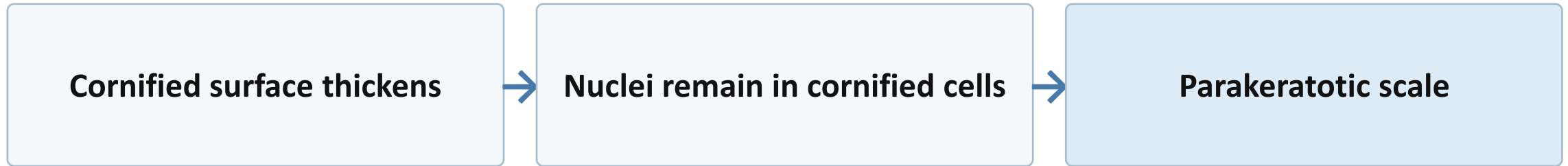
Dyskeratosis describes abnormal premature keratinization of individual keratinocytes.

Intercellular bridges help establish squamous identity

- Intercellular bridges may be recognized between atypical keratinocytes.
- This with basal cell carcinoma, where bridges are not visible.
- This is a morphologic clue, not a stand-alone immunohistochemical test.

Parakeratosis: The terminal differentiation defect

Abnormal cornification helps explain the characteristic scale.



- In normally cornified epidermis, mature surface corneocytes lose nuclei.
- Robbins explicitly describes retained nuclei in the stratum corneum.

Hyperkeratosis versus parakeratosis

Hyperkeratosis

- Thickness of stratum corneum is increased.
- Clinically contributes to scale and horns.
- Answers: “How much keratin?”

Parakeratosis

- Nuclei persist in cornified cells.
- Signals altered keratinocyte maturation.
- Answers: “How is cornification occurring?”

Solar elastosis: The dermal injury companion

- Superficial dermis contains thickened, blue-gray elastic fibers.
- The term elastosis for this appearance.
- It likely reflects abnormal elastic-fiber production by sun-damaged fibroblasts.

Compartment logic

Epidermal dysplasia and dermal elastosis are related signatures of sun injury, not the same lesion.

Three histologic compartments to examine

Cornified surface

- Hyperkeratosis may be conspicuous.
- Parakeratosis is commonly present.

Living epidermis

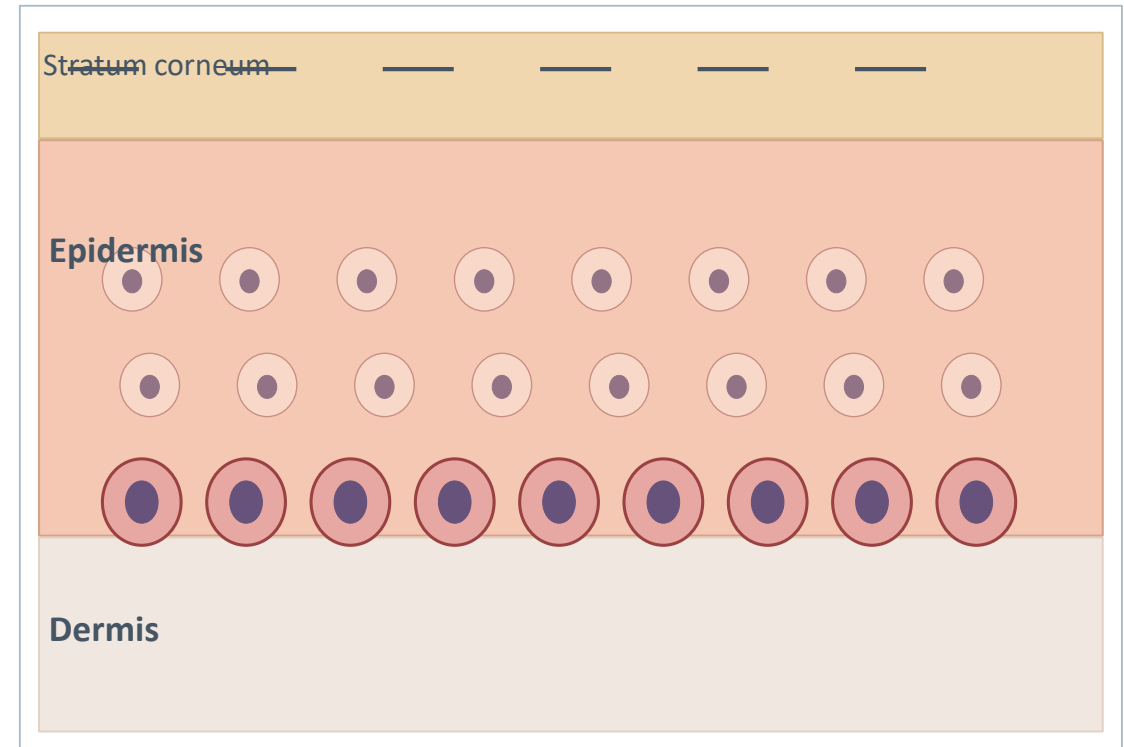
- Basal keratinocytic atypia is central.
- Hyperplasia or atrophy may occur.

Superficial dermis

- Solar elastosis may be visible.
- Elastosis points to chronic photodamage.

Integrating surface scale with lower-layer atypia

- The surface keratin is conspicuously expanded.
- Keratinocyte atypia is concentrated toward the base.
- Dermal solar injury supplies etiologic context.



Schematic · not a histologic section

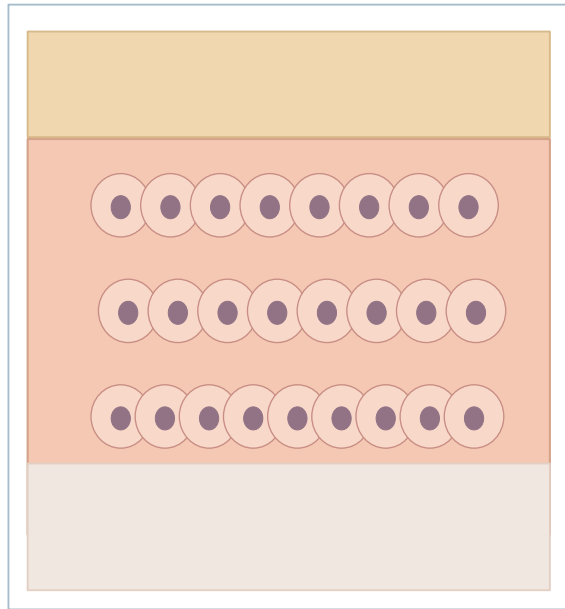
Schematic relationships only: Not a specimen Fig. 25.12.

Morphologic observations and what they establish

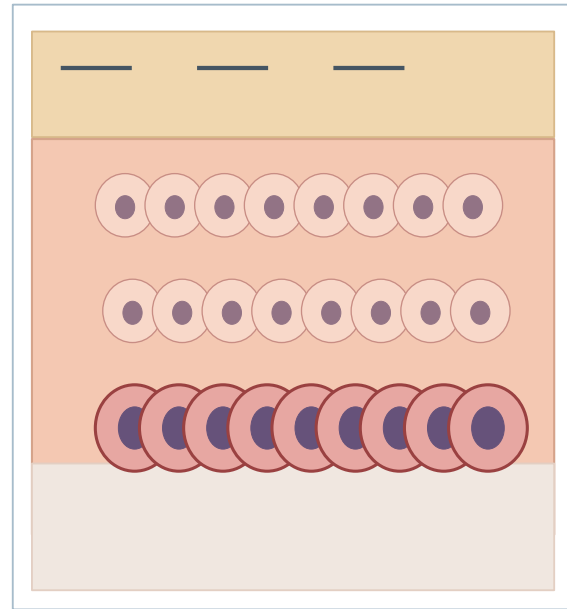
Observation	What it supports	What it does not prove
Rough scale	Surface keratin abnormality	Degree of invasion
Basal atypia	Epidermal dysplasia	Full-thickness in situ disease
Dermal elastosis	Background sun injury	Specific lesion subtype
Cutaneous horn	Marked keratin production	A unique histologic diagnosis

Progression is defined by atypia and invasion

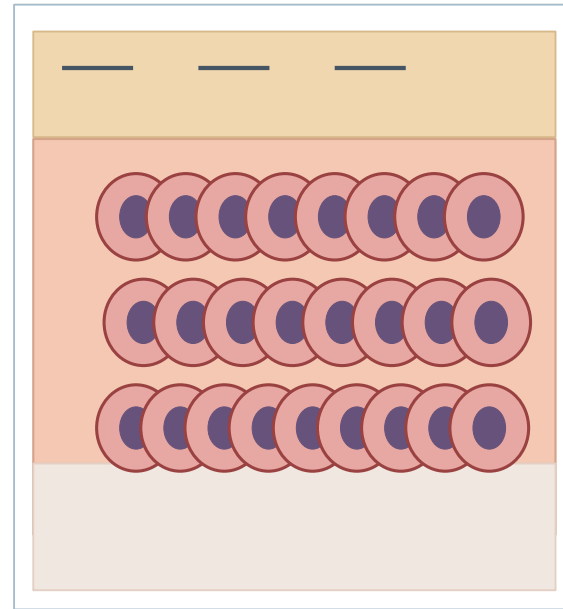
INCREASING EXTENT OF ATYPIA



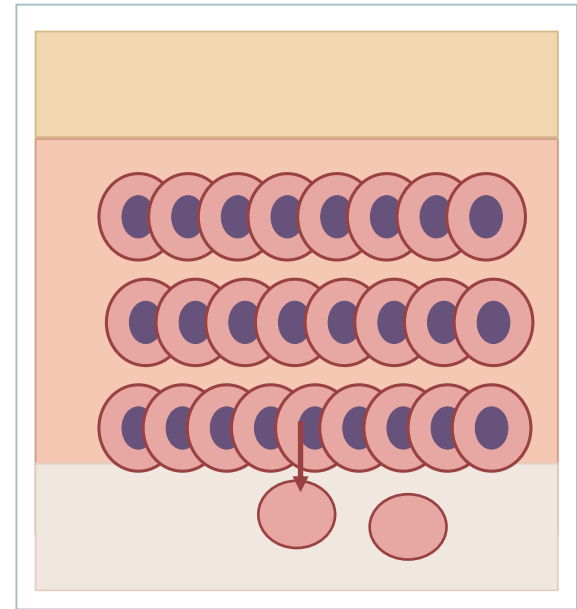
Orderly epidermis



Basal atypia (AK)



Full-thickness atypia

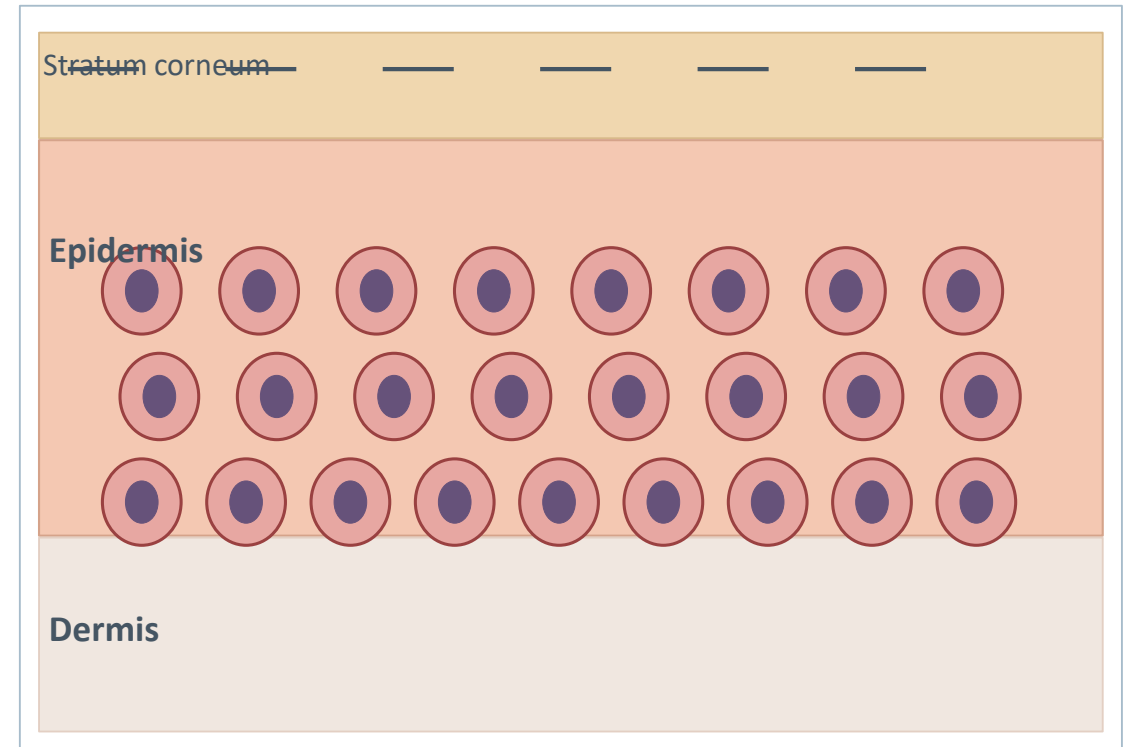


Breach of junction

Schematic illustration · conceptual epithelial compartments, not specimens

Full-thickness atypia indicates SCC in situ

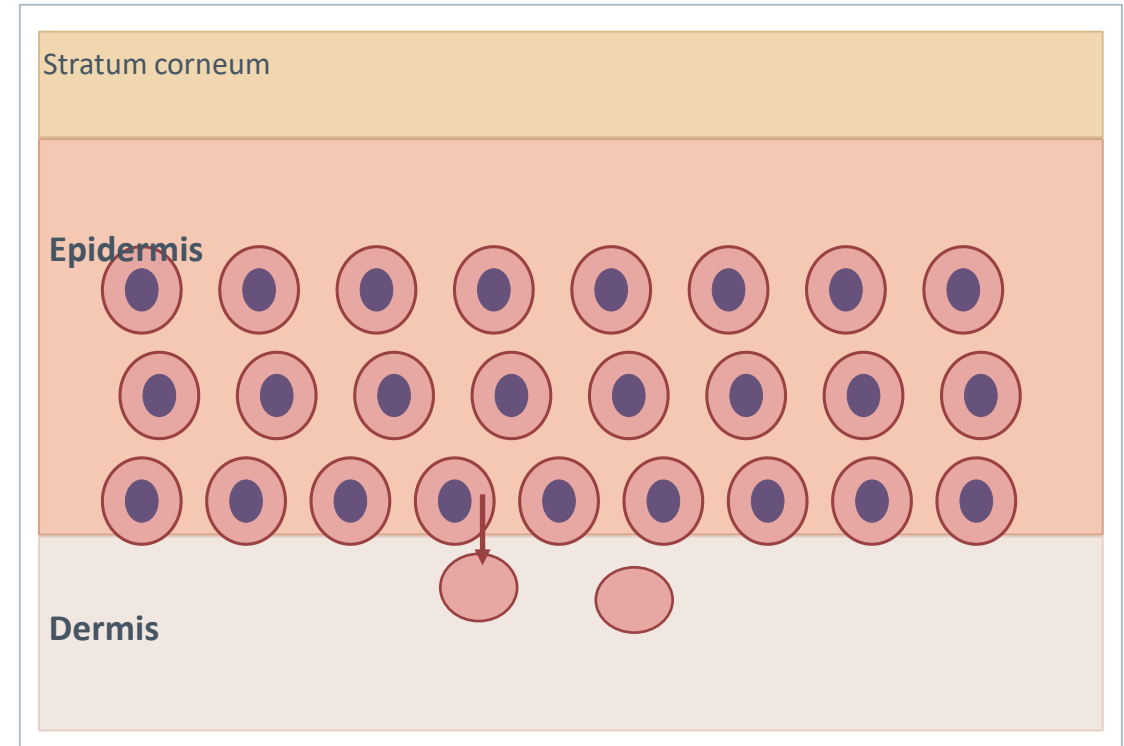
- Atypical enlarged, hyperchromatic nuclei extend through the epidermis.
- The basement membrane has not been breached.
- This is squamous cell carcinoma in situ.



Schematic · not a histologic section

Invasive SCC crosses the basement membrane

- Atypical squamous epithelium extends into dermal tissue.
- Dermal invasion—not merely thick surface scale—establishes invasive disease.
- The basement membrane is the decisive anatomic boundary.



Schematic · not a histologic section

Actinic keratosis versus SCC in situ

Actinic keratosis

- Basal or lower-epidermal atypia predominates.
- Marked hyperkeratosis/parakeratosis possible.
- Upper epidermal differentiation may persist.

Squamous carcinoma in situ

- Atypical nuclei involve all epidermal levels.
- No invasion beyond basement membrane.
- Often presents as a sharply defined red scaling plaque.

Carcinoma in situ versus invasive SCC

Carcinoma in situ

- Atypia extends through epidermal thickness.
- Atypical cells remain above the junction.
- Potential precursor to deeper invasion.

Invasive SCC

- Epithelial nests or tongues enter dermis.
- Nodular growth or ulceration may occur.
- Keratinization varies with differentiation.

From phenotype to mechanism

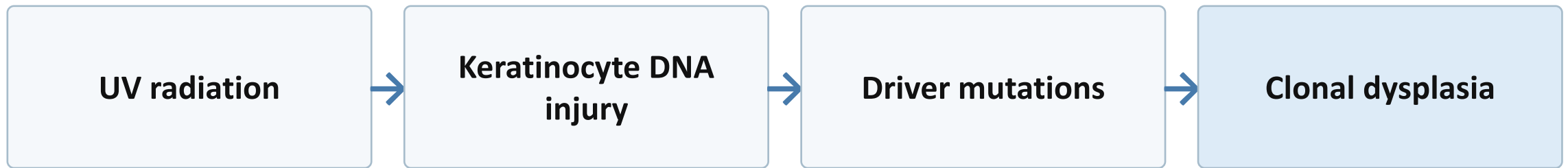
MOLECULAR PATHOGENESIS

Cumulative ultraviolet injury supplies a mutagenic background for keratinocytic neoplasia.

- Specific molecular findings are described in the adjacent SCC section.
- Mechanistic associations must not be treated as a universal deterministic pathway.

UV injury and the precursor–carcinoma pathway

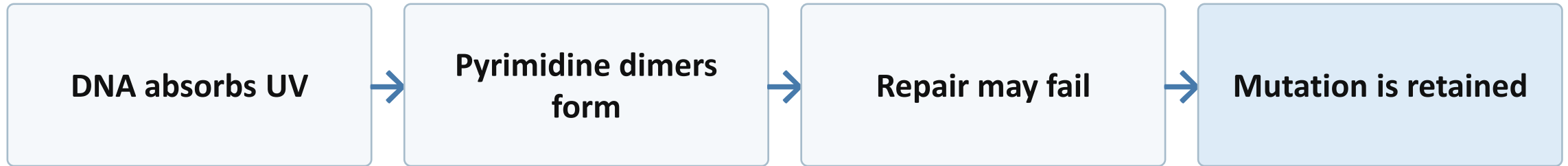
UV-mediated DNA damage as a dominant causal influence.



- The adjacent squamous carcinoma section discusses mutations in precursors, including AK.

The mutagenic signature: Pyrimidine dimers

Ultraviolet injury can create adjacent pyrimidine-base lesions.



- TP53 mutations in these tumors often map to UV-associated pyrimidine dimer sites.

TP53 dysfunction appears early

- TP53 mutations are frequent in AKs in lightly pigmented individuals.
- The pattern supports early p53 pathway dysfunction during UV-driven tumorigenesis.
- A precursor-associated mutation does not imply that invasion has already occurred.

Level of evidence in source

A high frequency is described, but no exact percentage is needed for this teaching point.

P53 pathway: Lesion state versus molecular event

Histologic lesion

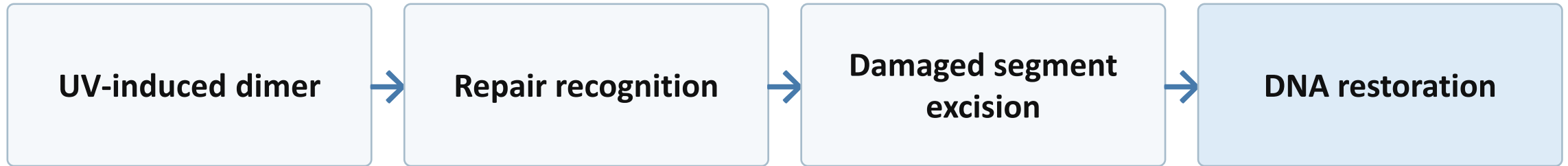
- Basal atypia defines the morphological diagnosis.
- Invasion remains a separately assessed feature.
- Surface keratin and dermal elastosis add context.

Molecular context

- TP53 changes may already be present in AK.
- UV-type sequence damage supplies an etiologic link.
- Molecular alteration is not synonymous with invasive SCC.

DNA repair determines persistence of UV injury

Nucleotide excision repair removes UV-induced pyrimidine lesions.



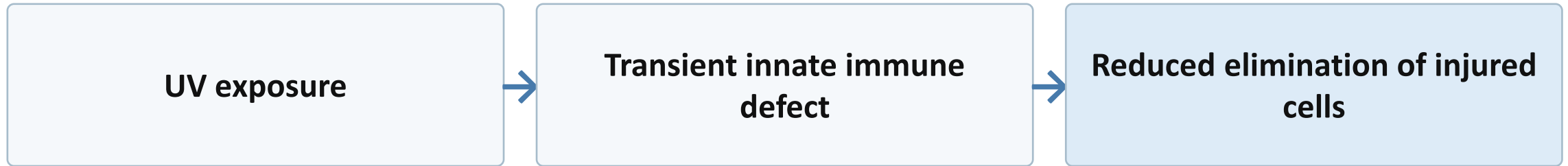
- The scheme is conceptual; Xeroderma pigmentosum to illustrate repair failure.

Xeroderma pigmentosum is a causal illustration

- Inherited defects in nucleotide excision repair impair dimer correction.
- Error-prone handling permits rapid mutation accumulation.
- The syndrome underscores why DNA maintenance limits skin carcinogenesis.

Sunlight also alters local immune defense

A transient effect on cutaneous innate immunity.



- The precise mechanism is described as uncertain.
- Do not portray this as a fully mapped pathway.

Three distinct influences on keratinocyte evolution

Damage input

- UV radiation introduces DNA lesions.
- Other physical or chemical insults may contribute.

Genome maintenance

- Repair competency modifies mutation persistence.
- TP53 dysfunction may emerge early.

Host response

- Immune surveillance can help remove damaged cells.
- UV-associated impairment is mechanistically uncertain.

Later SCC drivers are not AK diagnostic criteria

- RAS pathway activation and reduced Notch signaling are described in cutaneous SCC.
- These are mechanisms contributing to multistep malignant transformation.
- Robbins does not define an AK diagnosis by routine RAS/NOTCH testing.

Natural history has several possible paths

Regression

- Some lesions diminish spontaneously.
- Current lesion behavior is not fixed.

Persistence

- Some lesions remain stable for years.
- Stability does not eliminate precursor significance.

Progression

- Some evolve toward squamous carcinoma.
- Potential for malignancy motivates treatment.

Natural history must not be oversimplified

RISK INTERPRETATION

A lesion may regress or persist, yet the group has meaningful malignant potential.

- The source supports eradication, not a numerical patient-specific prediction.
- A deterministic “every AK becomes SCC” claim is incorrect.

What can—and cannot—be concluded from AK

Finding	Supported inference	Not supported
Sun-exposed site	Etiologic plausibility	Specific mutation status
Basal epidermal atypia	Precancerous morphology	Already invasive SCC
Persistent lesion	One possible disease course	Guaranteed future carcinoma
Hyperkeratotic horn	Marked surface keratin	Invasion by appearance alone

Actinic keratosis and basal cell carcinoma differ

Actinic keratosis

- Atypical squamous cells near epidermal base.
- Intercellular bridges may be apparent.
- May progress toward squamous carcinoma.

Basal cell carcinoma

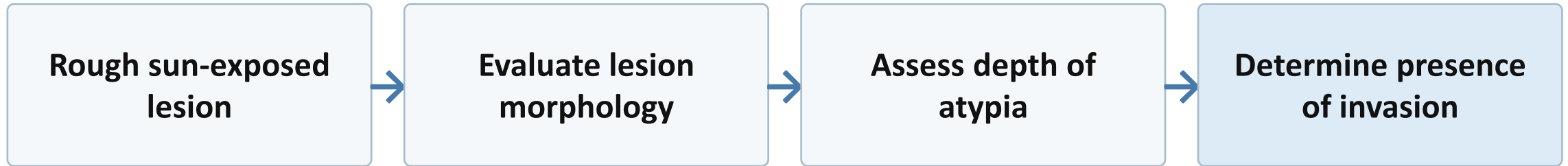
- Separate neoplasm associated with Hedgehog activation.
- Intercellular bridges are not visible.
- Not the endpoint of an AK-to-SCC sequence.

A focused differential based on architecture

Entity	Epidermal atypia	Defining boundary
Actinic keratosis	Mainly basal/lower layers	No invasive growth established
SCC in situ	Full epidermal thickness	Basement membrane intact
Invasive SCC	Variable epithelial differentiation	Dermal invasion present
Basal cell carcinoma	Basaloid tumor; Distinct phenotype	Separate Hedgehog-linked entity

Diagnostic reasoning: Clinical to microscopic

Start with clinical morphology; Establish the tissue-level distinction.



- The source describes distinguishing morphology but does not issue a modern biopsy triage guideline.

Why treatment is justified despite possible regression

- The course of an individual lesion cannot be predicted from appearance alone.
- Enough lesions transform to warrant local eradication.
- Intervention addresses a lesion with established malignant potential.

Core principle

A preventive rationale does not mean every individual actinic keratosis is destined to become cancer.

Local eradication methods

Gentle curettage

- Mechanical removal of the local lesion.
- A lesion-directed procedural approach.

Freezing

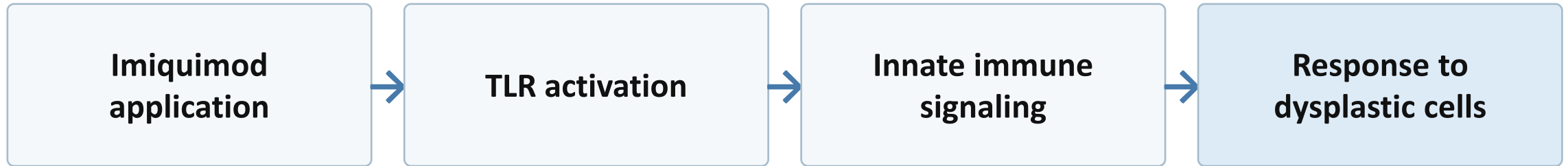
- Local destruction through cryotherapy.
- A lesion-directed physical approach.

Topical agents

- Drug-based treatment of affected epithelium.
- The text mentions topical chemotherapeutic agents.

Imiquimod illustrates immunologic therapy

A topical approach may recruit host innate immune recognition.



- Efficacy presumably to stimulation of host immunity; Causal wording remains qualified.

Direct destruction and immune activation

Physical / cytotoxic strategies

- Curettage removes altered epithelium.
- Freezing locally destroys affected tissue.
- Topical chemotherapy targets lesional cells.

Immune-oriented strategy

- Imiquimod activates Toll-like receptors.
- Innate immune response is engaged.
- Immune activity may contribute to clearance.

Interpreting the imiquimod efficacy statement

- Eradication of up to half of lesions in the described context.
- That statement is not a universal clearance rate for all regimens or populations.
- The excerpt supplies no comparator arm or modern treatment ranking.

Evidence calibration

Avoid turning a textbook teaching figure into a personalized treatment probability.

Applied case: Subtle facial plaque

Hypothetical teaching vignette

A lightly pigmented adult has a small facial lesion that is difficult to see but feels coarse and rough.

Which clinical observation most strongly supports actinic keratosis?

A. Rough sandpaper-like surface

B. A painless lesion

C. Uniform color

Case interpretation: The surface is informative

- The source specifically emphasizes sandpaper-like consistency.
- Typical sun-exposed distribution increases etiologic plausibility.
- Appearance supports a working diagnosis; Cellular dysplasia remains microscopic.

Applied case: Markedly keratinized projection

Hypothetical teaching vignette

A small sun-exposed plaque produces a tall compact projection of surface keratin.

What is the most precise descriptive term?

A. Cutaneous horn

B. Invasive SCC confirmed clinically

C. Basal cell carcinoma

Case interpretation: Horn does not equal carcinoma

- A cutaneous horn may arise from excessive keratin in actinic keratosis.
- Keratin accumulation is distinct from tumor-cell invasion.
- The underlying epithelial architecture establishes the lesion category.

Applied case: Basal keratinocyte atypia

Hypothetical teaching vignette

A conceptual epidermal section shows dysplastic cells mainly in lower epidermal layers, with parakeratosis and solar elastosis.

Which diagnosis best matches this pattern?

A. Actinic keratosis

B. SCC in situ

C. Invasive SCC

Case interpretation: Lower-layer dysplasia

- Basal-predominant atypia is the characteristic AK distribution.
- Parakeratosis and elastosis reinforce the morphologic context.
- Full-thickness atypia or basement-membrane breach would alter the classification.

Applied case: Full-thickness epidermal atypia

Hypothetical teaching vignette

A conceptual section shows atypical nuclei in the entire epidermis, with no cells extending into dermis.

Which tissue-level conclusion follows?

A. Squamous cell carcinoma in situ

B. Actinic keratosis limited to basal cells

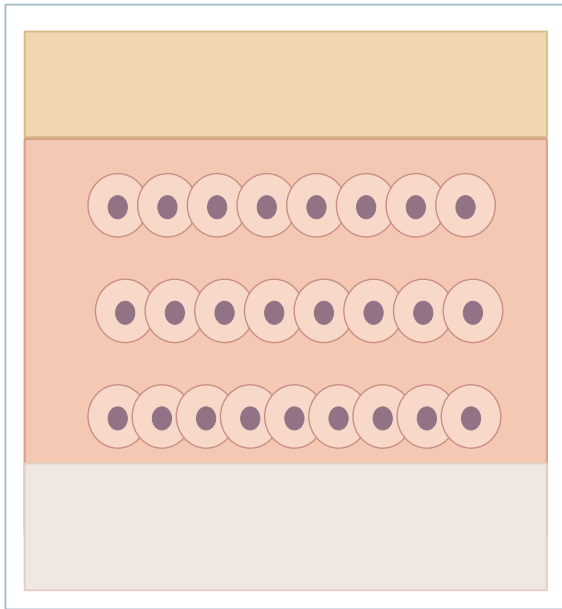
C. Invasive squamous carcinoma

Case interpretation: In situ is not invasive

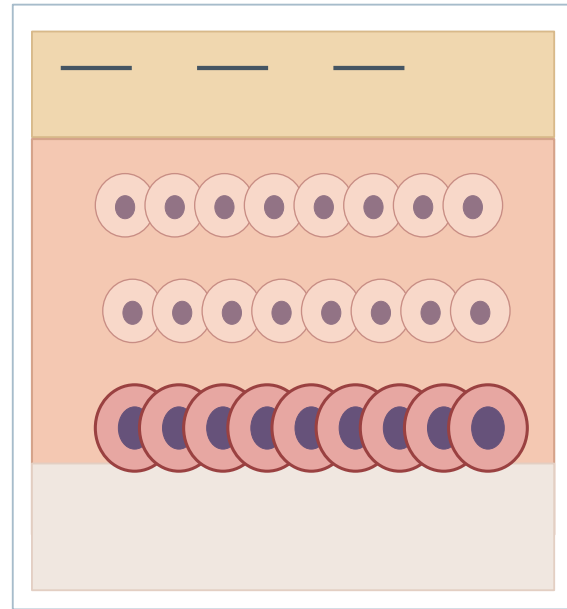
- The distinguishing change is full-epidermal-thickness atypia.
- Carcinoma remains in situ while the basement membrane is intact.
- Invasive growth requires atypical tumor epithelium in underlying dermis.

A final morphology-based classification exercise

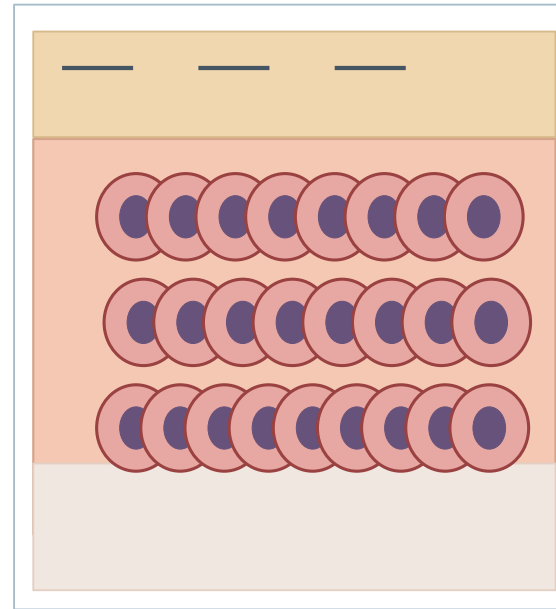
READ FROM LEFT TO RIGHT, THEN NAME THE TISSUE BOUNDARY



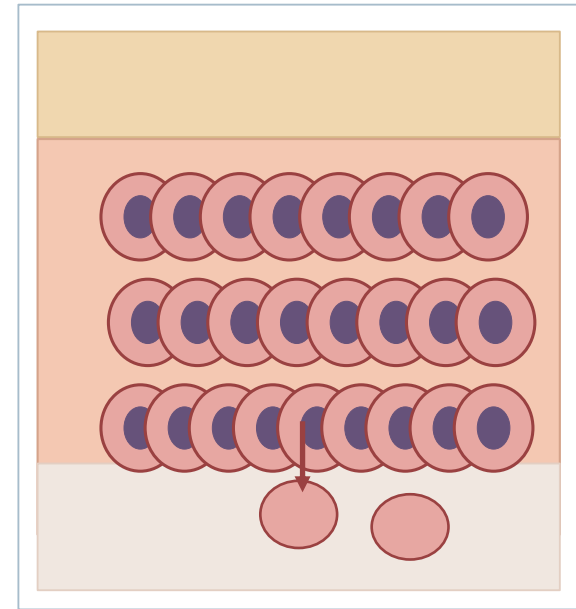
Normal



Basal dysplasia



Carcinoma in situ



Invasive SCC

Schematic illustration · conceptual epithelial compartments, not specimens

Three evidence layers in a good pathology diagnosis

Clinical morphology

- Rough scale, size, color, distribution.
- Cutaneous horn and lip involvement are variants.

Histologic morphology

- Basal atypia, hyperkeratosis, parakeratosis.
- Dyskeratosis and dermal elastosis may support.

Biologic context

- UV-linked mutations, including TP53.
- Uncertain progression and potential SCC evolution.

Consolidation: Five high-yield propositions

- AK is a sun-associated dysplastic keratinocytic lesion.
- The surface is often rough and hyperkeratotic.
- Atypia is concentrated in the lower epidermis.
- Full-thickness atypia means SCC in situ; Dermal invasion means invasive SCC.
- Lesion eradication is justified by nonzero malignant potential.

References and source scope

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026).
- Chapter 25, The Skin: Actinic Keratosis, pp. 1039–1040.
- Adjacent context: Squamous Cell Carcinoma, pp. 1040–1041.
- The lecture diagrams are original editable conceptual schematics—not histologic specimens.