

Mycosis Fungoides and Sézary Syndrome

Clinical evolution · skin pathology · extracutaneous disease

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Learning outcomes

- Define the two cutaneous mature T-cell neoplasms and their skin-homing biology.
- Relate clinical phases of mycosis fungoides to histologic architecture.
- Recognize the characteristic skin–blood–node presentation of Sézary syndrome.
- Explain the principal course, prognostic and therapy distinctions.

Two related neoplasms, two clinical patterns

Mycosis fungoides

- Typically evolves from patches to plaques and tumors
- May remain skin-localized for years
- Blood circulation may be molecularly detectable without overt dissemination

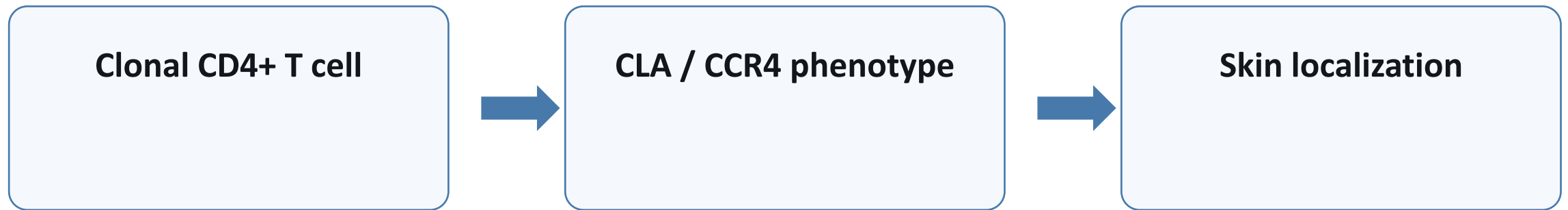
Sézary syndrome

- Generalized exfoliative erythroderma
- Leukemia of atypical cerebriform T cells
- Generalized lymphadenopathy

Position within lymphoid neoplasia

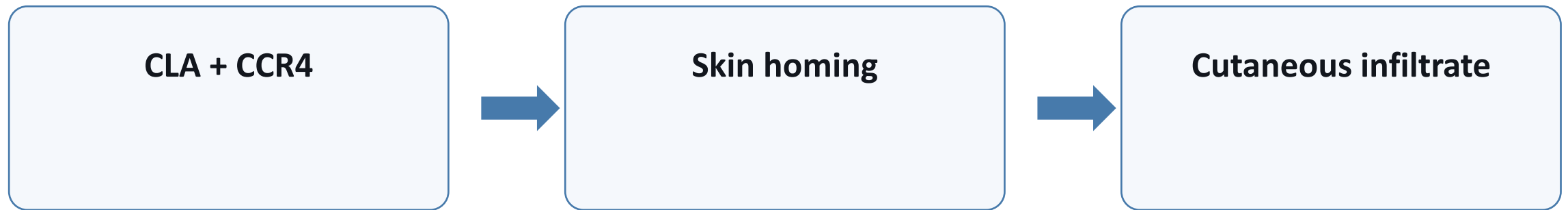
- Both are neoplasms of mature helper T lymphocytes.
- Their shared biology is cutaneous tropism rather than a common clinical presentation.
- They belong to the peripheral T-cell neoplasm discussion.
- MF is also covered as a cutaneous T-cell lymphoma in the skin chapter.

The neoplastic cell: A skin-homing CD4+ T cell



- The lymphoid lineage is helper T cell (CD4+).
- The cells express molecules associated with cutaneous trafficking.
- Clonal expansion produces the malignant infiltrate, not merely a reactive T-cell influx.

Skin-homing biology explains cutaneous presentation



- Skin-directed trafficking is an integral property of these malignant T cells.
- Cutaneous lymphocyte antigen (CLA) and CCR4.
- The same kinds of homing molecules also operate in normal CD4+ T cells.

Cutaneous lymphocyte antigen (CLA)

- CLA is an adhesion-related surface determinant associated with skin homing.
- Expression provides a biologic explanation for preferential cutaneous involvement.
- CLA expression alone does not establish a malignant process.

Teaching distinction

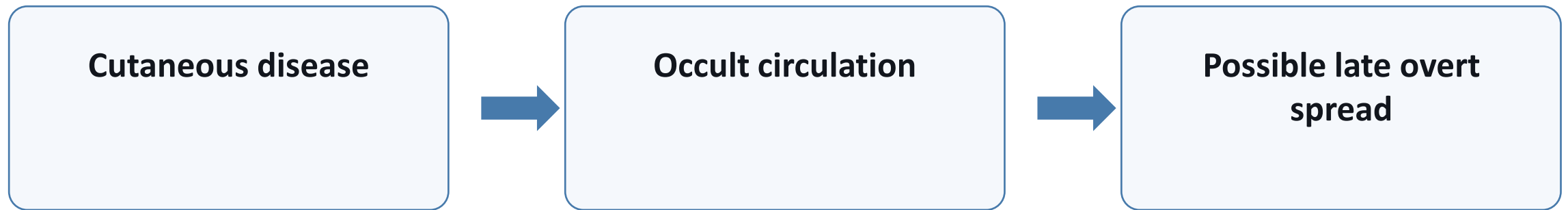
- Skin tropism is a biological property.
- Malignancy requires additional morphologic and clonal evidence.

CCR4 and the skin-tropic phenotype



- CCR4 is a chemokine receptor identified by Robbins in these neoplasms.
- Its presence accompanies other molecules that contribute to cutaneous localization.
- The excerpt does not define a unique oncogenic CCR4 mutation or a specific ligand pathway.

Homing is not equivalent to confinement



- A tumor can preferentially involve skin while its cells circulate through other compartments.
- MF may show circulating cells by sensitive molecular methods early in its course.
- Clinically evident extracutaneous disease in MF generally emerges late.

A compartment-based framework

Skin-dominant phenotype

- Patches, plaques, and cutaneous nodules
- Superficial or deep dermal infiltration
- MF often has an extended cutaneous phase

Multicompartment phenotype

- Diffuse erythroderma
- Peripheral blood leukemia
- Generalized lymphadenopathy: Typical of Sézary syndrome

Clonal T-cell receptor rearrangement



- The neoplastic lymphocytes in MF harbor clonal T-cell receptor gene rearrangements.
- T-cell receptor clonality provides molecular support for a T-cell clone.
- Integrate a molecular result with lesion morphology and clinical context.

No single specific driver mutation defines CTCL

- A wide variety of altered oncogenes and tumor-suppressor genes.
- None of these reported driver alterations is described as specific for CTCL.
- The source therefore does not justify a single-mutation diagnostic algorithm.

Interpretive implication

- Molecular heterogeneity $\neq$ a pathognomonic gene.
- Preserve separation between clonality and a specific driver mutation.

Phenotypic aberrancy can provide supportive evidence

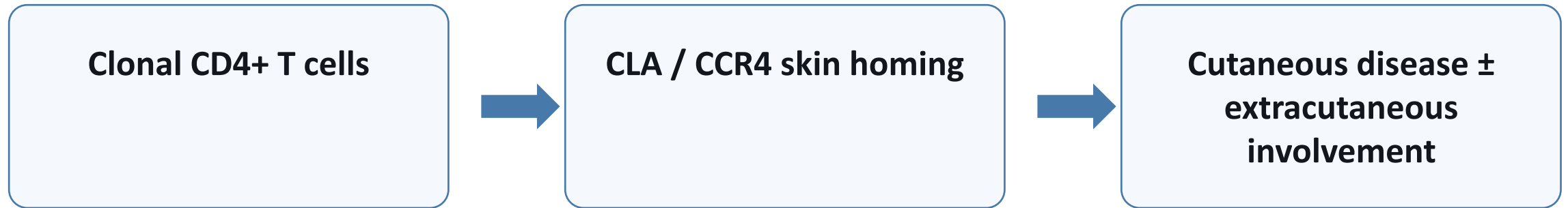
Supported by Robbins

- CD4+ helper T lineage
- Possible aberrant T-cell antigen patterns
- Clonal TCR rearrangements

Not established in this extract

- A unique obligatory phenotype
- A numerical immunophenotypic threshold
- A pathognomonic mutation

Integrated biological model of MF and Sézary syndrome



Mycosis fungoides: Essential definition

- A cutaneous T-cell lymphoma of skin-homing helper T lymphocytes.
- Typically presents with chronic evolving skin lesions.
- In many patients it remains confined to skin clinically for years.

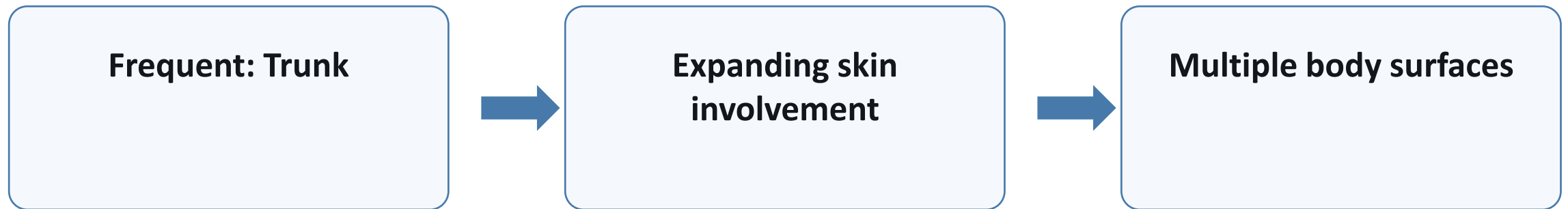
Central pathology concept

- Atypical lymphocytes in superficial dermis + epidermis.
- Clinical evolution and lesion architecture are connected.

Clinical setting of mycosis fungoides

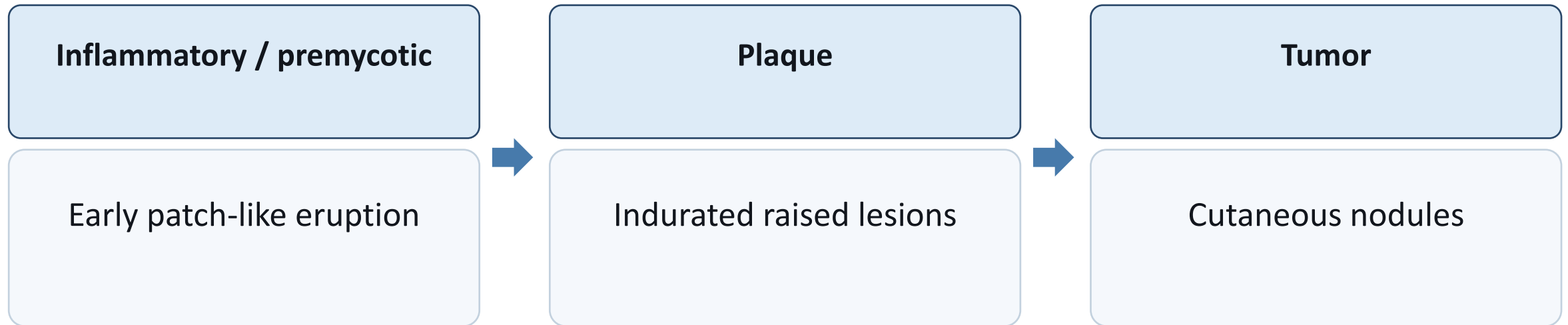
- MF can develop at any age.
- It most often affects adults older than 40 years.
- Age is contextual—not a defining diagnostic requirement.

Preferred distribution of skin lesions



- Truncal skin is a usual location of early lesions.
- Disease may eventually involve extremities, face and scalp.
- The geographic distribution can broaden as cutaneous disease evolves.

Three partially overlapping phases



The premycotic phase resembles dermatitis

Observed appearance

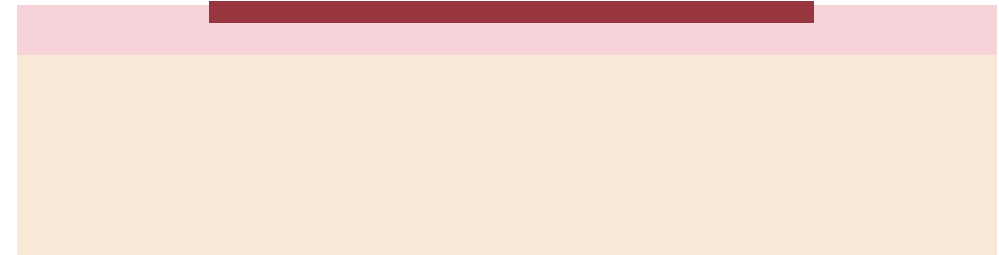
- Eczema-like lesions
- Scaly, erythematous patches
- Subtle or variable extent

Underlying process

- Skin-homing neoplastic T-cell infiltrate
- Potential epidermal invasion
- Disease remains cutaneous clinically in many patients

Patch lesions: Clinical morphology

- Scaly red-brown patches are a typical form of MF.
- Patches can resemble common inflammatory dermatoses.
- Their appearance must be interpreted alongside clinical evolution and pathology.



Flat, red-brown scaly patch

Schematic illustration — not a clinical or histologic specimen

Why patch disease is easily confused with eczema

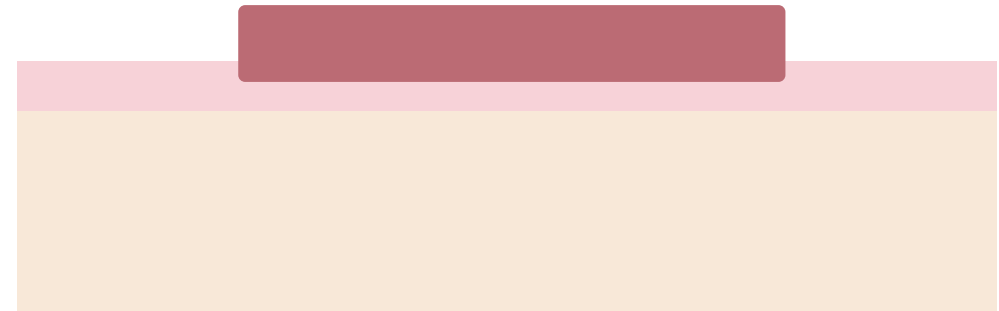
- The early cutaneous phenotype is as eczema-like.
- Inflammatory clinical morphology can coexist with a clonal neoplastic infiltrate.
- Clinical appearance and histology address different aspects of the same lesion.

Practical reasoning

- Inflammatory appearance does not exclude lymphoma.
- Anatomic infiltrate pattern helps explain the suspicion.

Plaque lesions: The second recognizable pattern

- Raised, indurated erythematous plaques may follow patches.
- Plaques may have irregular outlines and scaling.
- They indicate a more conspicuous cutaneous tumor burden.



Raised, indurated scaling plaque

Schematic illustration — not a clinical or histologic specimen

A psoriasis-like appearance can mislead

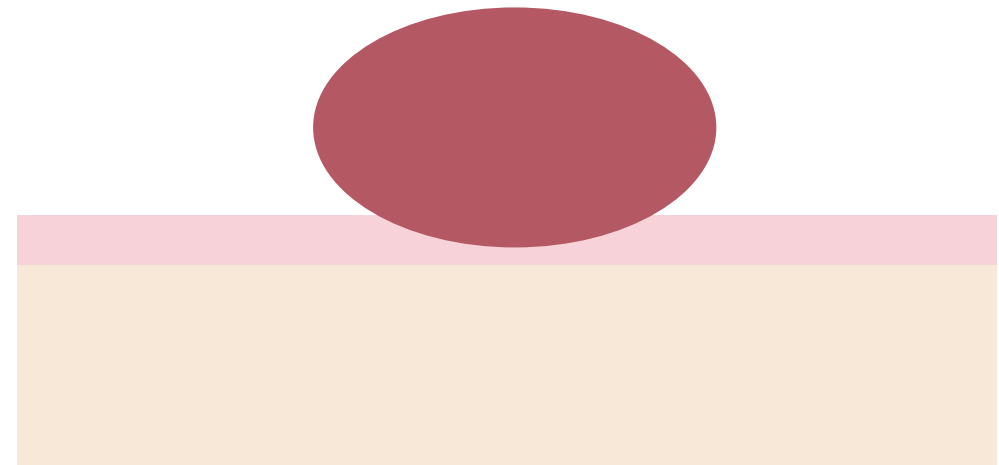
- Scaling plaques of MF can resemble psoriasis.
- The clinical overlap does not mean their underlying mechanisms are the same.
- Epidermal and superficial dermal lymphoid architecture becomes informative.

Compare the descriptions

- Psoriasis-like: Raised, scaling plaque.
- MF histology: Atypical T cells with epidermotropism.

Tumor phase: Nodules become prominent

- MF may develop multiple nodules or fungating tumors.
- Nodules represent a change in the depth and distribution of tumor growth.
- Progression to this phase correlates with greater systemic risk.



Protruding nodule / tumor

Schematic illustration — not a clinical or histologic specimen

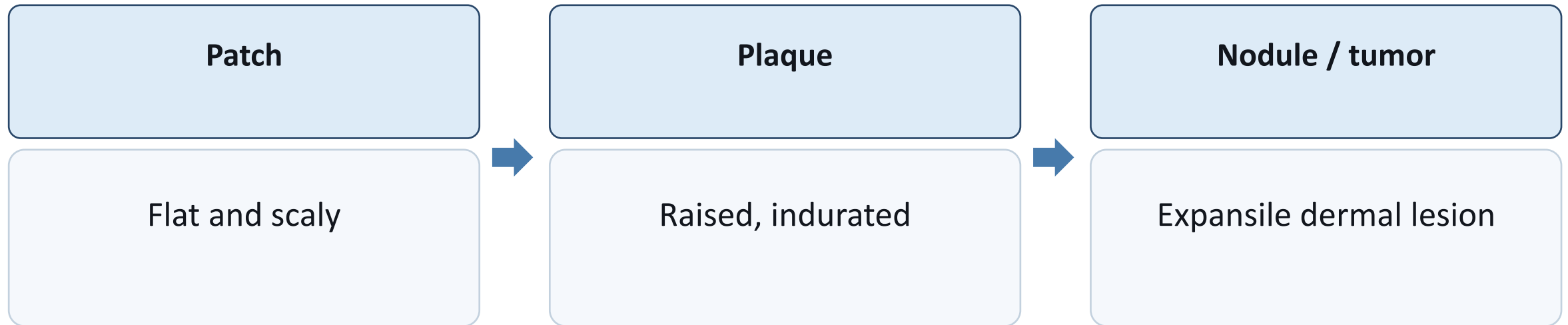
Ulceration and advanced cutaneous lesions

- Plaques and tumor nodules can ulcerate.
- An ulcerated lesion is a clinically important destructive cutaneous manifestation.
- The presence of nodules or systemic spread is prognostically unfavorable.

Course relationship

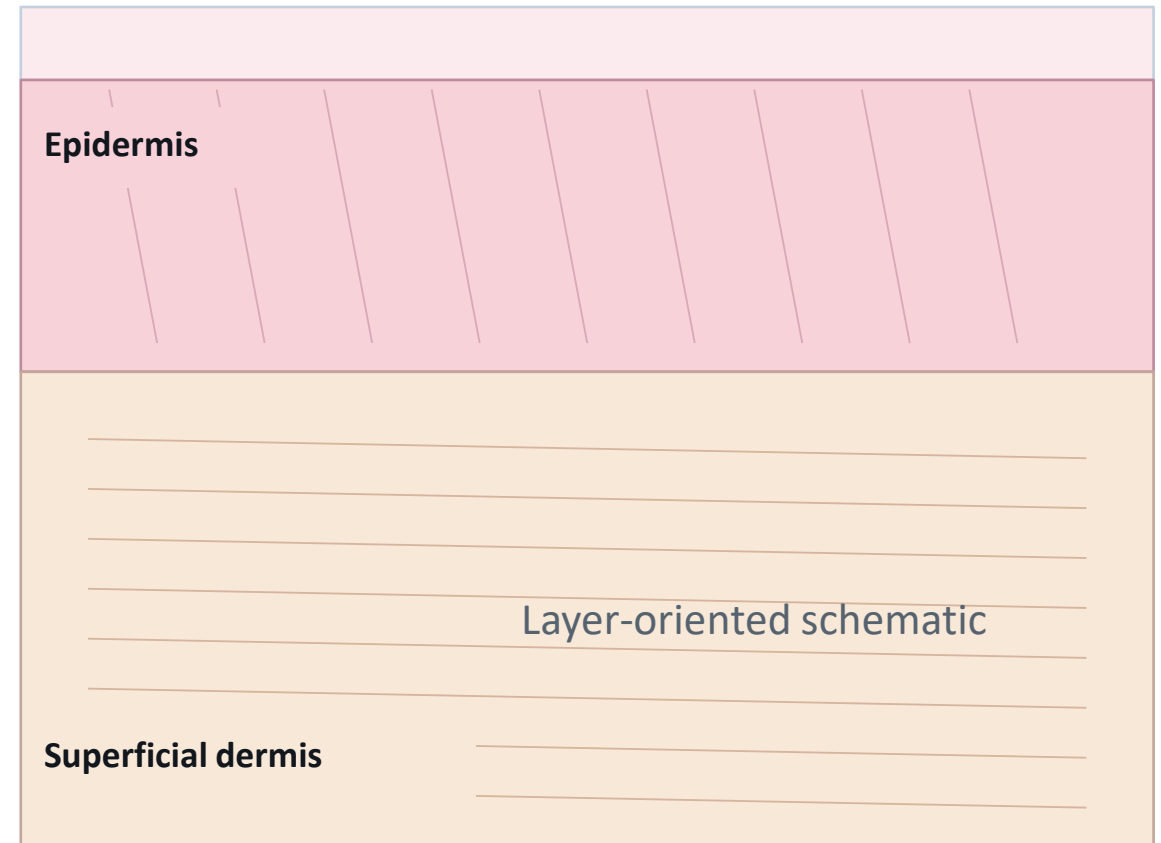
- Plaque or nodule → possible ulceration.
- Tumor nodules → association with extracutaneous spread.

Morphologic progression: External appearance



Histologic orientation: Epidermis and dermis

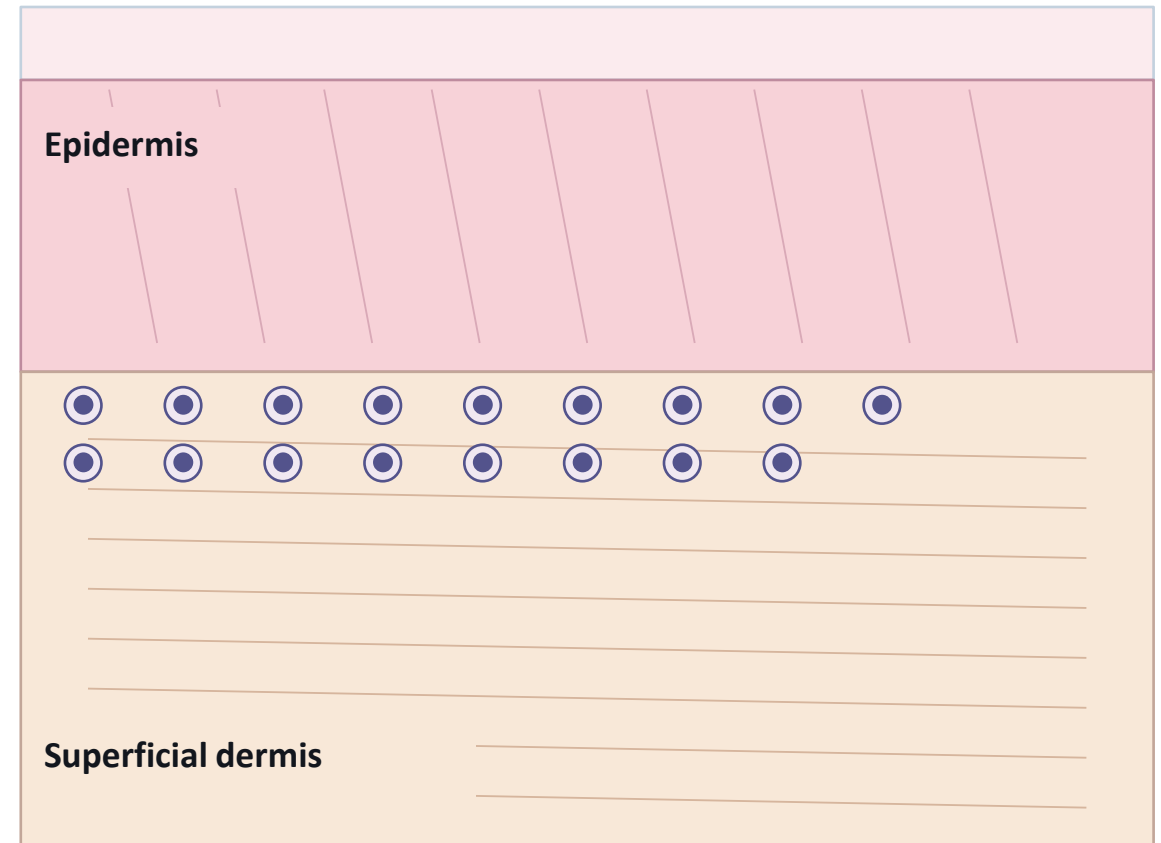
- The epidermis is the superficial epithelial compartment.
- The upper dermis lies immediately beneath it.
- MF may involve both compartments, producing epidermotropism and a dermal infiltrate.



Schematic illustration — not a clinical or histologic specimen

Superficial dermal band-like aggregates

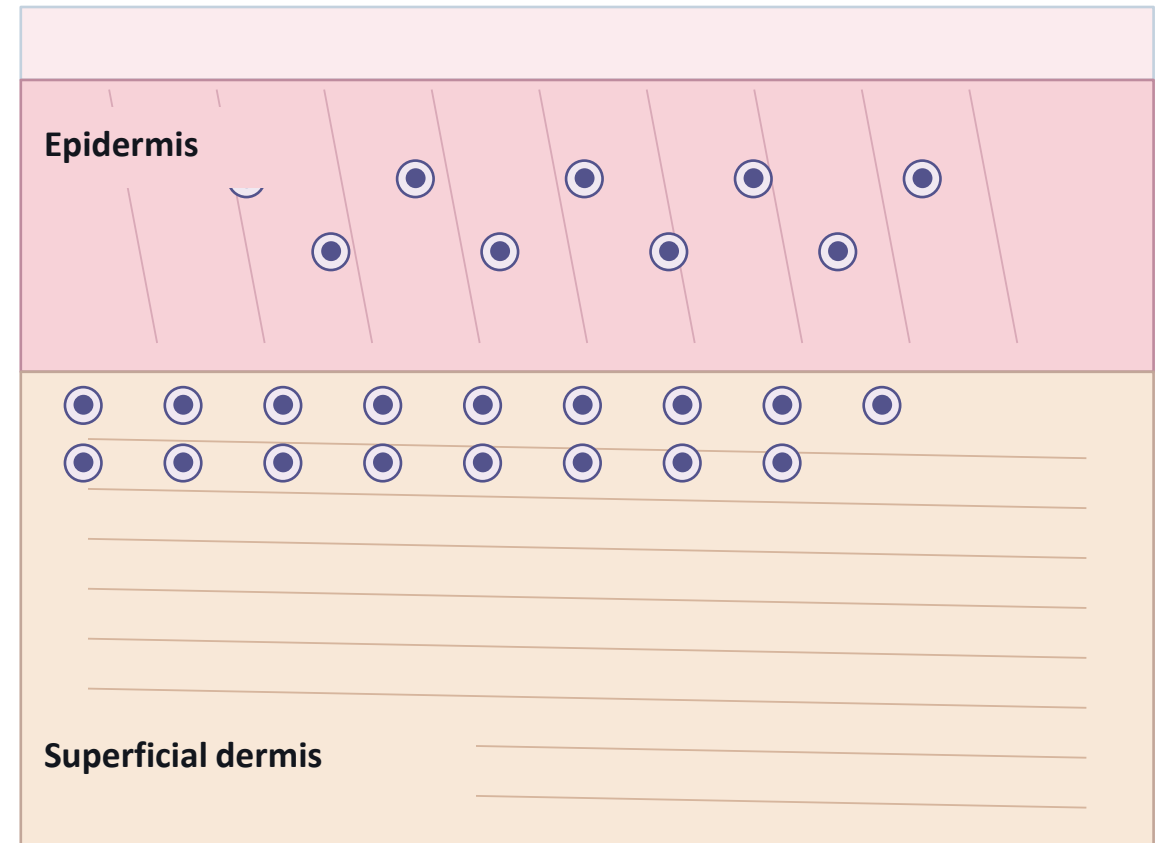
- Atypical lymphocytes characteristically accumulate in the superficial dermis.
- The infiltrate often forms a band-like distribution below the epidermis.
- This arrangement must be considered alongside epidermal invasion.



Schematic illustration — not a clinical or histologic specimen

Epidermotropism: Atypical lymphocytes in epidermis

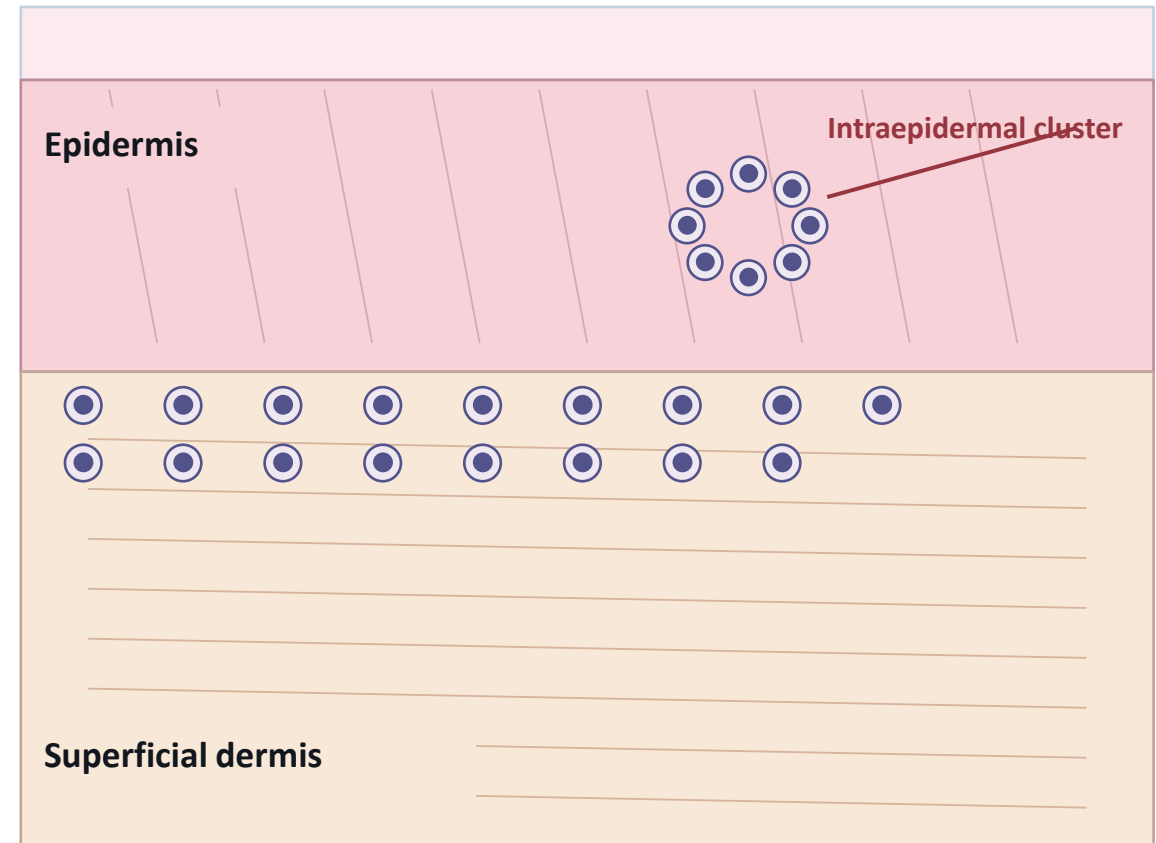
- Neoplastic lymphocytes move from their dermal distribution into epidermis.
- Epidermal cells may be present singly or in small groups.
- This epidermal invasion as a hallmark of patch/plaque MF.



Schematic illustration — not a clinical or histologic specimen

Pautrier microabscesses are intraepidermal clusters

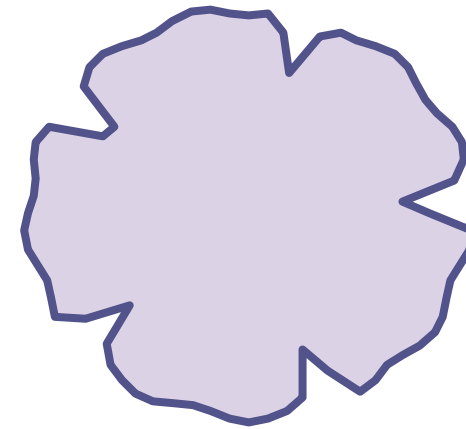
- Groups of atypical T lymphocytes can form small epidermal collections.
- These collections are termed Pautrier microabscesses.
- Despite the name, they are clusters of lymphocytes—not ordinary neutrophilic abscesses.



Schematic illustration — not a clinical or histologic specimen

Cerebriform nuclear contours

- Tumor T cells frequently possess markedly irregular nuclear membranes.
- The nuclear membrane folds give a convoluted, cerebriform appearance.
- This nuclear feature occurs in both cutaneous MF cells and Sézary blood cells.

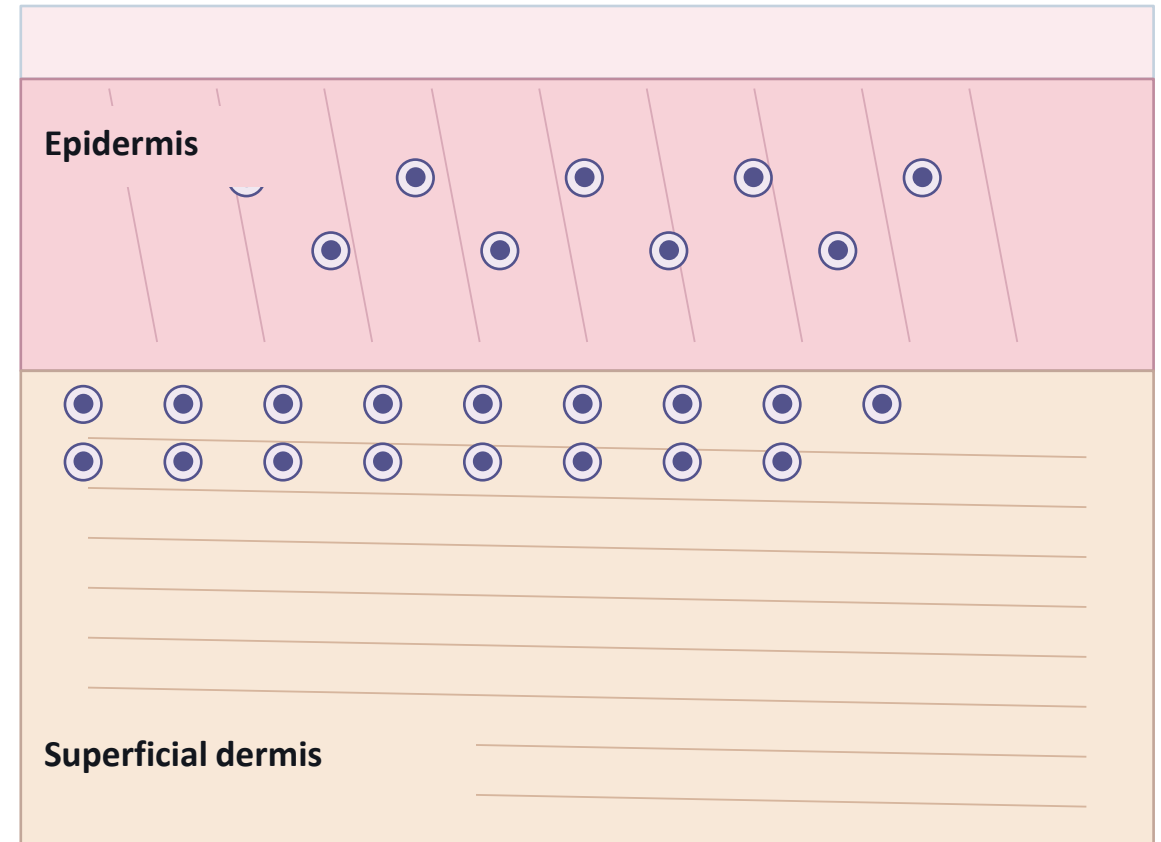


Marked nuclear membrane infolding

Schematic illustration — not a clinical or histologic specimen

Patch and plaque histology: A compartment pattern

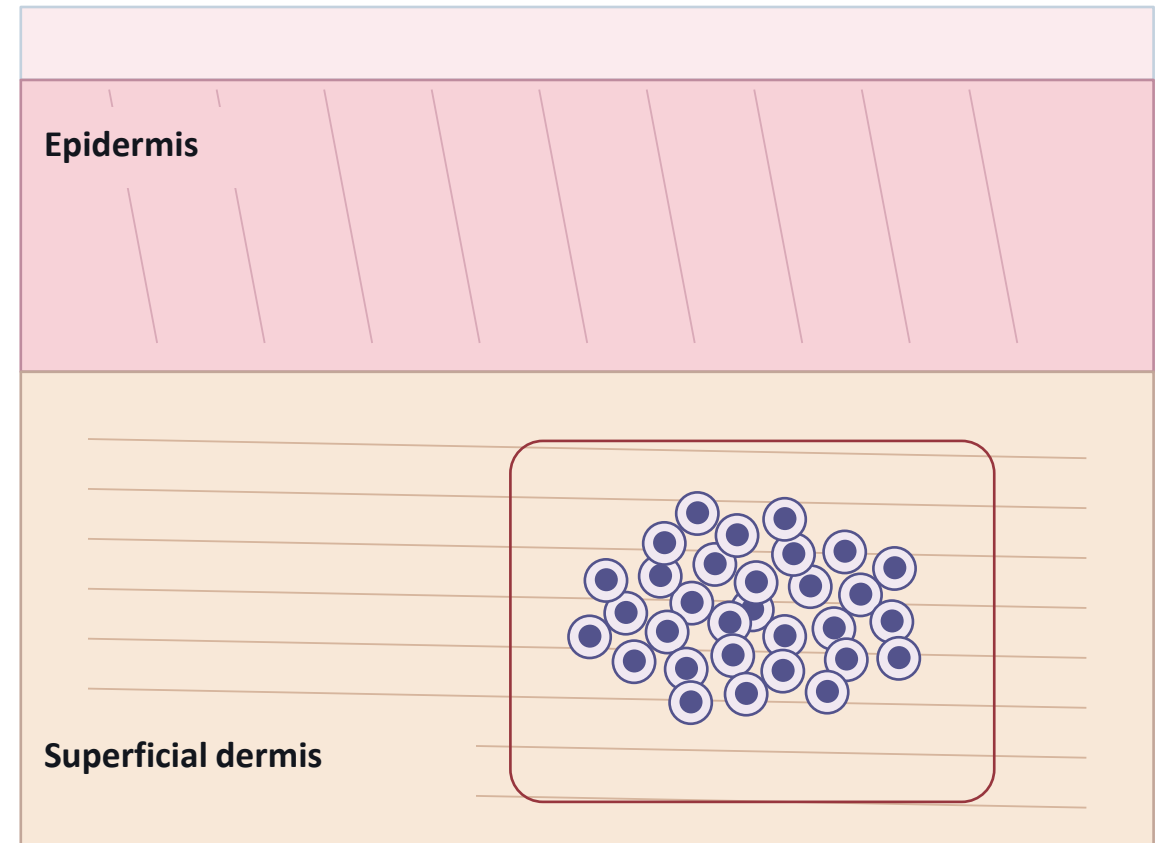
- Epidermotropism: Single atypical T cells within the epidermis.
- Band-like infiltration beneath the epidermis.
- Together, these encode the patch/plaque lesion pattern.



Schematic illustration — not a clinical or histologic specimen

The tumor phase changes the architectural pattern

- Advanced cutaneous nodules often show less conspicuous epidermotropism.
- Malignant lymphocytes extend deeper into the dermis.
- A nodular dermal growth pattern becomes clinically visible.



Deep dermal tumor mass
Schematic illustration — not a clinical or histologic specimen

Loss of epidermotropism does not exclude advanced MF

Patch / plaque

- Epidermal entry conspicuous
- Upper dermal infiltrate
- Small epidermal clusters may occur

Advanced tumor nodule

- Epidermotropism may diminish
- Deeper dermal growth prominent
- Expansile nodular disease

Why cutaneous nodules matter prognostically



- The presence of tumor nodules is associated with a worse course.
- Tumor nodules correlate with the risk of systemic dissemination.
- Surface area and extracutaneous involvement provide additional prognostic context.

Subclinical blood and tissue circulation in MF

Molecularly detectable

- Low-level tumor-cell circulation
- May occur in apparently skin-limited disease
- Requires interpretation of test sensitivity

Clinically overt

- Nodal or visceral involvement becomes manifest
- Typically later in MF course
- Carries adverse clinical significance

Histology and the clinical phase should agree logically

Clinical phase	Cutaneous finding	Pathologic pattern
Patch	Scaly erythematous patch	Epidermotropism + superficial infiltration
Plaque	Raised, indurated lesion	Epidermotropic atypical cells in skin
Tumor	Nodular or fungating mass	Deeper dermal tumor; epidermotropism may fade

MF is not synonymous with every cutaneous T-cell lymphoma

- CTCL includes several lymphoproliferative disorders affecting skin.
- Robbins focuses here on MF as a distinctive skin-homing CD4+ neoplasm.
- The clinicopathologic description should not be transferred to all CTCL entities.

Classification principle

- Category: Cutaneous T-cell lymphomas.
- Entity: Mycosis fungoides.

A source-grounded evaluation sequence

Evolving skin morphology



**Epidermal / dermal
atypical T cells**



**Phenotype + TCR
clonality**

What molecular testing contributes—and does not

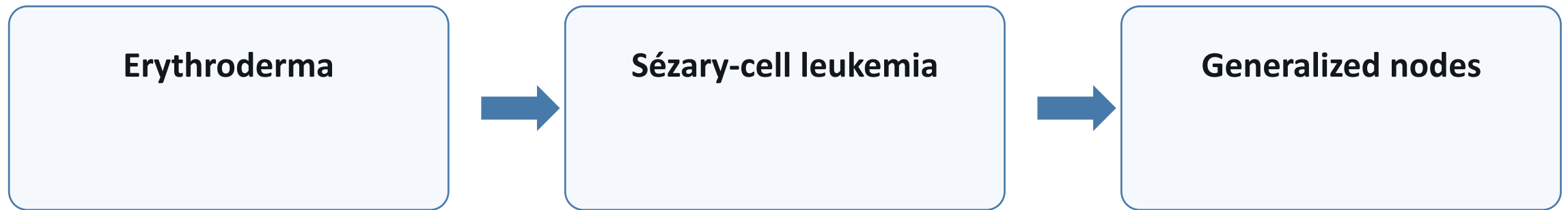
Useful molecular evidence

- Clonal TCR rearrangement
- Possible aberrant antigen expression
- Clonal nature of cutaneous infiltrate

Must also assess

- Clinical presentation and evolution
- Atypical cytomorphology
- Epidermal versus dermal location

Sézary syndrome: A distinct presentation



- Sézary syndrome is another tumor of skin-homing CD4+ T cells.
- Its presentation combines generalized cutaneous and extracutaneous features.
- It follows a more aggressive course than typical MF.

Generalized exfoliative erythroderma

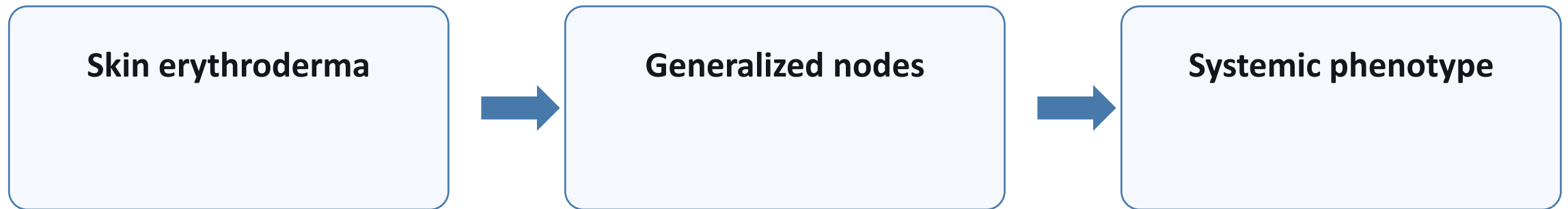
Mycosis fungoides

- Patches / plaques / sometimes tumors
- Often initially localized to skin
- Stepwise but overlapping cutaneous phases

Sézary syndrome

- Diffuse exfoliative erythroderma
- Extensive skin involvement at presentation
- Often accompanied by blood and nodal disease

Generalized lymphadenopathy in Sézary syndrome



- Generalized lymph node enlargement is part of the characteristic clinical syndrome.
- This finding marks involvement beyond the skin compartment.
- Consider the nodes together with erythroderma and leukemic cells.

Leukemic peripheral blood involvement

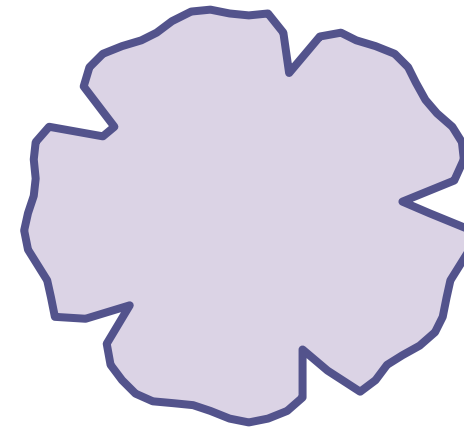
- Sézary syndrome includes circulating malignant T cells detectable in peripheral blood.
- This as a leukemia of Sézary cells.
- Overt blood involvement distinguishes its clinical phenotype from the indolent skin-dominant MF course.

Compartment distinction

- MF: Subclinical circulation is possible.
- Sézary syndrome: Leukemic blood disease is evident.

Sézary cells have folded nuclear membranes

- Circulating Sézary cells characteristically show cerebriform nuclei.
- The convoluted nuclear contour parallels the morphology of cutaneous malignant T cells.
- Blood morphology is one component of the characteristic clinical triad.



Marked nuclear membrane infolding

Schematic illustration — not a clinical or histologic specimen

Tumefaction is unusual in Sézary syndrome

MF tumor progression

- Cutaneous nodules can develop
- Tumors may ulcerate
- Deeper dermal growth

Sézary presentation

- Diffuse erythroderma predominates
- Tumefaction is uncommon
- Blood/nodal disease prominent

Three affected compartments in Sézary syndrome

Skin: Erythroderma



Blood: Leukemic T cells



**Nodes: Generalized
enlargement**

MF versus Sézary syndrome: Core discrimination

Dimension	Mycosis fungoides	Sézary syndrome
Presentation	Patches → plaques → tumors	Generalized exfoliative erythroderma
Tumor nodules	Can become prominent	Rarely develops tumefaction
Blood involvement	Occult circulation can occur	Overt Sézary-cell leukemia
Lymph nodes	Overt spread typically late	Generalized lymphadenopathy characteristic
Course	Usually relatively indolent	More aggressive

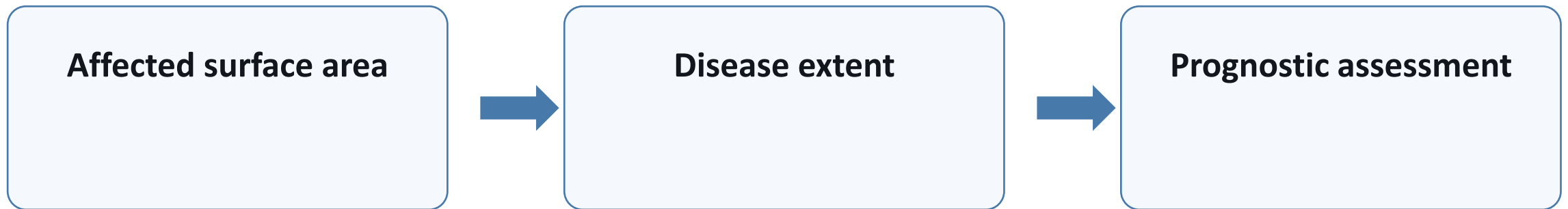
Typical course of mycosis fungoides

- MF generally develops over a long interval.
- Cutaneous disease may remain the dominant problem for years.
- A median survival of roughly 10 years (textbook-level estimate).

Do not overgeneralize

- Prognosis is heterogeneous.
- Skin extent and nodules alter risk.

Skin surface area matters to prognosis



- The percentage of body surface area affected contributes to prognosis.
- Greater extent reflects more widespread cutaneous disease.
- The supplied source does not provide stage cutoffs for body surface area.

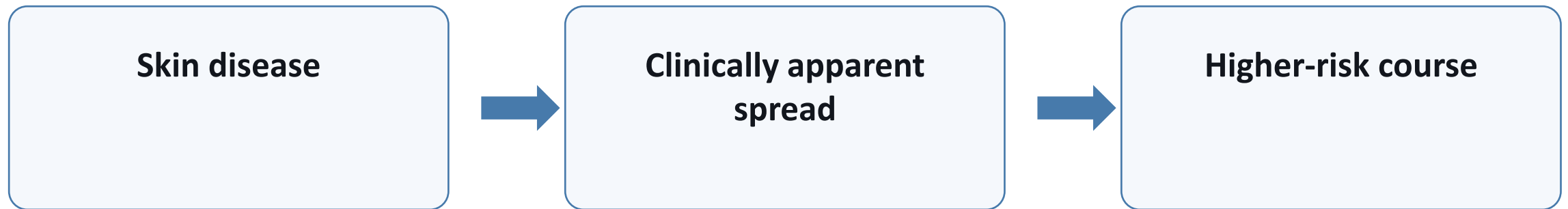
Tumor nodules indicate more aggressive disease

- Development of cutaneous tumor nodules is linked with worse prognosis.
- Nodular disease may coincide with more extensive lymphoid infiltration.
- The presence of nodules is clinically meaningful beyond lesion count alone.

Morphology → prognosis

- Patch / plaque predominant
- Vs. Nodular tumor phase

Systemic spread changes the clinical outlook



- Nodal or visceral involvement is an adverse event during MF progression.
- Tumor nodules and systemic spread are associated with aggressive disease.
- The distinction between molecular circulation and overt spread remains important.

Transformation to an aggressive T-cell lymphoma

- Transformation of MF to an aggressive T-cell lymphoma can occur.
- Robbins characterizes this as an occasional terminal event.
- Do not equate every tumor-phase skin nodule with proven transformation.

Important distinction

- Tumor-phase cutaneous progression
- ≠ necessarily aggressive transformation

Sézary syndrome has a more guarded prognosis

MF: General course

- Often prolonged skin-limited period
- Median survival roughly 10 years
- Prognosis worsens with extent/spread

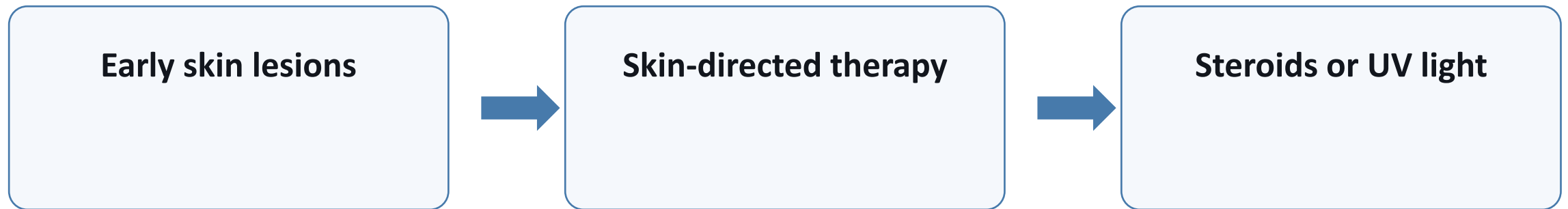
Sézary: General course

- Blood, nodes and erythroderma at presentation
- More aggressive natural history
- Fewer patients survive five years description

Risk assessment is multidimensional

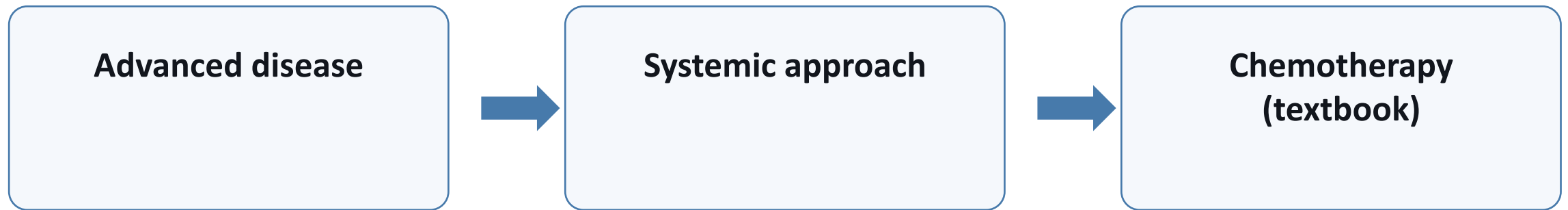
Dimension	Why it matters
Cutaneous extent	Percent of body surface involved correlates with prognosis
Cutaneous tumor nodules	Associated with greater aggressiveness
Clinically overt extracutaneous spread	Signals systemic progression
Syndromic presentation	Sézary syndrome differs from typical MF in course

Early lesions: Skin-directed treatment



- Topical corticosteroids are used for early cutaneous lesions.
- Ultraviolet light treatment is another described option.
- These therapies in the context of early skin disease, not advanced systemic involvement.

Advanced disease: Systemic treatment considerations



- Systemic chemotherapy for advanced CTCL disease.
- The trigger for changing approach is disease advancement beyond early skin lesions.
- Specific regimens and current guideline hierarchies are not covered in the supplied excerpt.

Therapy follows anatomic and clinical burden

Earlier localized disease

- Skin-dominant clinical pattern
- Topical corticosteroids
- Ultraviolet light

Advanced disease

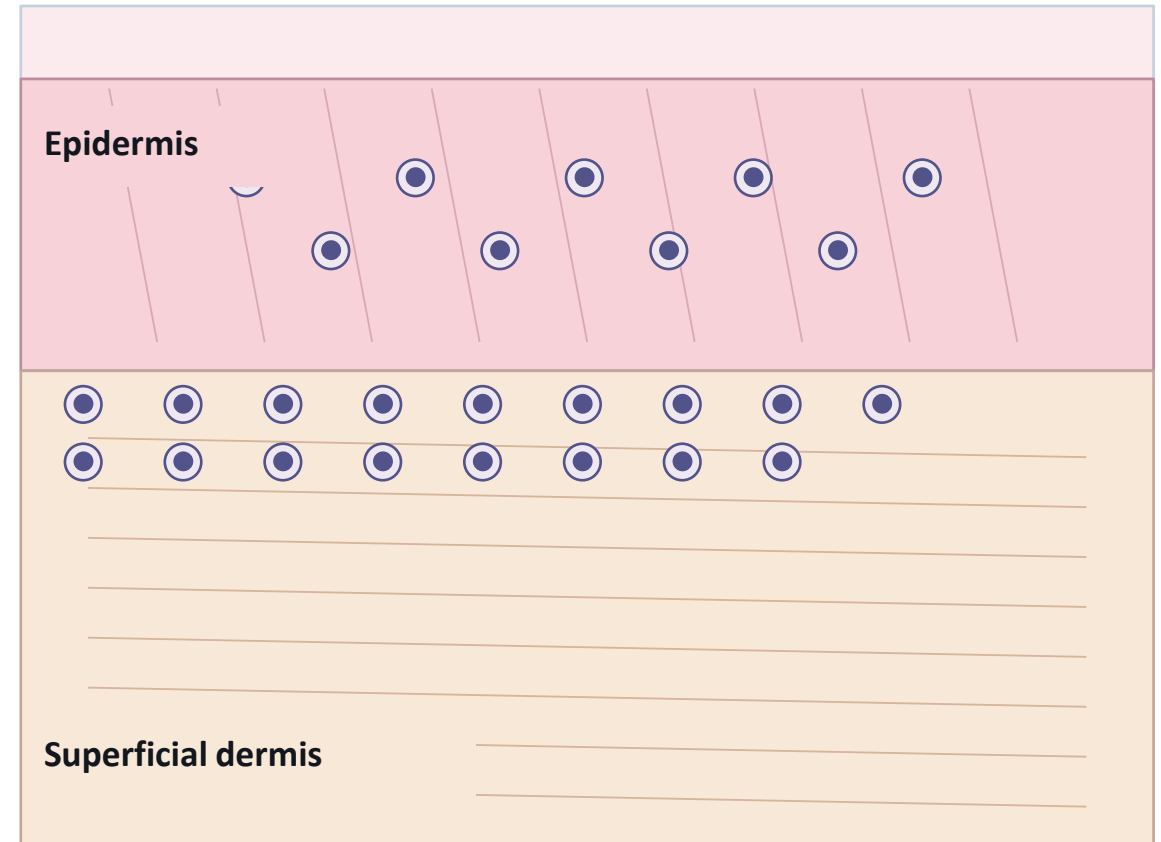
- Deep tumor / systemic involvement
- More aggressive treatment approach
- Systemic chemotherapy

Case 1: A chronic erythematous patch

- Illustrative patient: Persistent scaly, red-brown patch on the trunk.
- Early eruption has an eczema-like clinical appearance.
- Biopsy description: Atypical superficial dermal T-cell infiltrate with epidermal migration.
- Question: Which disease and phase best fit?

Case 1: Interpret clinical and microscopic clues

- Mycosis fungoides—early patch / premycotic phase—is the most consistent pattern.
- Clinical mimicry explains why initial appearance can be misleading.
- Epidermotropism connects the lesion to the characteristic MF architecture.



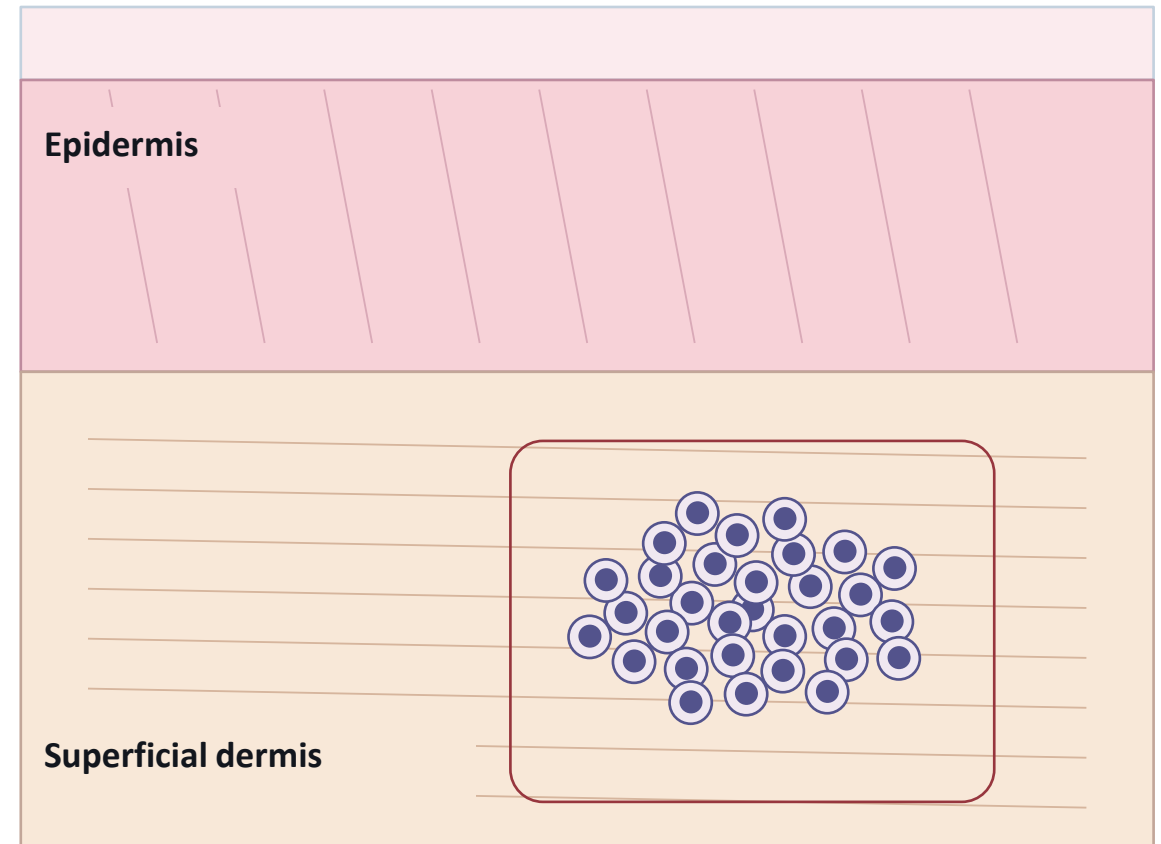
Schematic illustration — not a clinical or histologic specimen

Case 2: Plaques progress to a nodule

- Illustrative patient: Longstanding scaly plaques become raised and indurated.
- A cutaneous nodule subsequently develops.
- Biopsy of the nodule shows deeper dermal lymphoid growth with less epidermotropism.
- Question: Which feature indicates progression?

Case 2: Progression does not require epidermotropism

- Tumor-phase MF is favored by the nodular clinical lesion and deep dermal pattern.
- Epidermotropism can decrease in advanced nodules.
- Tumor nodules justify concern about more aggressive disease and spread.

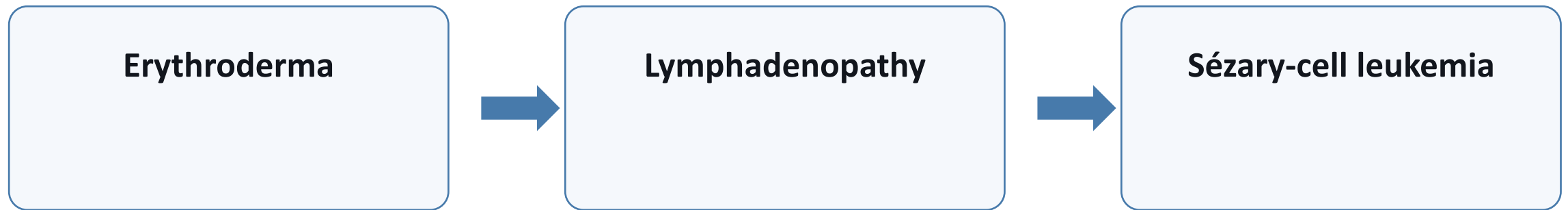


Deep dermal tumor mass
Schematic illustration — not a clinical or histologic specimen

Case 3: Erythroderma plus abnormal blood cells

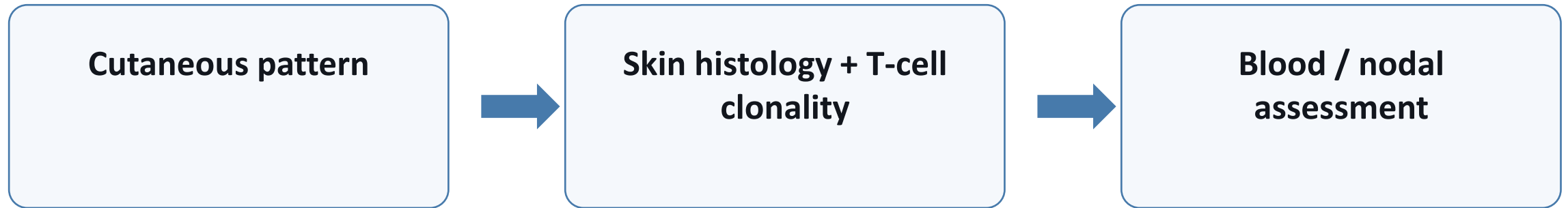
- Illustrative patient: Generalized exfoliative erythroderma.
- Generalized lymphadenopathy accompanies the skin eruption.
- Blood film reveals atypical T lymphocytes with markedly folded nuclear outlines.
- Question: Which T-cell neoplasm unifies all three sites?

Case 3: The defining triad identifies Sézary syndrome



- Diffuse erythroderma + generalized nodes + leukemic Sézary cells.
- The presentation is systemic from the clinical standpoint.
- It is not simply the ordinary plaque-to-tumor progression of MF.

A clinicopathologic reasoning map



Summary: Morphology that carries diagnostic meaning

- Patch and plaque MF: Epidermotropic atypical T cells + superficial dermal infiltrates.
- Pautrier microabscesses: Intraepidermal groups of malignant lymphocytes.
- Tumor-phase MF: Deep dermal growth; Epidermotropism may be lost.
- Sézary syndrome: Cerebriform leukemic lymphocytes accompanying erythroderma.

Summary: Two distinct clinical trajectories

Mycosis fungoides

- Long cutaneous course
- Patches → plaques → nodules
- Clinical dissemination mainly later

Sézary syndrome

- Diffuse exfoliative erythroderma
- Blood and node involvement
- Generally more aggressive

Principal references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Elsevier; 2026. Chapter 13, pp. 551–552.
- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Elsevier; 2026. Chapter 25, pp. 1044–1045.
- Clinical descriptions, molecular observations and prognosis are interpreted within the supplied textbook scope.