

Verrucae (Warts)

Human papillomavirus–associated epithelial proliferations

Etiology • Clinicopathologic variants • Histomorphology • Oncogenic context

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Learning objectives

Classify verrucae by their appearance and anatomic location.

Connect HPV effects on keratinocytes with verrucous architecture and koilocytosis.

Recognize common wart morphology and distinguish low- from high-risk HPV disease.

Interpret selected clinicopathologic vignettes without equating every wart with dysplasia.

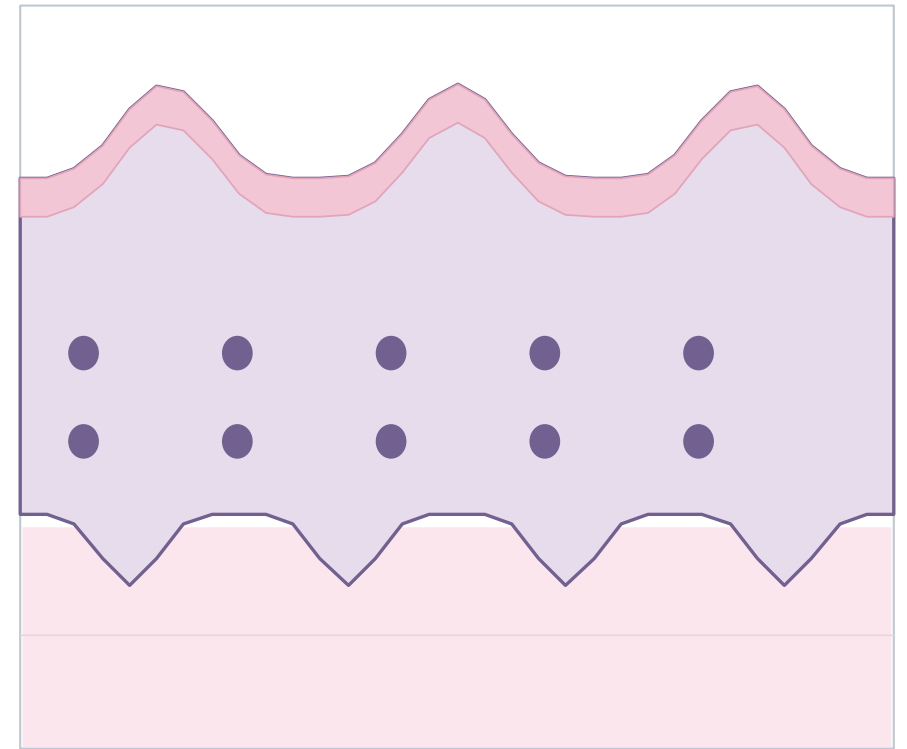
Verrucae are HPV-driven epithelial proliferations

Warts are proliferative lesions caused by human papillomaviruses (HPVs).

The epithelial growth pattern, rather than invasive destruction, characterizes ordinary verrucae.

Clinical naming reflects morphology and distribution.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Warts are frequent in the young but not age-restricted

Children and adolescents as commonly affected groups.

Verrucae may occur at any age.

Age and site help the differential diagnosis but do not establish HPV type.

Children / adolescents; Any age

Children

Adolescents

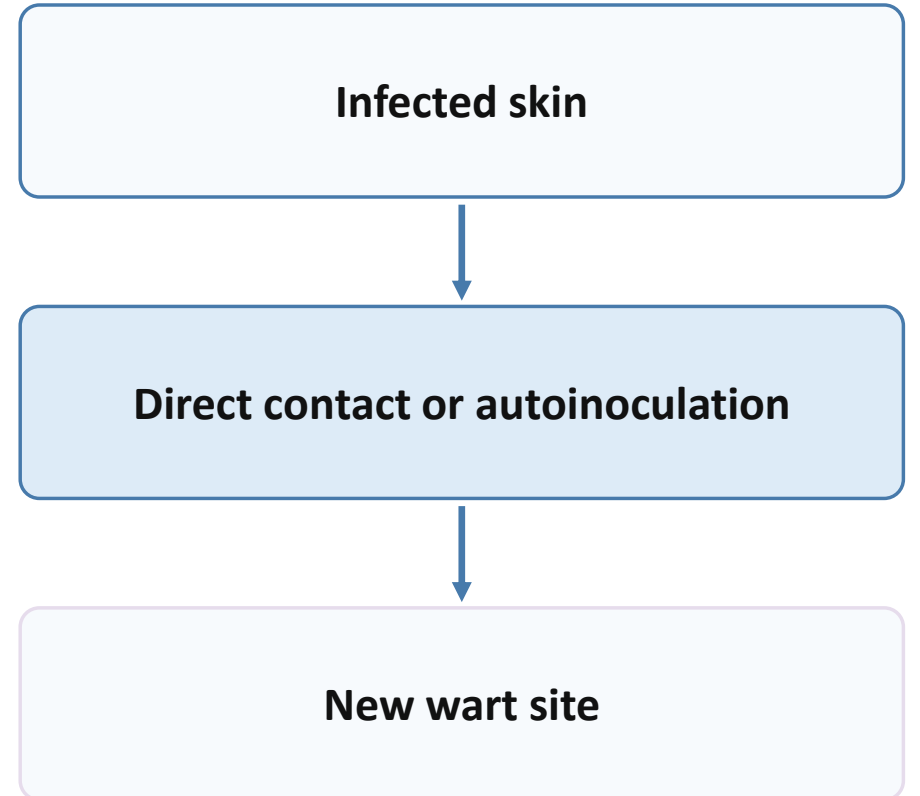
Adults

Transmission: Contact and autoinoculation

Transmission usually involves direct person-to-person contact.

Autoinoculation transfers infection to another location on the same individual.

Multiple lesions do not automatically imply multiple HPV genotypes.

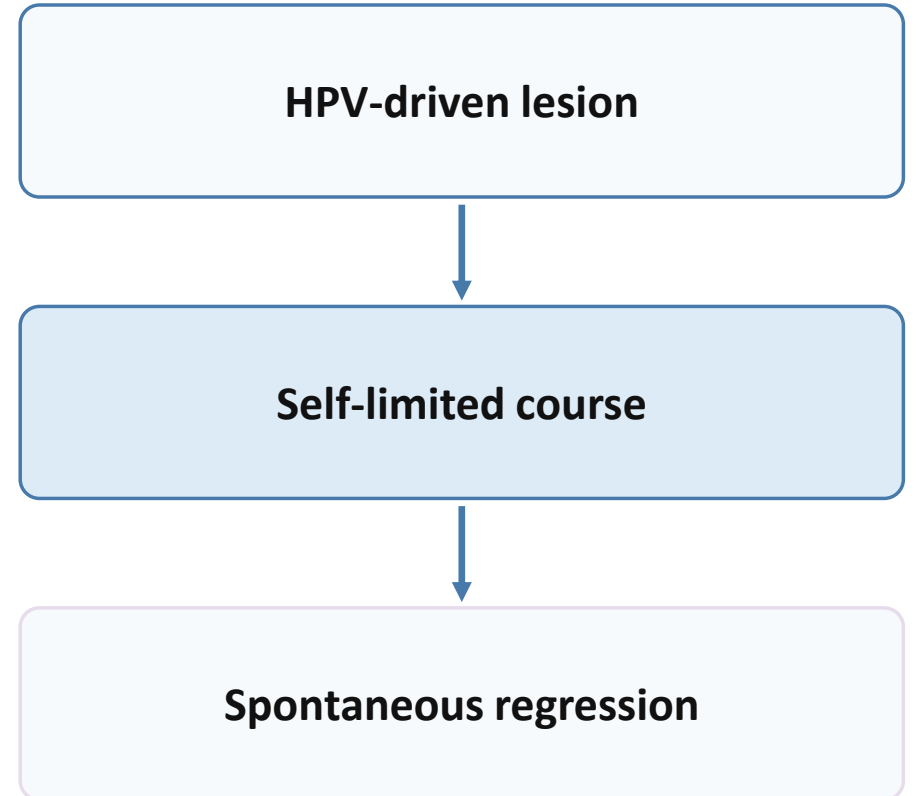


Natural history: Spontaneous regression

Verrucae are generally self-limited.

Spontaneous regression within approximately 6 months to 2 years.

Persistence at an individual site does not by itself prove malignant change.



HPV comprises multiple biologically distinct types

More than 150 HPV types are described in this dermatopathology section.

Many of these types can produce human warts.

Certain wart variants show associations with particular HPV types.

Genotype diversity

Clinical phenotype

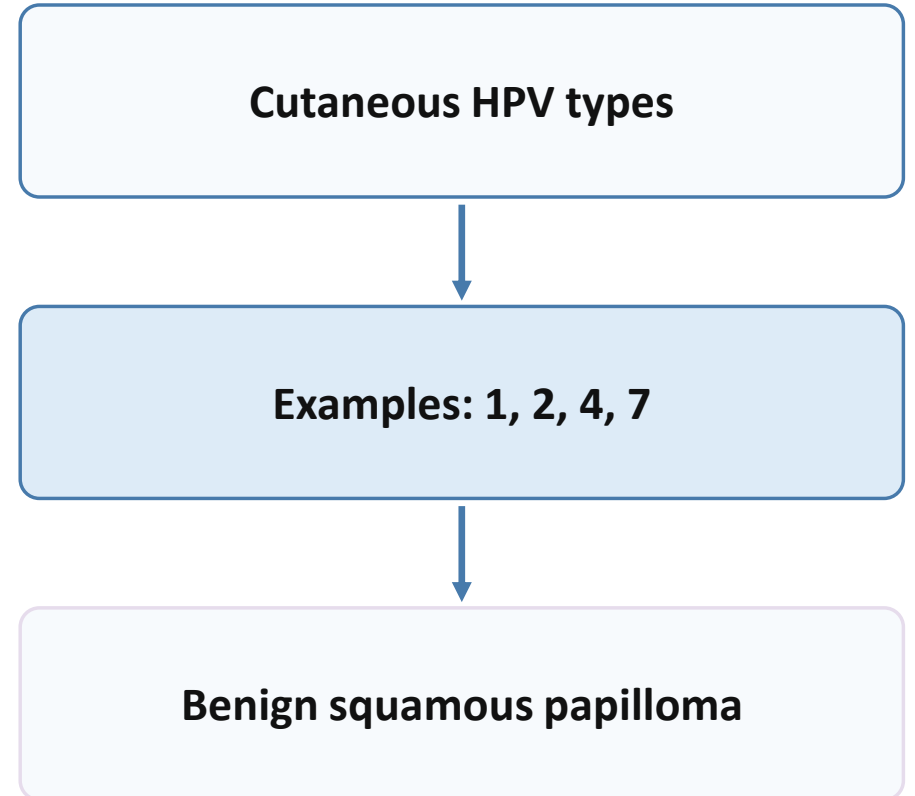
Oncogenic context

Benign cutaneous wart–associated HPV types

The neoplasia chapter gives HPV 1, 2, 4, and 7 as examples associated with benign squamous papillomas.

This is an illustrative group, not an exhaustive taxonomy of cutaneous HPV.

The clinical label “wart” does not specify a single viral genotype.



Anogenital condylomata: Predominantly HPV 6 and 11

Condyloma acuminatum is a common anogenital wart phenotype.

HPV types 6 and 11 are the predominant associated types.

The neoplasia chapter identifies these as low-malignant-potential HPV types.

HPV 6 → Low-risk

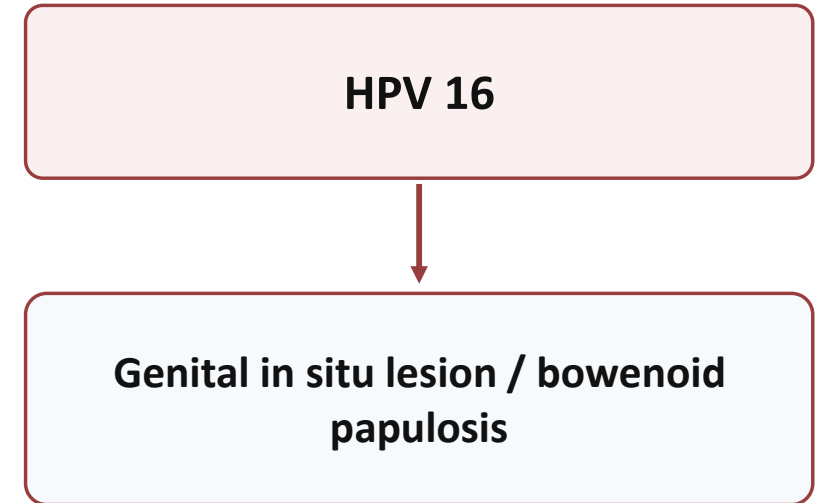
HPV 11 → Low-risk

HPV 16 is associated with genital precursor lesions

HPV 16 with genital squamous carcinoma in situ.

It also associates HPV 16 with bowenoid papulosis.

Bowenoid papulosis has an in situ carcinoma–like histology yet often regresses.

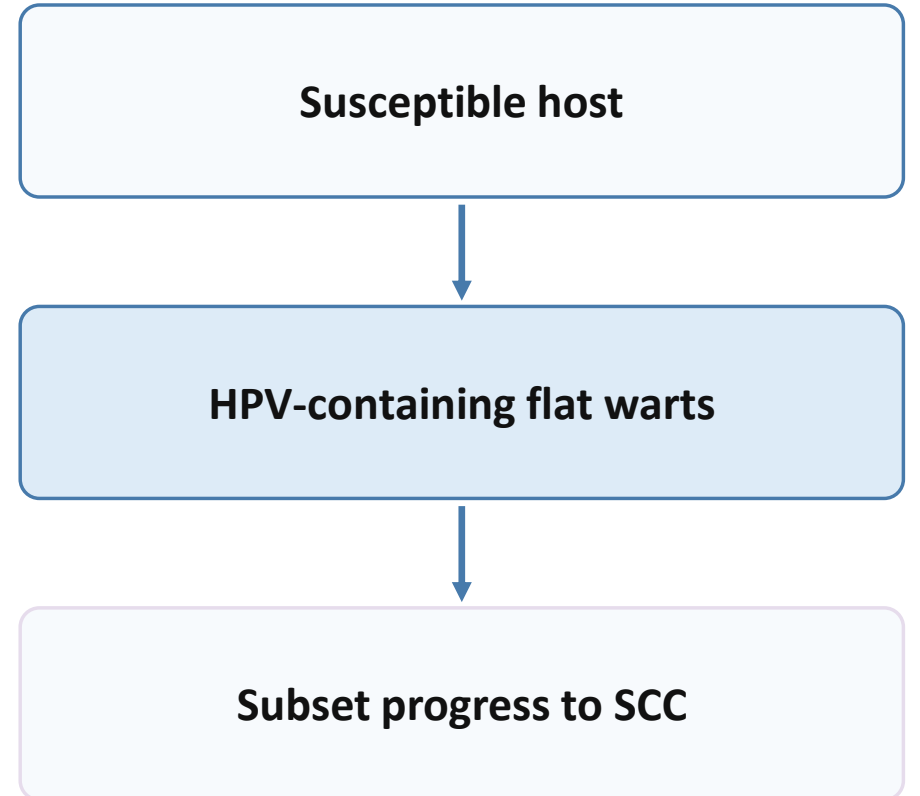


HPV 5 and 8: The epidermodysplasia context

HPV 5 and 8 are discussed in relation to epidermodysplasia verruciformis.

In affected individuals, some HPV-containing flat warts progress to cutaneous carcinoma.

This is a syndrome-specific association, not the expected outcome of ordinary warts.



Three HPV-associated phenotypes require separation

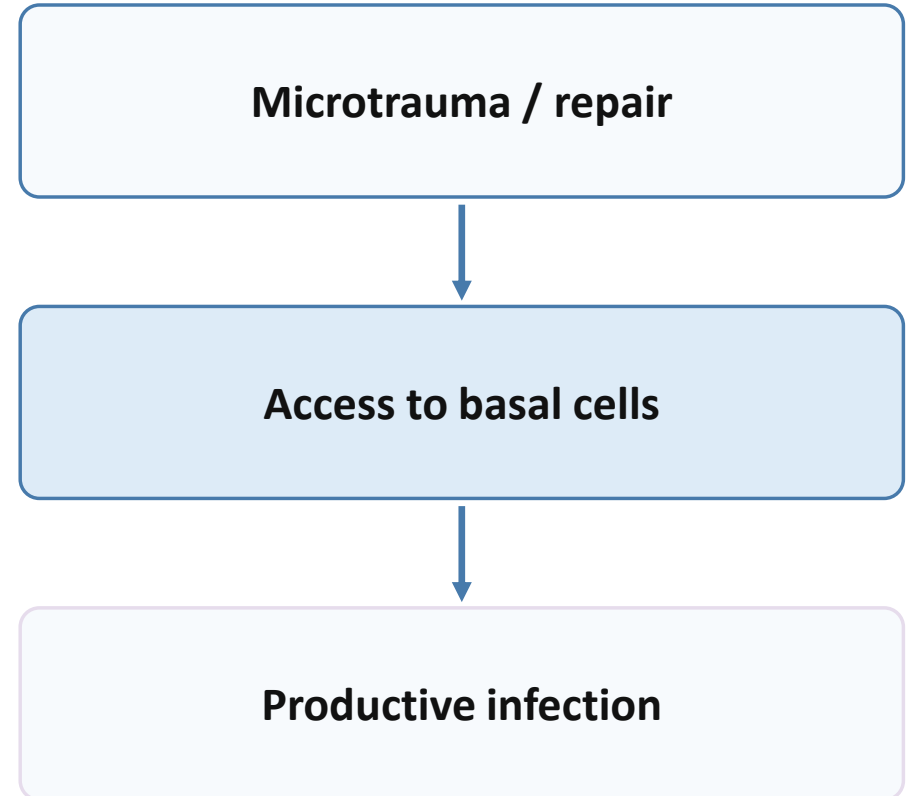
Clinical category	HPV context	Pathologic emphasis
Cutaneous verrucae	Benign cutaneous HPV types	Papillomatosis + koilocytosis
Condyloma acuminatum	Predominantly HPV 6 / 11	Soft papillary proliferation
Genital in situ lesions	HPV 16 association	High-grade atypia may be present

HPV infection requires access to susceptible epithelium

Genital HPV persistence requires entry into immature basal epithelial cells.

Microtrauma and epithelial repair can provide access to susceptible basal cells.

This mechanism provides context; Anatomy and exposures differ between sites.



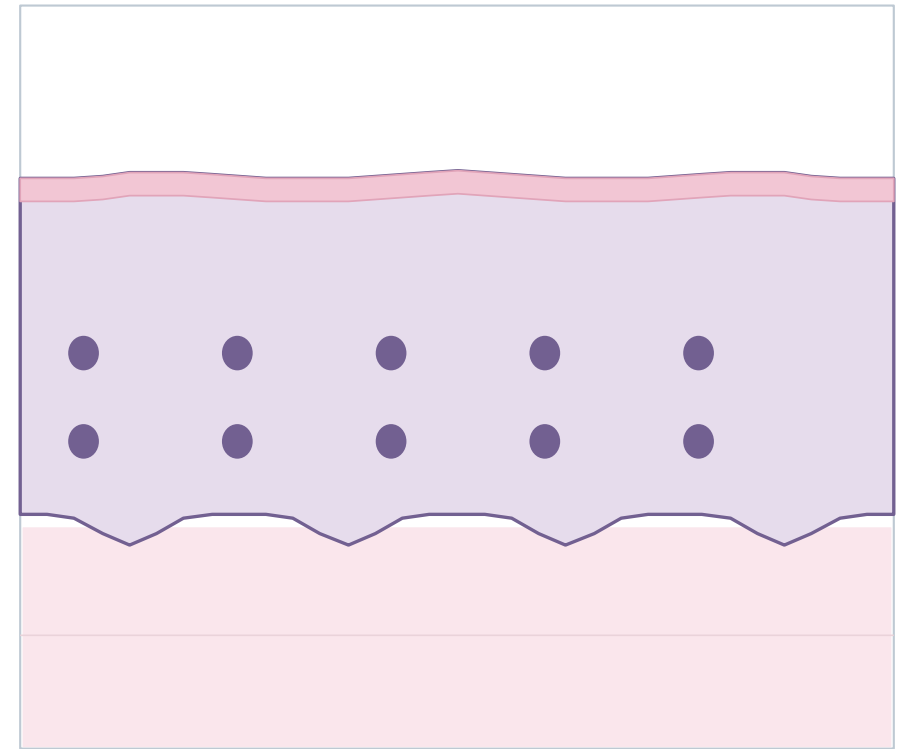
Replication is linked to keratinocyte maturation

HPV infects immature squamous cells, but viral replication takes place in maturing squamous cells.

Infected differentiating cells retain cell-cycle activity.

This coupling explains why superficial epithelial cells may show viral changes.

Schematic — not a micrograph



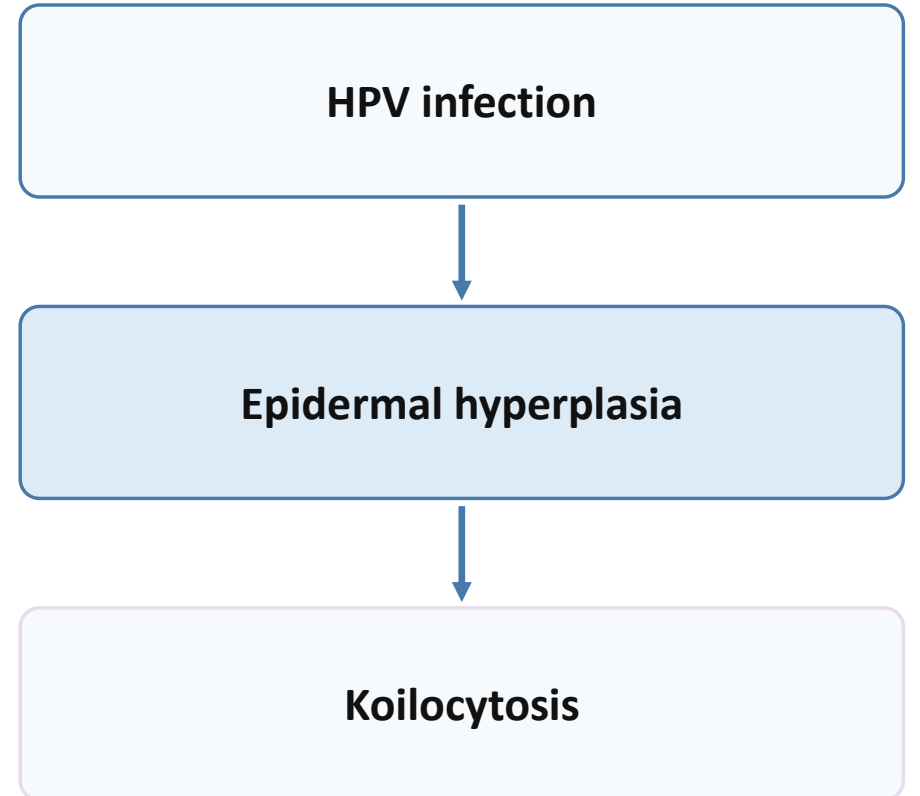
Continuous epidermal proliferation over dermis

Productive infection modifies epithelial maturation

Infected epithelium may develop conspicuous superficial cytopathic change.

The epidermis simultaneously shows hyperplastic architecture.

Low-power architecture and high-power cytopathy therefore answer different diagnostic questions.

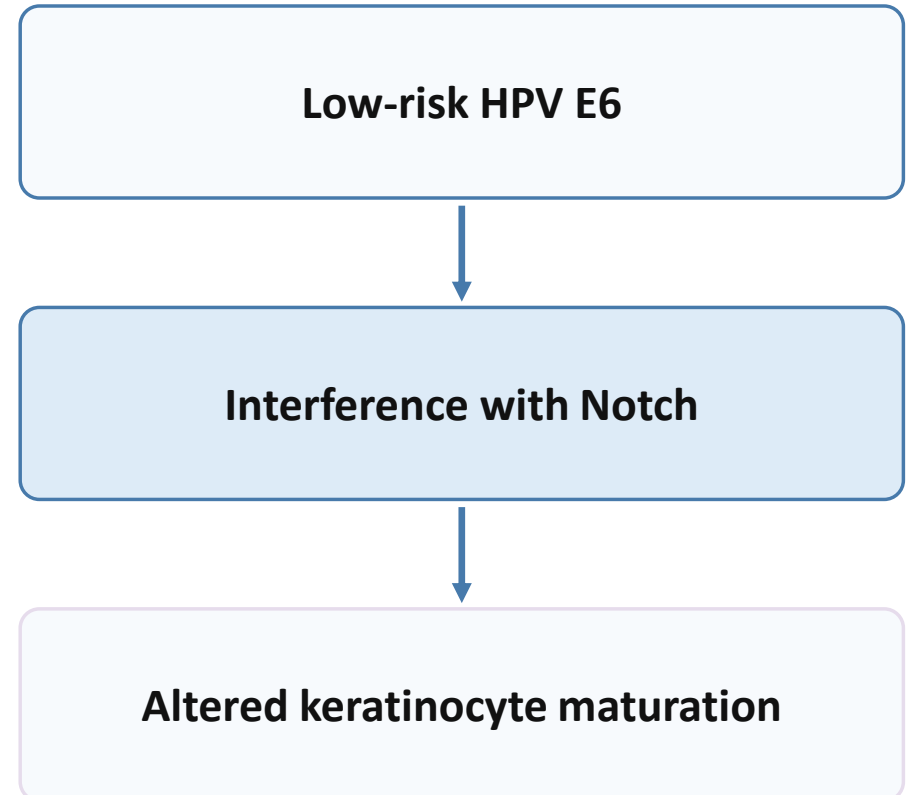


Low-risk E6 affects Notch-mediated differentiation

The skin chapter describes interference with Notch signaling by low-risk HPV E6.

Notch signaling contributes to normal keratinocyte maturation.

Altered maturation is proposed to contribute to wart-associated epidermal hyperplasia.



Low-risk versus high-risk HPV is a mechanistic distinction

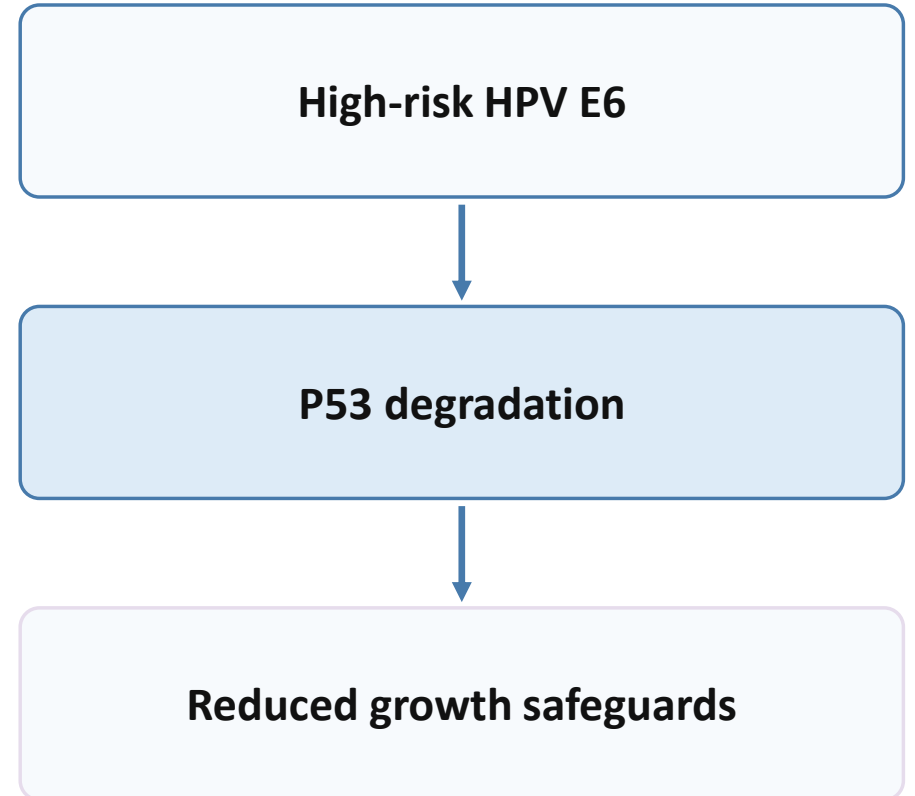
Feature	Low-risk HPV context	High-risk HPV context
Illustrative types	6, 11	16, 18
Prominent disease	Condyloma / benign papilloma	Intraepithelial neoplasia / carcinoma
E6 behavior	Notch interference	p53 degradation
E7 behavior	Lower-affinity RB interaction	Strong RB disruption

High-risk E6 antagonizes p53

High-risk HPV E6 promotes p53 degradation.

Reduced p53 function weakens the DNA damage and apoptosis response.

The oncogenic mechanism belongs to the high-risk HPV context—not to all cutaneous warts.

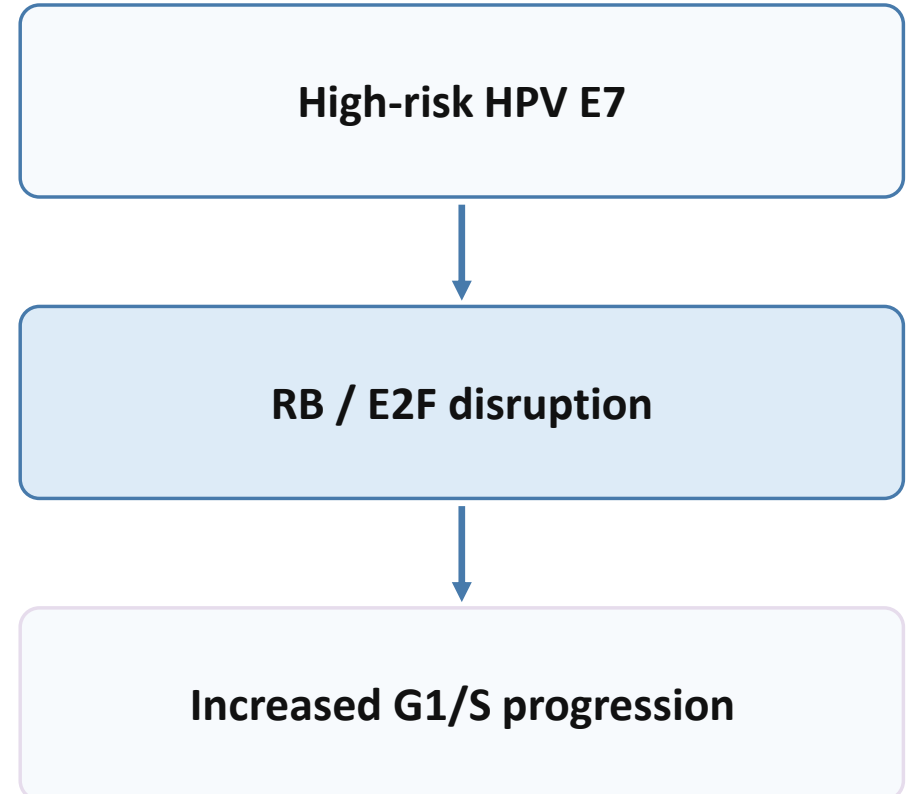


High-risk E7 disrupts RB–E2F control

High-risk HPV E7 binds RB and releases E2F transcription factors.

It also inhibits p21 and p27, favoring G1/S progression.

E7 effects complement E6-mediated loss of p53 signaling.



Viral genome status differs between benign and malignant settings

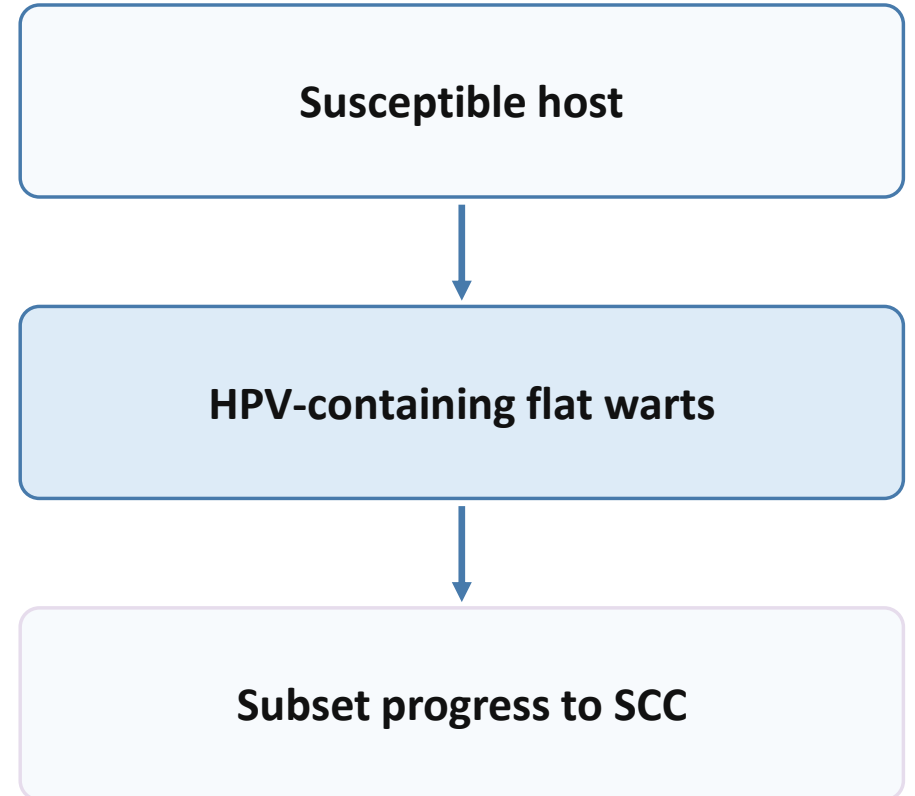
Feature	Benign wart	HPV-associated cancer
Common viral DNA state	Episomal	Often integrated
E6 / E7 oncogenic drive	Less pronounced	Frequently increased
Clinical inference	Viral presence $\neq$ malignancy	Other changes contribute to cancer

Epidermodysplasia verruciformis: A host susceptibility state

This as a rare autosomal recessive disorder.

Patients develop multiple flat warts containing HPV genomes.

Some lesions progress to carcinoma, establishing a special host–virus interaction.

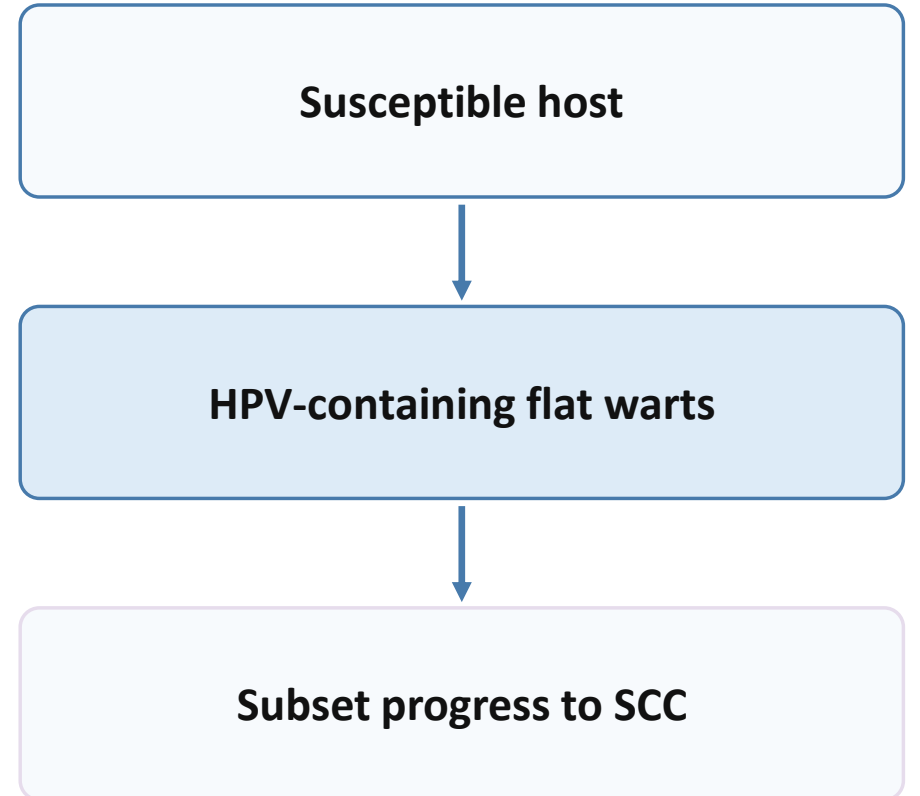


HPV 5/8 and cutaneous SCC require context

The chapter links HPV 5/8 to SCC especially in epidermodysplasia verruciformis.

Its discussion does not justify diagnosing SCC in an ordinary wart.

Host background, lesion architecture, and cytologic atypia remain distinct questions.



Classification is clinical: Shape plus location

Variant	Typical location	Clinical surface
V. vulgaris	Dorsal / periungual hands	Rough, pebblelike
V. plana	Face, dorsal hands	Smooth, flat
V. palmaris / plantaris	Palm / sole	Rough, scaly
Condyloma acuminatum	Anogenital sites	Soft, cauliflower-like

Verruca vulgaris favors dorsal and periungual hands

Verruca vulgaris is the commonest wart variant.

Lesions can occur anywhere but are especially frequent on hands.

Dorsal surfaces and periungual regions are emphasized.

Dorsal hand | periungual sites

Location

Dorsal hand | periungual sites

Morphology

Variant defined by clinical pattern

Correlation

Match location with architecture

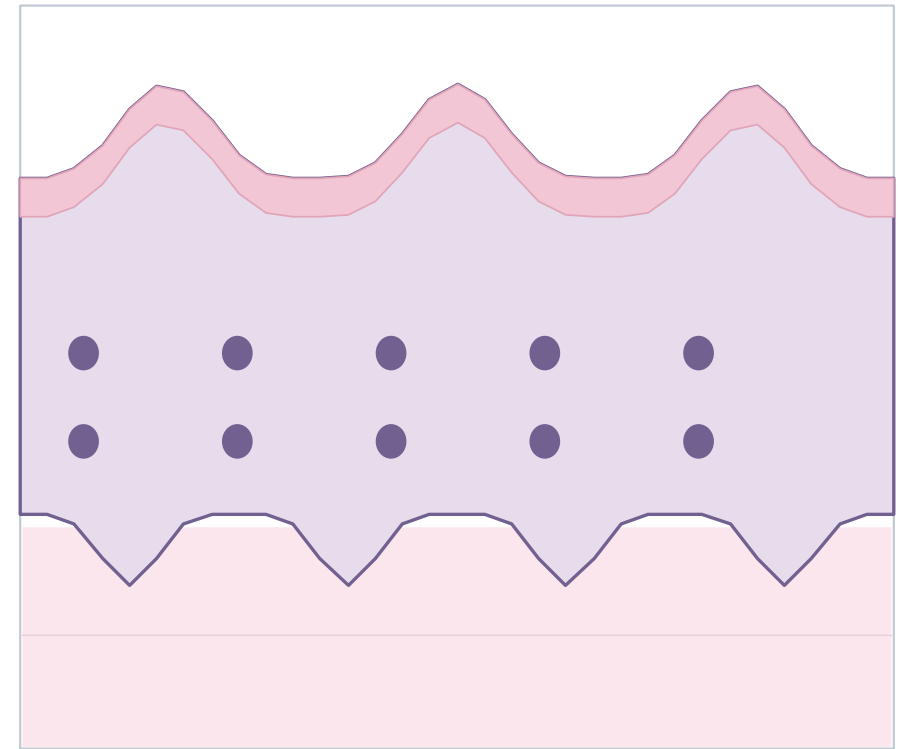
Verruca vulgaris: Gross appearance

Typically flat-to-convex papules with a rough, pebblelike surface.

On lighter skin, typical described color is gray-white to tan.

Individual papules of approximately 0.1–1 cm.

Schematic — not a micrograph



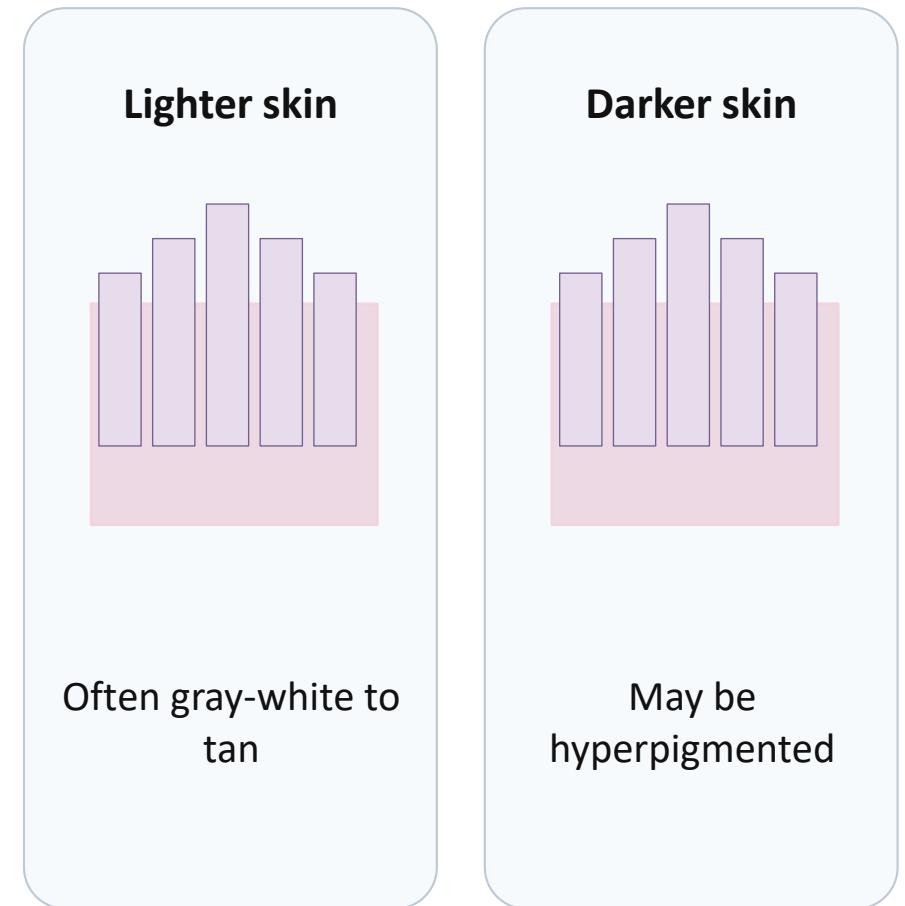
Continuous epidermal proliferation over dermis

Pigmentation modifies visual recognition

On more deeply pigmented skin, verrucae may appear hyperpigmented.

Texture, shape, and distribution remain useful when hue changes.

Avoid treating a single photographic color appearance as universal.



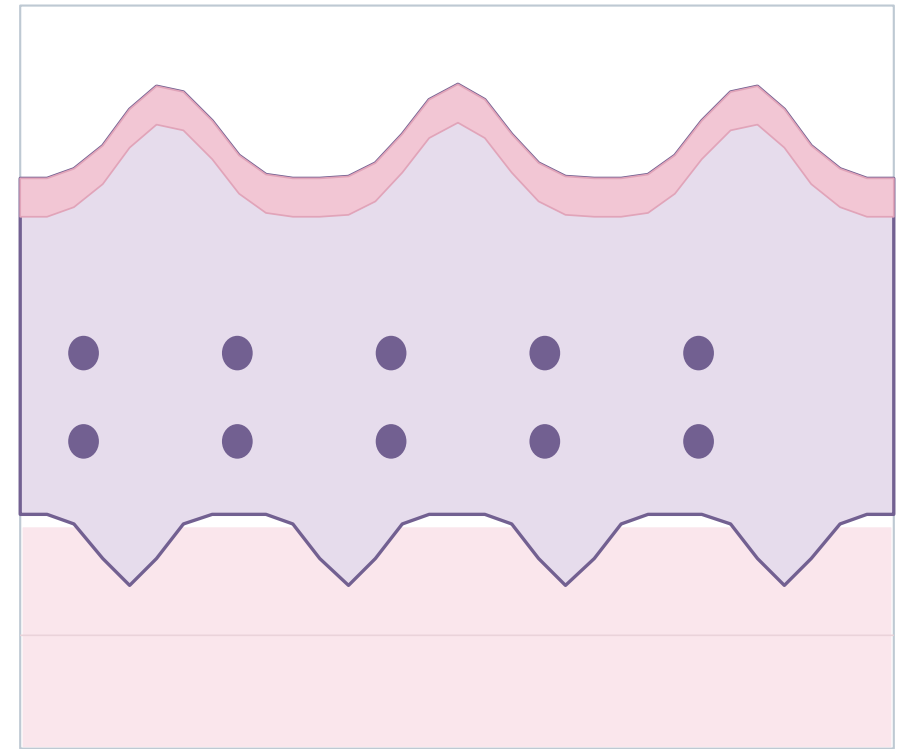
The rough surface reflects a papillomatous process

A verrucous papule is not simply an elevated patch of normal epidermis.

Its uneven contour corresponds to proliferative epithelial architecture.

Microscopy reveals the epithelial pattern responsible for the gross texture.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

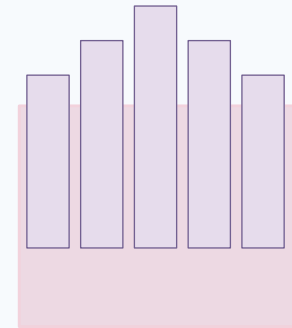
Verruca plana: A low-profile wart

Verruca plana is slightly elevated and typically flat topped.

Its surface is smooth rather than markedly pebblelike.

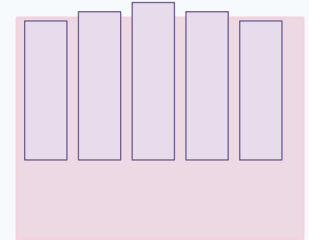
Lesions are generally smaller than verruca vulgaris.

Common wart



Raised rough
surface; Often
convex

Flat wart



Smooth, flat-
topped, slightly
elevated

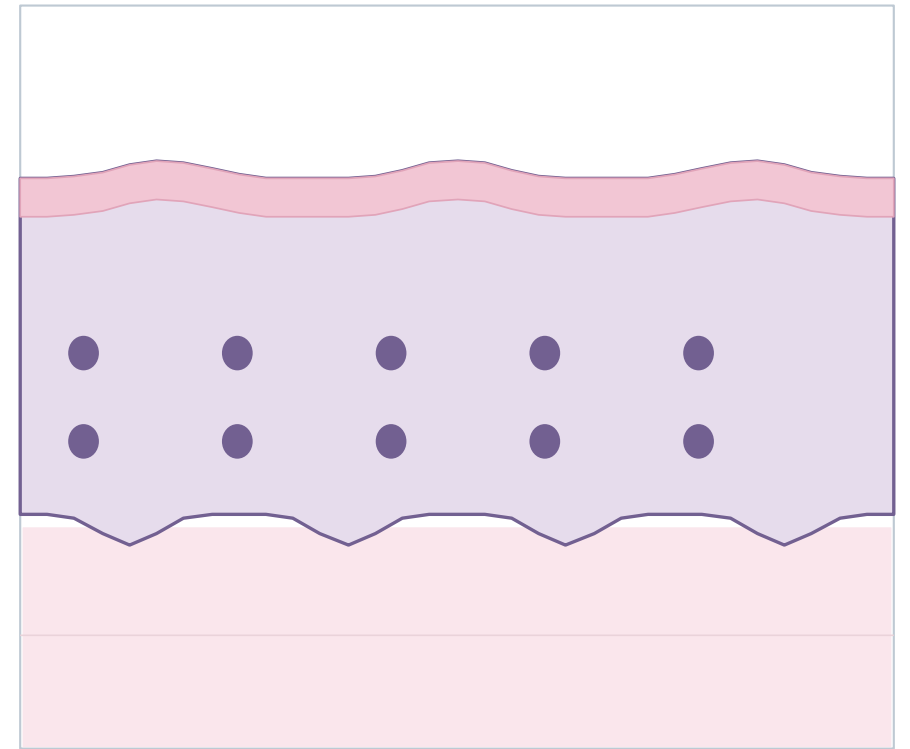
Flat warts: Typical distribution

The face is a classic site.

The dorsal hands are another frequent site.

A smooth low papule at these sites can be more compatible with verruca plana than a rough common wart.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Verruca vulgaris versus verruca plana

Feature	V. vulgaris	V. plana
Profile	Flat to convex	Slightly raised, flat-topped
Surface	Rough / pebbled	Smooth
Distribution	Hands, periungual	Face / dorsal hands
Relative size	Usually 0.1–1 cm	Generally smaller

Plantar verrucae: Warts of the sole

“Plantaris” identifies the sole as the anatomic location.

Rough, scaly lesions.

Palmoplantar verrucae may reach about 1–2 cm.

Plantar surface

Location

Plantar surface

Morphology

Variant defined by clinical pattern

Correlation

Match location with architecture

Palmar verrucae: Warts of the palm

“Palmaris” identifies the palm.

Surface roughness and scale overlap with plantar lesions.

Location is therefore essential to the naming convention.

Palmar surface

Location

Palmar surface

Morphology

Variant defined by clinical pattern

Correlation

Match location with architecture

Palmoplantar wart versus callus

Feature	Palmoplantar verruca	Callus
Appearance	Rough, scaly	Keratinized mimic
Location	Palm / sole	Weight or friction–related sites can overlap
Diagnostic concern	HPV-associated epithelial lesion	Can look similar clinically
Tissue correlation	Papillomatosis + koilocytosis	HPV cytopathic pattern not expected

Condyloma acuminatum: Anatomic distribution

Lesions occur on the penis and female genitalia.

Additional sites include the urethra, perianal region, and rectum.

The term describes the anogenital distribution and papillomatous appearance.

Penis, vulva, urethra, perianal and rectal sites

External genital

Urethral / anorectal

Perianal / rectal

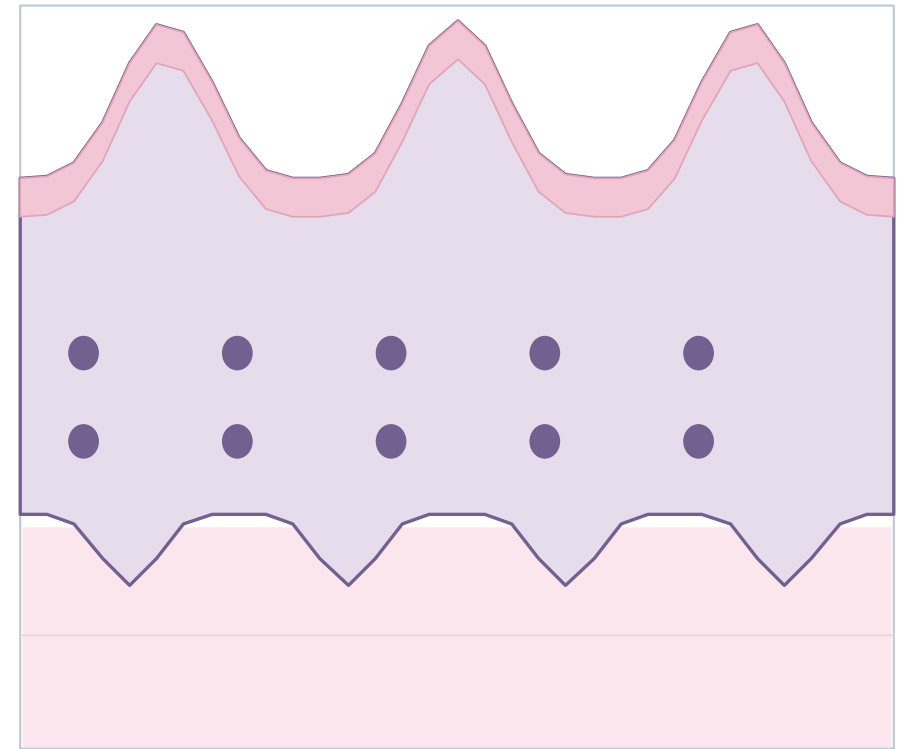
Condyloma acuminatum: Exophytic architecture

The clinical surface is soft and cauliflower-like.

Tan masses.

Lesions can occasionally reach several centimeters.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Genital wart is not synonymous with high-grade dysplasia

Finding	Condyloma acuminatum	High-risk HPV lesion
Typical HPV context	6 and 11	HPV 16 is an important type
Architecture	Papillary hyperplasia	May show intraepithelial atypia
Risk interpretation	Usually low malignant potential	Assess dysplasia / carcinoma risk

Clinical variants at a glance

Variant	Typical surface / morphology	Characteristic site
Vulgaris	Rough, convex or flat papule	Dorsal hand, periungual
Plana	Small, smooth, flat-topped	Face, dorsal hand
Plantaris / palmaris	Coarse and scaly	Sole / palm
Condyloma	Soft, cauliflower-like	Anogenital

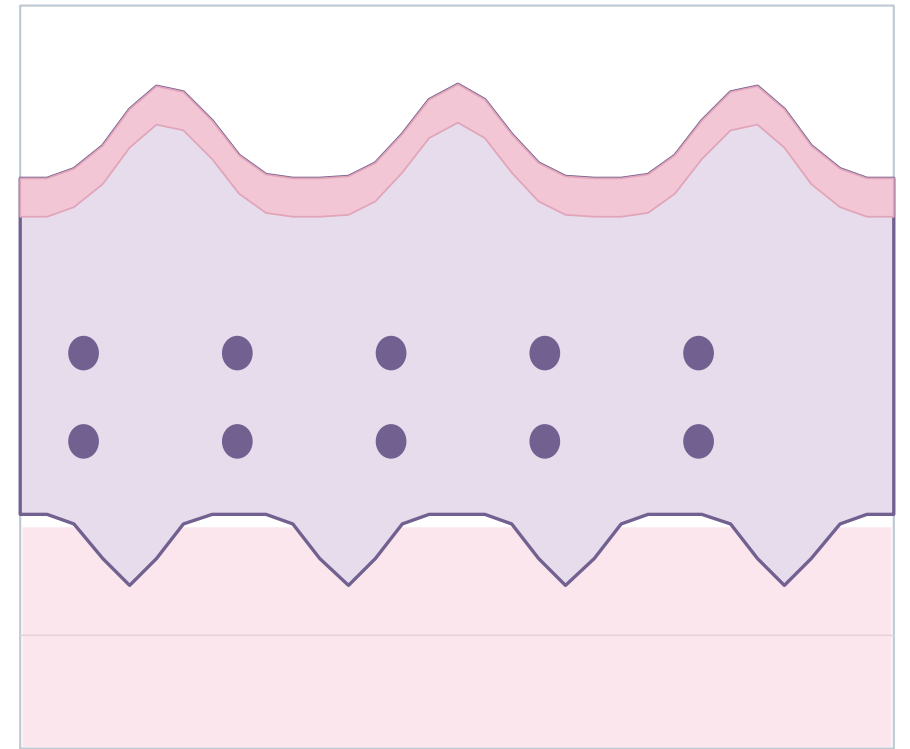
Microscopy: Orient the epidermal compartments

Stratum corneum caps the lesion.

Superficial viable epidermis is where koilocytic change is described.

Deeper epidermal proliferation produces the papillary contour.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

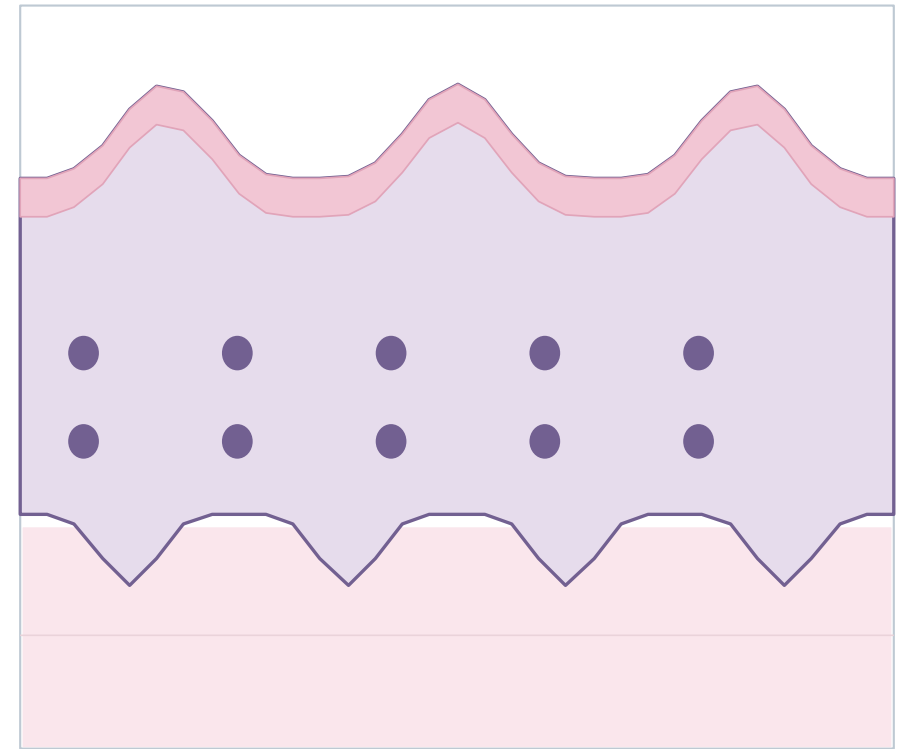
Verrucous / papillomatous epidermal hyperplasia

The epidermis expands in an undulating or spire-like pattern.

The term “papillomatosis” describes the surface architecture.

A broad low-power view is especially useful for recognizing this configuration.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

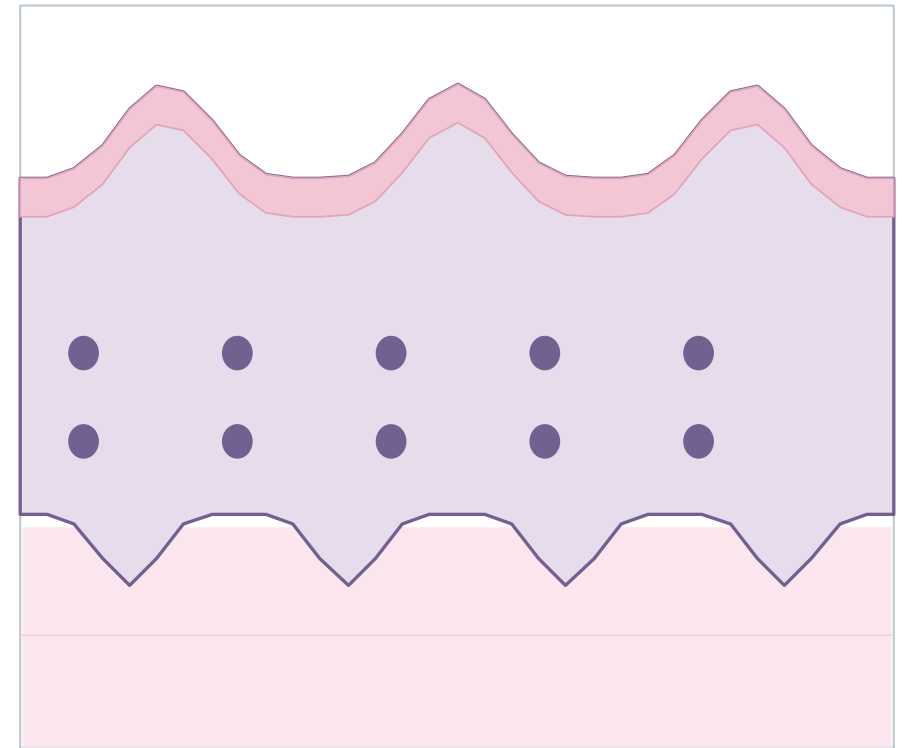
Acanthosis and epidermal thickening

The epithelial proliferation expands the viable epidermal compartment.

The thickening accompanies the clinically elevated lesion.

Describe the location and configuration of thickened epidermis, not only its presence.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

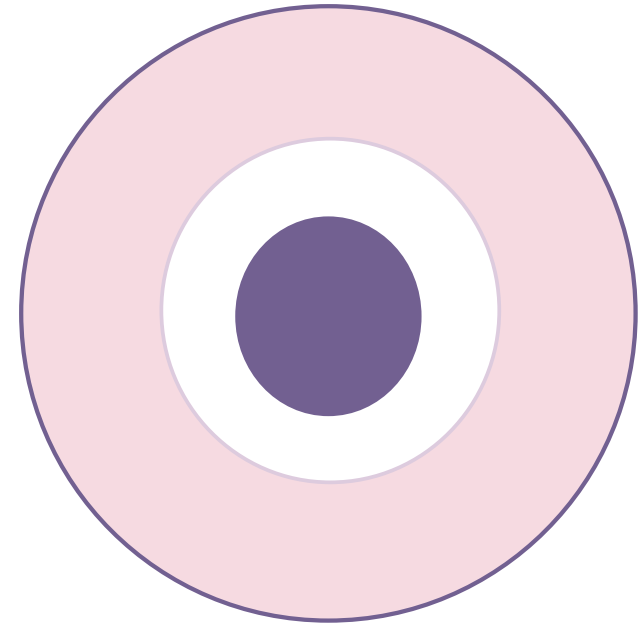
Koilocytosis is a superficial viral cytopathic effect

Koilocytes show cytoplasmic clearing around the nucleus.

The resulting pale perinuclear halo is a characteristic HPV-associated change.

The vacuolated cells in more superficial epidermal layers.

Schematic — HPV cytopathic cell



Perinuclear halo

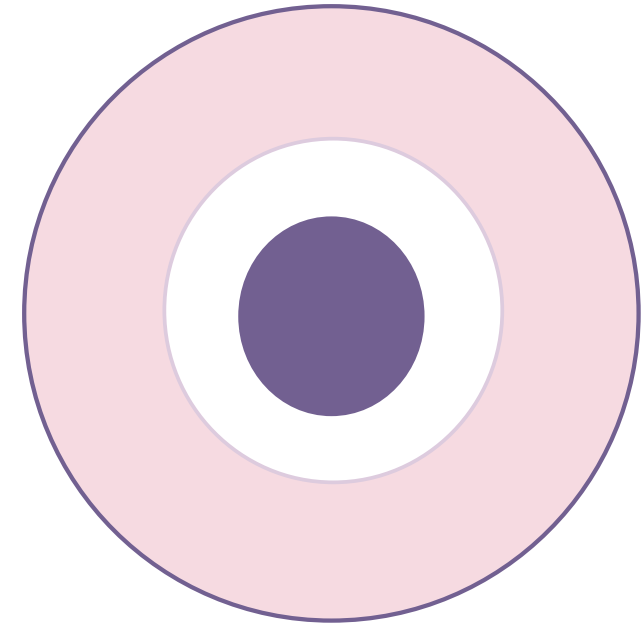
Why the perinuclear halo matters

The halo highlights a virus-related epithelial cell change.

It is a cellular finding, distinct from the papillary architecture.

Koilocytosis should be interpreted alongside tissue pattern and site.

Schematic — HPV cytopathic cell



Perinuclear halo

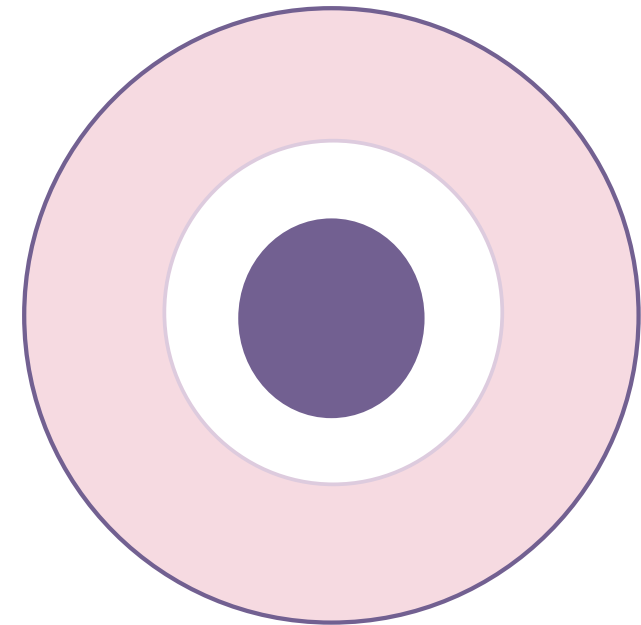
Additional virally altered keratinocyte features

Prominent, condensed keratohyaline granules may be visible.

Jagged eosinophilic intracytoplasmic keratin aggregates are described.

These changes accompany, rather than replace, the diagnostic emphasis on papillomatosis and koilocytosis.

Schematic — HPV cytopathic cell



Perinuclear halo

Electron microscopy: Intranuclear HPV virions

Numerous HPV virions within nuclei of affected superficial zones.

This is a biologic observation supporting the viral etiology.

Routine morphologic interpretation does not require demonstrating virions in every lesion.

Infected superficial keratinocyte



HPV virions observed in nuclei



Evidence of viral etiology

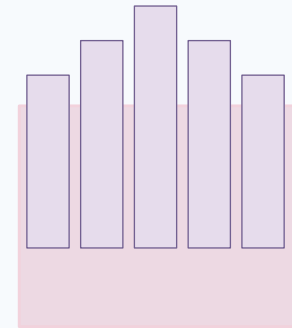
Low-power versus high-power recognition

Low power: Assess epidermal profile, surface undulations, and epithelial proliferation.

High power: Assess superficial cytoplasmic vacuoles and accompanying keratinization changes.

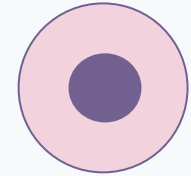
Combining architecture and cytopathology is more informative than a single isolated feature.

Low magnification



Architecture:
Papillomatosis

High magnification



Cells: Superficial
koilocytosis

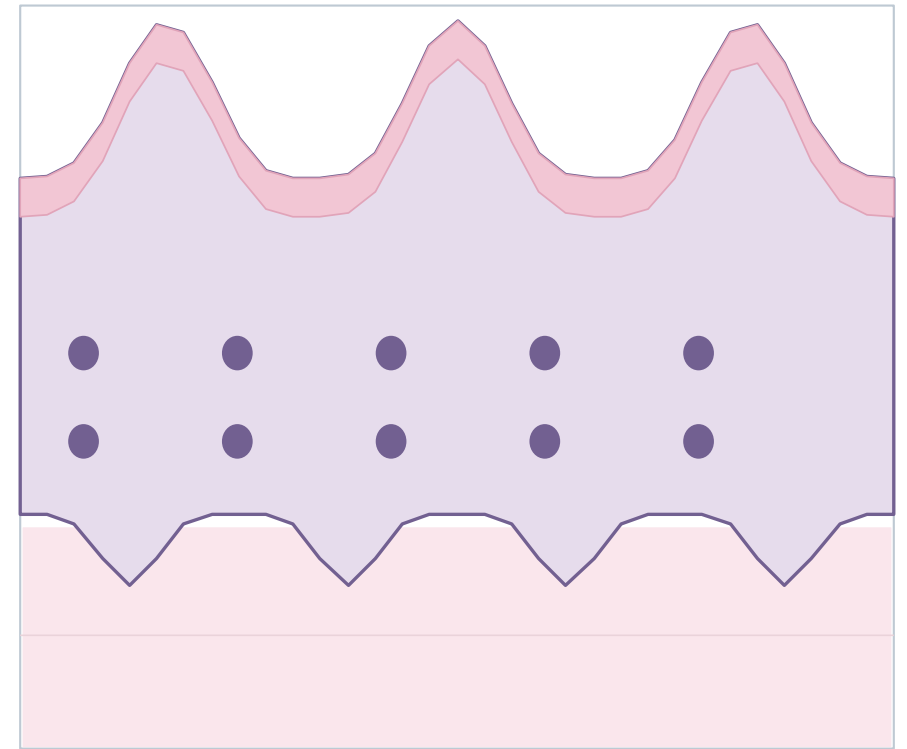
Condyloma: Papillary architecture is especially important

Condylomata are hyperplastic papillary lesions.

Koilocytic changes may be less conspicuous than in common cutaneous warts.

Wedge-shaped zones of koilocytosis within papillae are described.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

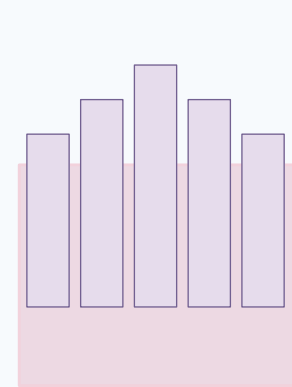
Do not overrequire dramatic koilocytosis in condyloma

A weakly expressed cytopathic effect does not negate the papillary pattern.

Site and soft papillary gross morphology remain relevant.

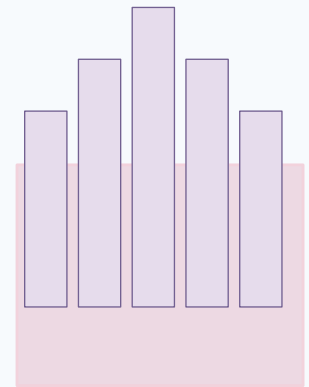
Assessment for dysplasia remains conceptually separate from proving papillomavirus-associated change.

Common wart



Koilocytosis often
conspicuous

Condyloma



Papillary
architecture helps
when koilocytosis is
subtle

Differential: Molluscum contagiosum

Feature	Verruca	Molluscum
Virus	Human papillomavirus	Poxvirus
Architecture	Papillomatous hyperplasia	Verrucous hyperplasia can occur
Signature cytology	Koilocytosis	Large cytoplasmic inclusions
Primary conclusion	HPV-driven wart	Distinct viral infection

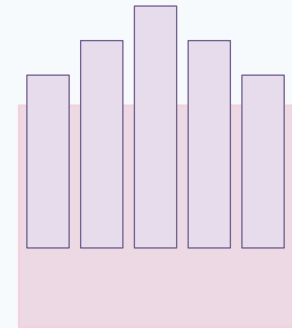
Differential: Reactive callus

Callus is explicitly noted as a potential clinical mimic of palmoplantar warts.

Both may display prominent surface keratinization.

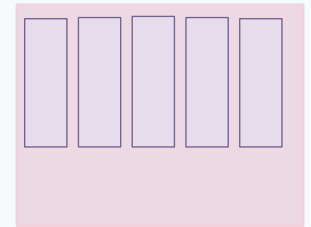
Viral cytopathic change and papillomatous architecture support a verruca when tissue is examined.

Palmoplantar wart



Viral cytopathic changes can support wart

Reactive callus



Keratinized mimic;
Viral cytopathy is not implied

Differential: High-grade HPV-associated lesions

Entity	Typical clue	Diagnostic issue
Ordinary verruca	Papillomatosis with koilocytes	Benign viral proliferation
Bowenoid papulosis	Genital lesion; in situ–like histology	May regress, but atypia is high grade
Squamous carcinoma in situ	Full-thickness atypia	Not classified as a simple wart

When HPV typing is used, two techniques are described

Viral typing can be accomplished by in situ hybridization.

Polymerase chain reaction is another described option.

These methods identify viral material; Histologic architecture is a separate line of evidence.

Lesion requiring viral identity



In situ hybridization OR PCR



HPV material / genotype

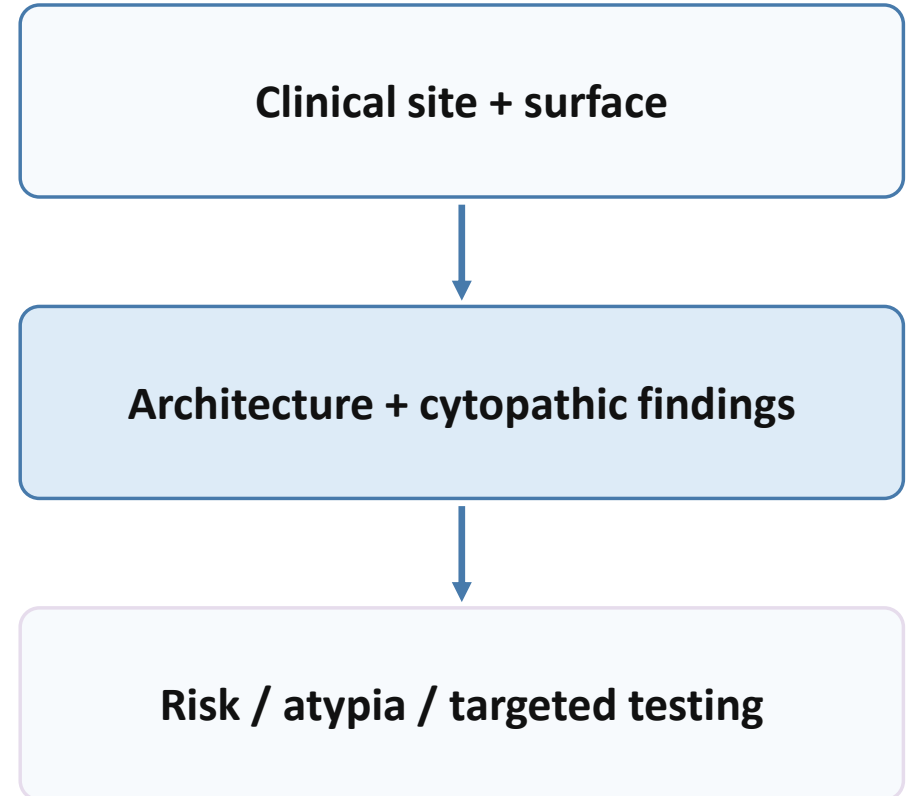
Clinicopathologic evaluation: A structured sequence

Start with anatomic site and clinical surface morphology.

Correlate with low-power epithelial architecture.

Assess superficial cytopathic features and any concerning atypia.

Use virologic methods selectively when the diagnostic question requires viral identity.



Case 1: Rough papules on a dorsal hand

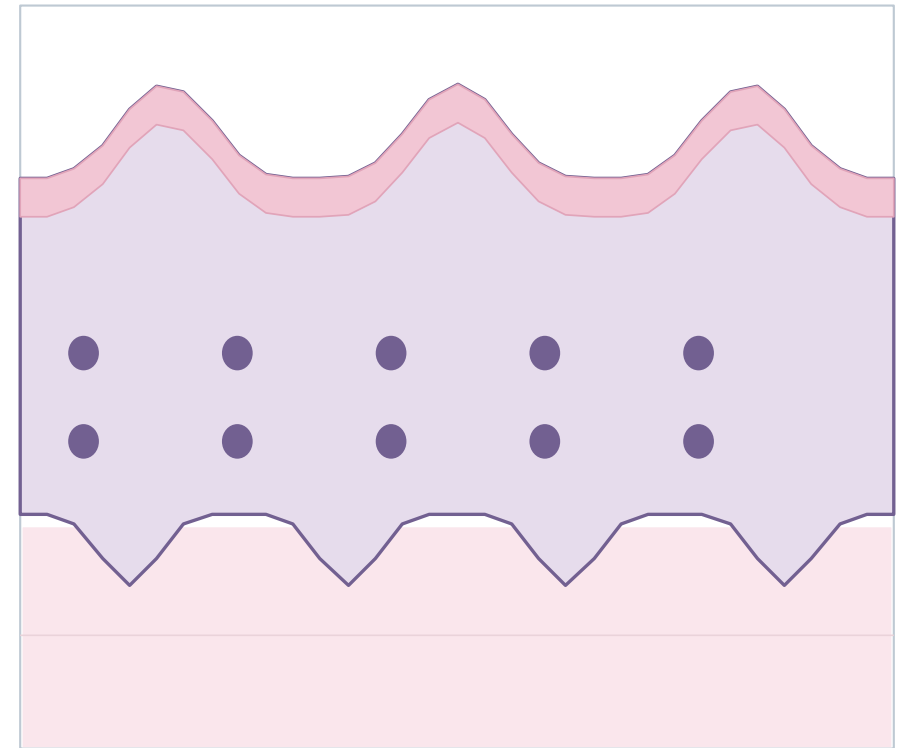
Constructed teaching vignette

Constructed vignette: An adolescent has several gray-tan, rough, elevated papules over the dorsal hand.

Which clinical wart variant is most likely?

Which low- and high-power histologic findings would support the diagnosis?

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

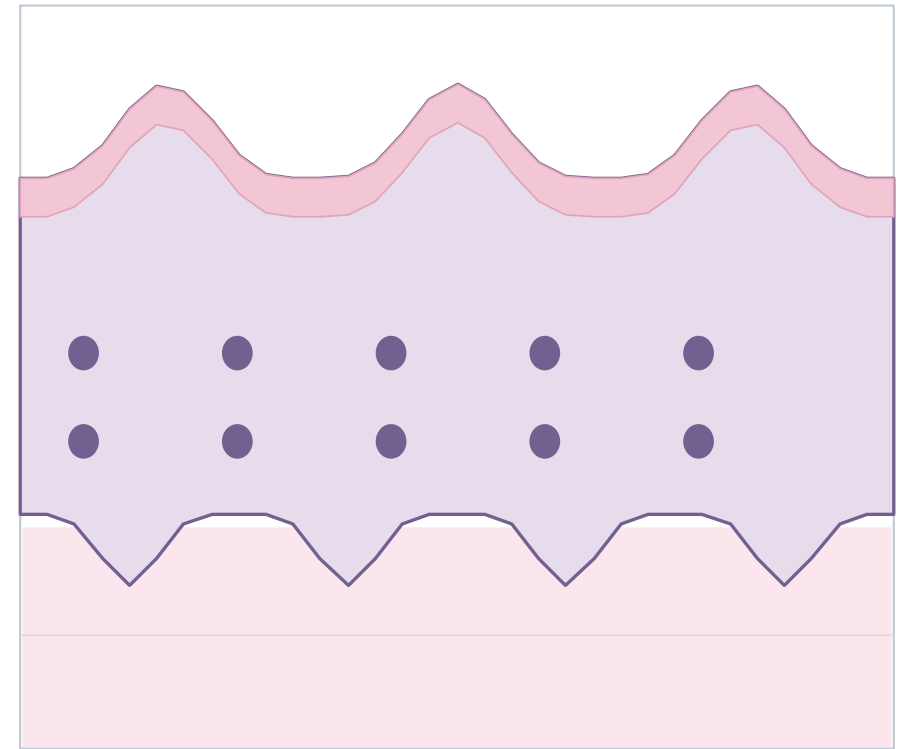
Case 1: Morphology establishes the pattern

Likely clinical phenotype: Verruca vulgaris.

Expected architecture: Verrucous/papillomatous epidermal hyperplasia.

Expected cytopathology: Superficial koilocytosis with perinuclear halos.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Case 2: Multiple smooth facial papules

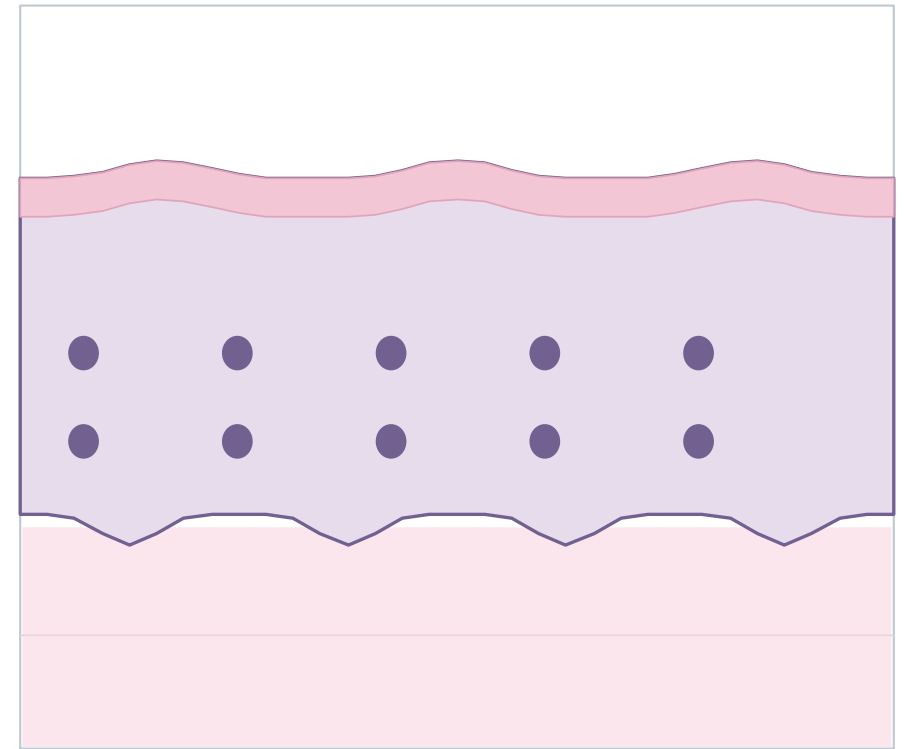
Constructed teaching vignette

Constructed vignette: Several small, slightly raised, smooth, flat-topped facial papules.

Which wart class best matches this morphology?

Why would a rough pebblelike surface favor another variant?

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

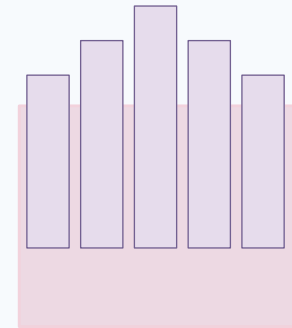
Case 2: Flat architecture changes the clinical name

Likely clinical phenotype: *Verruca plana*.

The description emphasizes smooth, low, flat papules.

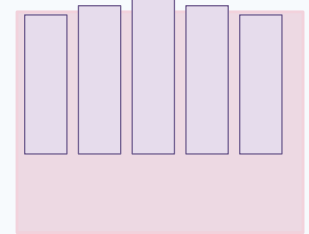
The face and dorsal hands are characteristic sites.

Common wart



Raised rough
surface; Often
convex

Flat wart



Smooth, flat-
topped, slightly
elevated

Case 3: A scaly lesion on the sole

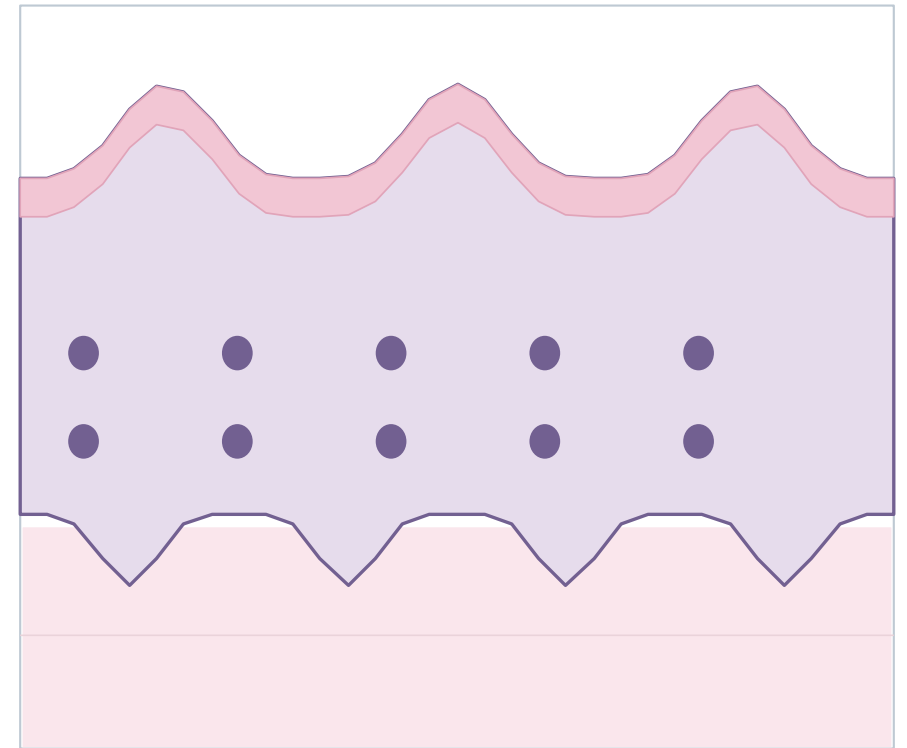
Constructed teaching vignette

Constructed vignette: A coarse, scaly plantar lesion clinically resembles a callus.

Name the wart variant suggested by the site.

Identify the specific diagnostic ambiguity emphasized.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Case 3: Site and mimic must both be considered

Feature	Palmoplantar verruca	Callus
Appearance	Rough, scaly	Keratinized mimic
Location	Palm / sole	Weight or friction–related sites can overlap
Diagnostic concern	HPV-associated epithelial lesion	Can look similar clinically
Tissue correlation	Papillomatosis + koilocytosis	HPV cytopathic pattern not expected

Case 4: A soft anogenital cauliflower-like mass

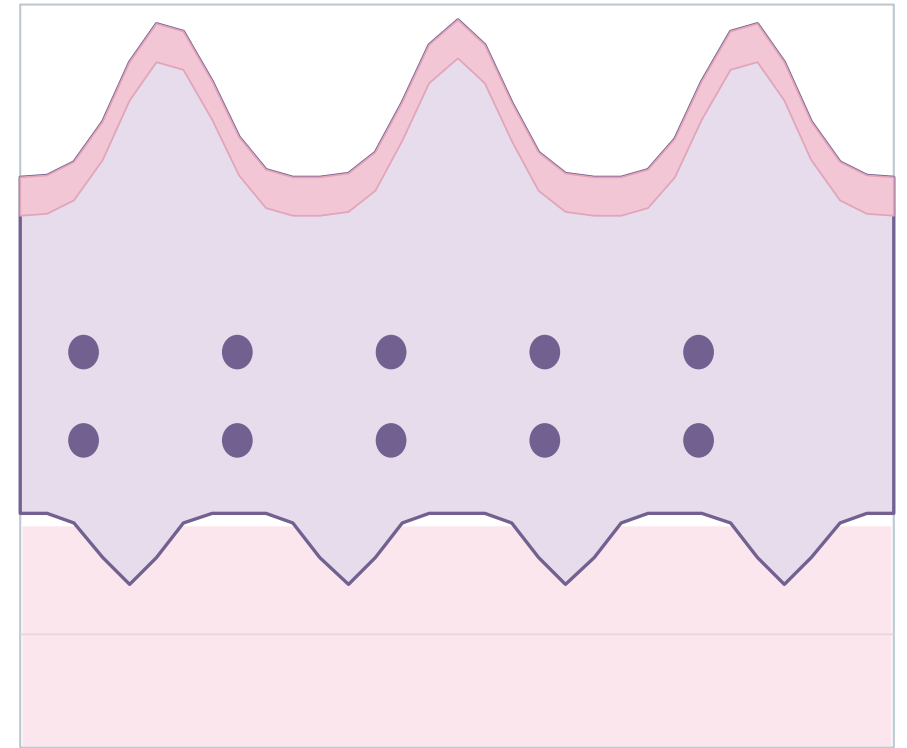
Constructed teaching vignette

Constructed vignette: A soft papillary anogenital lesion forms an exophytic tan mass.

What is the clinical classification?

Which HPV types are most often associated with this phenotype?

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

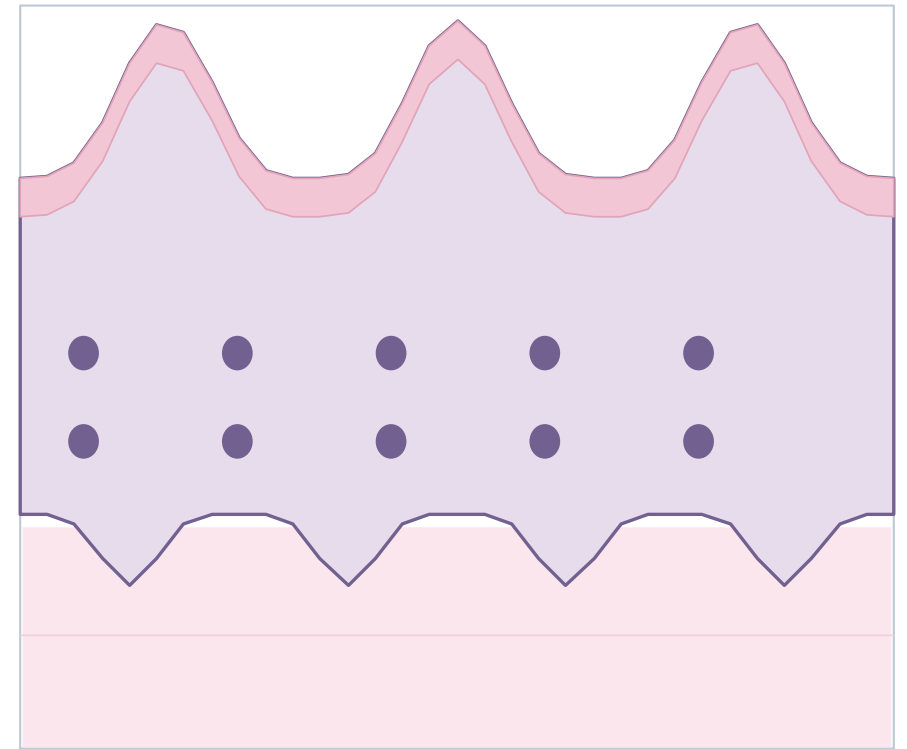
Case 4: Distinguish condyloma from oncogenic HPV disease

Clinical pattern: Condyloma acuminatum.

Usual type association: HPV 6 and 11.

Assess cytologic atypia separately; HPV 16-associated precursor lesions have different implications.

Schematic — not a micrograph



Continuous epidermal proliferation over dermis

Frequent diagnostic reasoning errors

Do not identify HPV genotype solely from the papule surface.

Do not assume absence of conspicuous koilocytosis excludes condyloma.

Do not mistake an ordinary plantar wart for callus without considering HPV.

Do not equate all HPV-related papillary lesions with high-grade neoplasia.

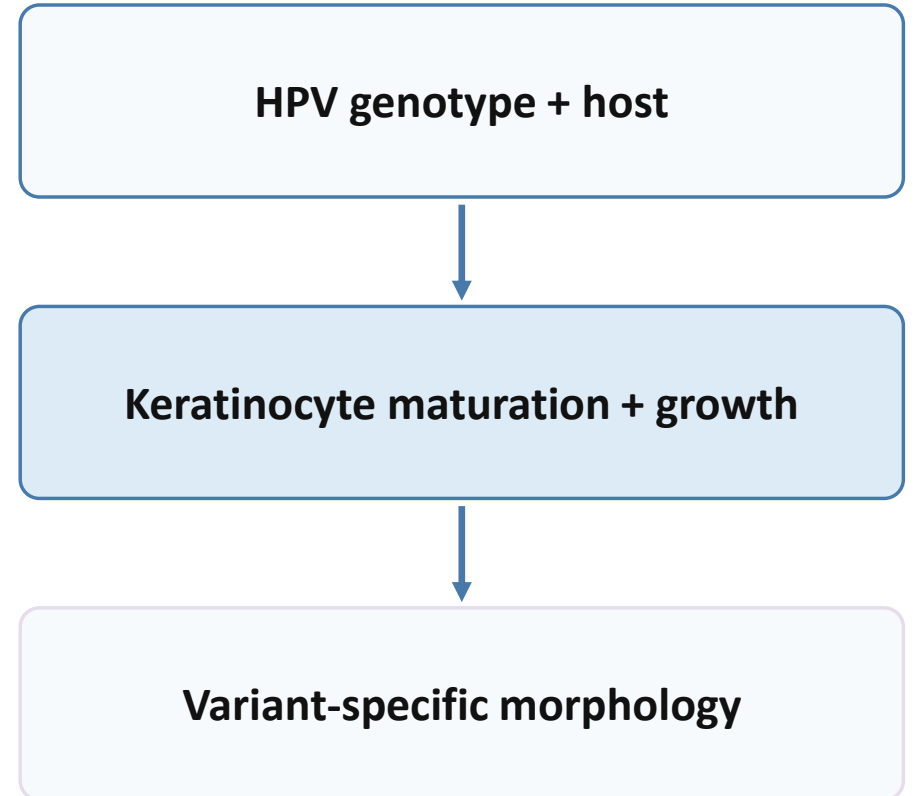
Morphology integrates virus, epithelium, and location

Virus: HPV subtype influences phenotype and oncogenic context.

Epidermis: Proliferation produces papillomatosis;
Cytopathy produces koilocytosis.

Location: Distribution distinguishes common, flat, palmoplantar, and anogenital lesions.

Cancer risk: Genotype and host setting require separate interpretation.



Core references and scope

Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 25: The Skin, pp. 1059–1060.

Supporting context: Chapter 7, HPV and oncogenic DNA viruses; Chapter 22, HPV pathogenesis.

All schematics are newly constructed, editable conceptual illustrations—not clinical photographs or histologic specimens.