Mycosis Fungoides

Definition

- Mature T-cell lymphoma
- Presents in skin with patches/plaques
- Characterized by epidermal and dermal infiltration of small to medium-sized T-cells with cerebriform nuclei

Epidemiology

- Most common primary T-cell lymphoma of skin
- Incidence 0.29/100,000/year
- 0.5% of NHL
- Adults/elderly
- M:F = 2:1

Sites of involvement

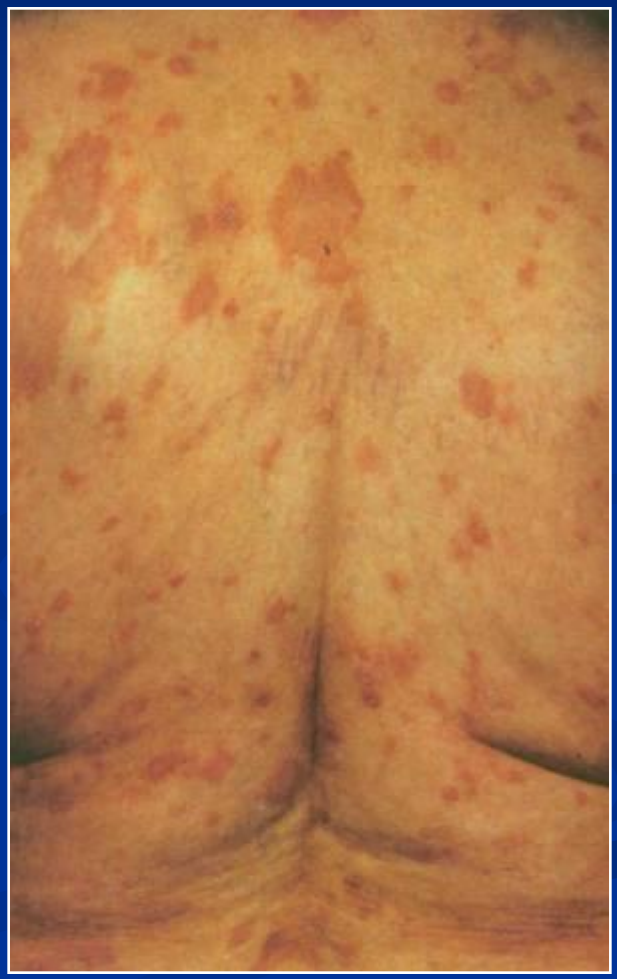
- Early stages
  - Limited to skin
- Advanced stages
  - Skin
  - Extracutaneous dissemination
    - LN
    - Liver
    - Spleen
    - Lungs
    - PB
    - BM (rare)

Clinical features

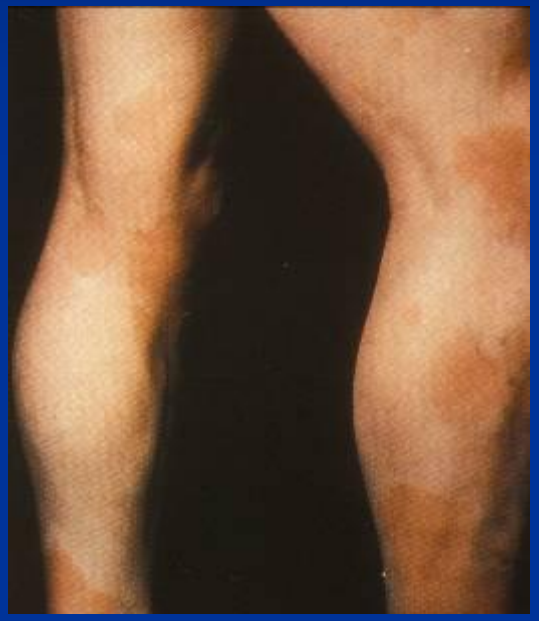
- Long natural history
- Non-specific scaly eruptions years before diagnostic histology develops

Clinical features

- Initial diagnostic lesions
  - Limited patches and/or plaques
    - Frequently on trunk
    - May persist for years
- Later diagnostic lesions
  - More generalized plaques
  - Tumors

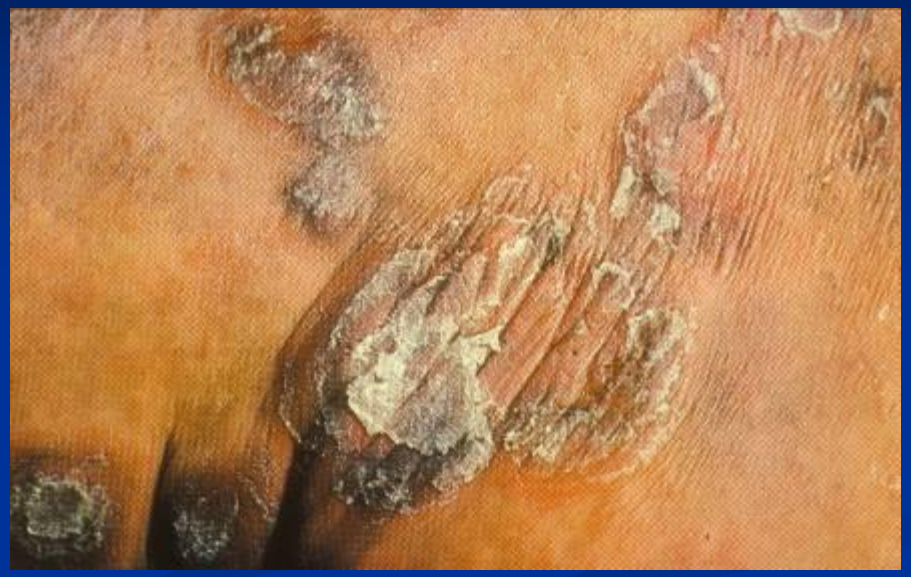


Mycosis Fungoides

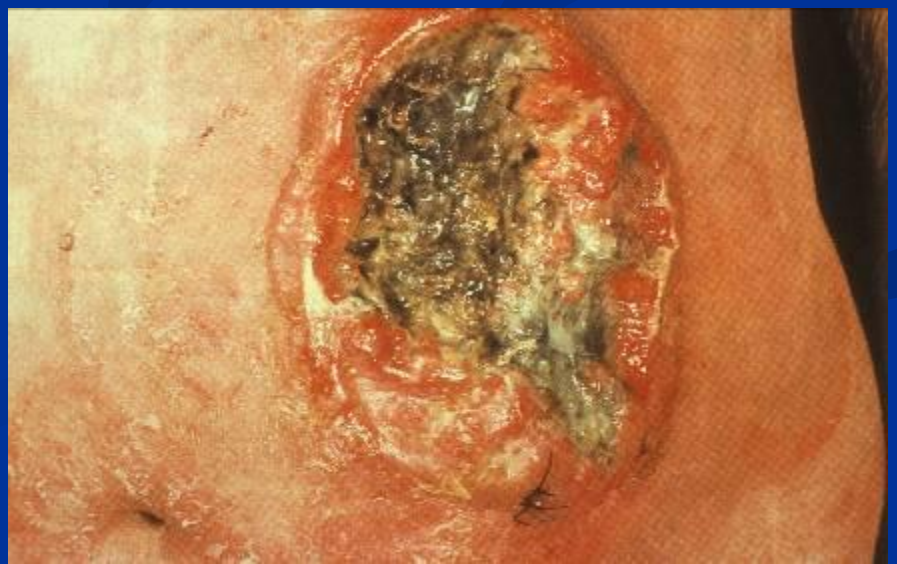


Early stage

Plaque stage

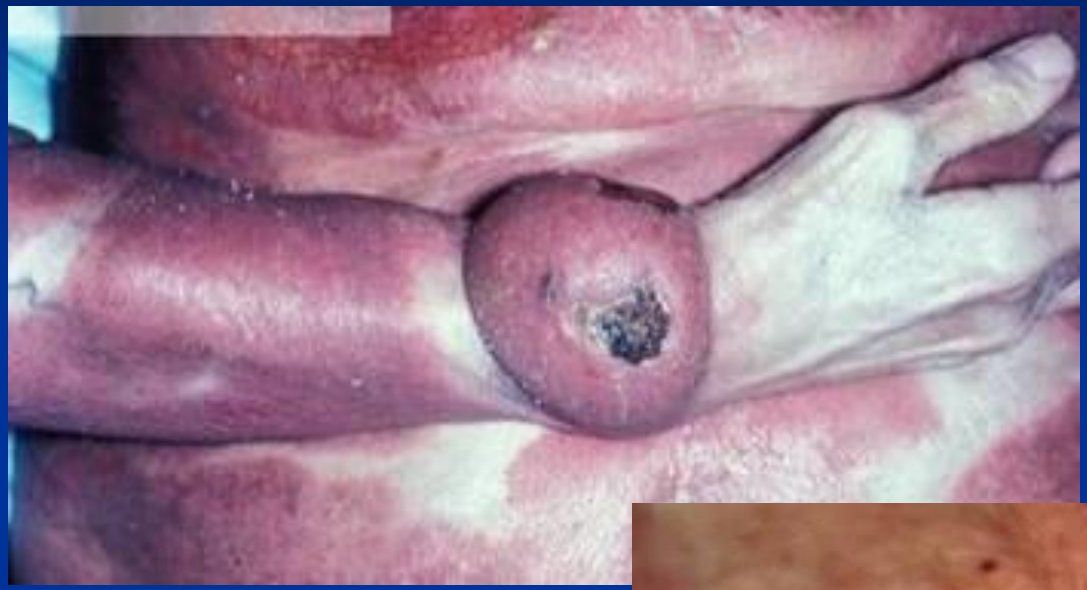


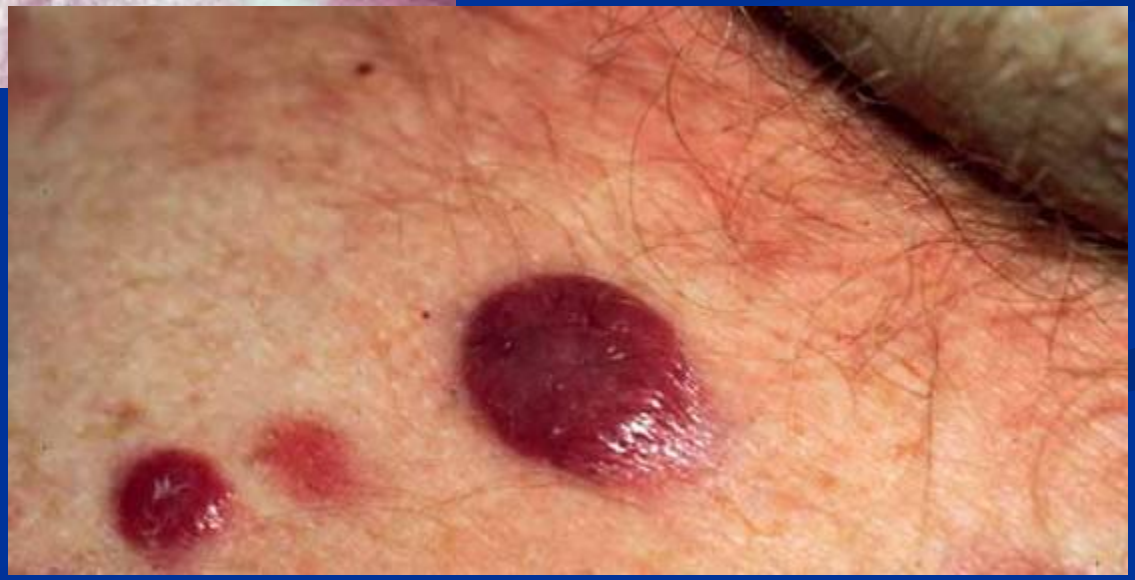
Tumor stage



Mycosis Fungoides

Tumor Stage





Clinical features

- Rare patients may develop generalized disease with erythroderma
  - May overlap with Sézary syndrome
- Extracutaneous dissemination
  - Late event
  - Predominantly in patients with extensive/advanced cutaneous disease

Clinical features

- D'emblée lesions
  - Skin tumors without a preceding patch/plaque stage
  - Rare
  - "not entirely well defined"
  - May represent other subtypes of T-cell lymphoma with preferential cutaneous infiltration

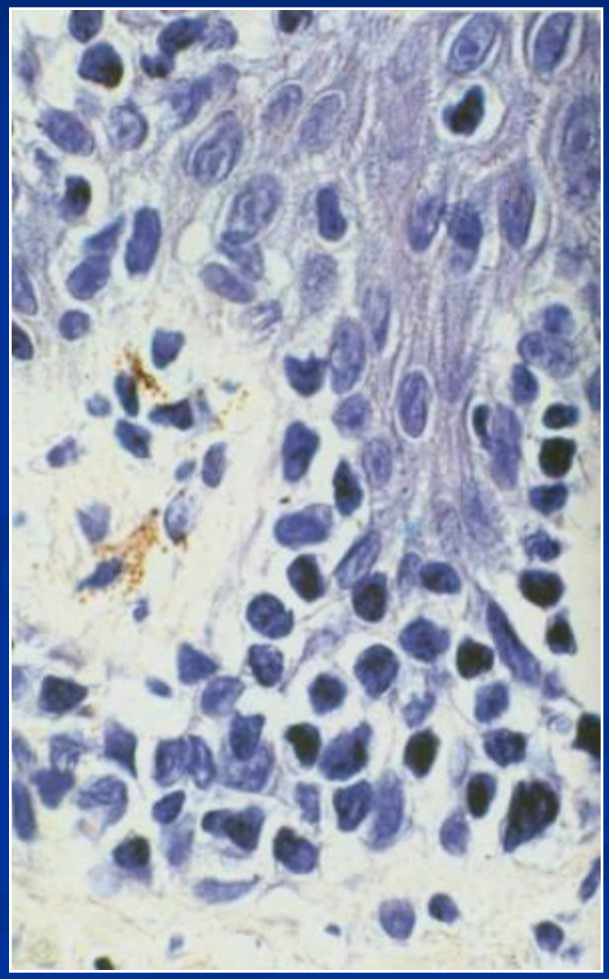
Etiology

- Unknown pathogenesis

- HTLV-1 (or similar virus) implicated in one series (Pancake et al. 1995)
  - 50 patients
  - Truncated proviral sequences similar to tax and/or pol detected by PCR in 30-90%
  - Majority of patients have antibodies to tax, but not to the structural proteins of HTLV-1
  - Whether the virus is the cause or secondary event is unknown
  - Not identified in a European series

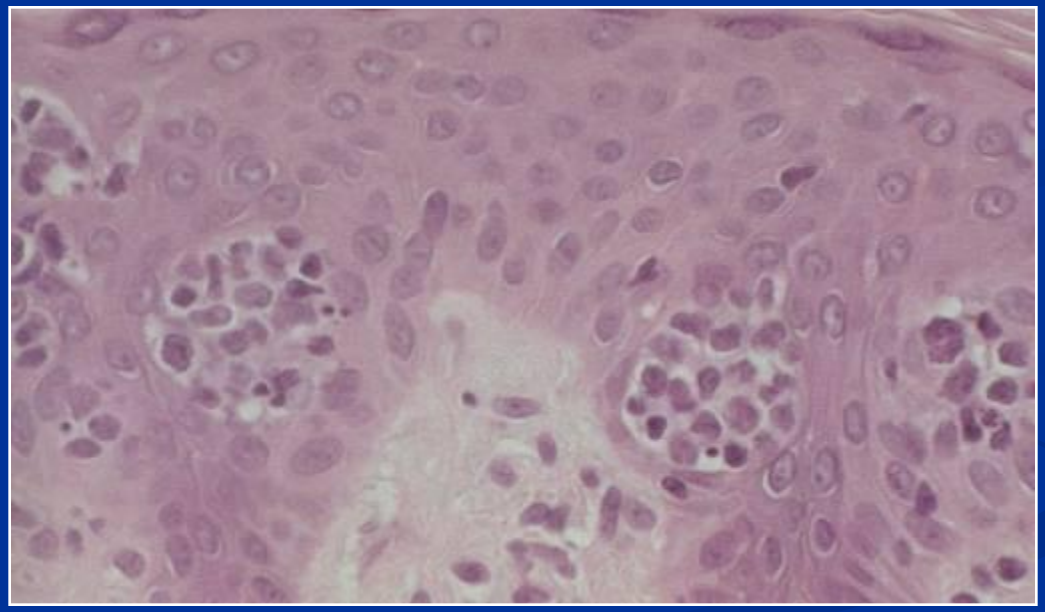
Morphology

- Epidermotropism
  - Small to medium-sized cells with irregular (cerebriform) nuclei
  - Larger cells with similar nuclei (minority)
  - Involvement with single cell exocytosis is most common form of epidermotropism

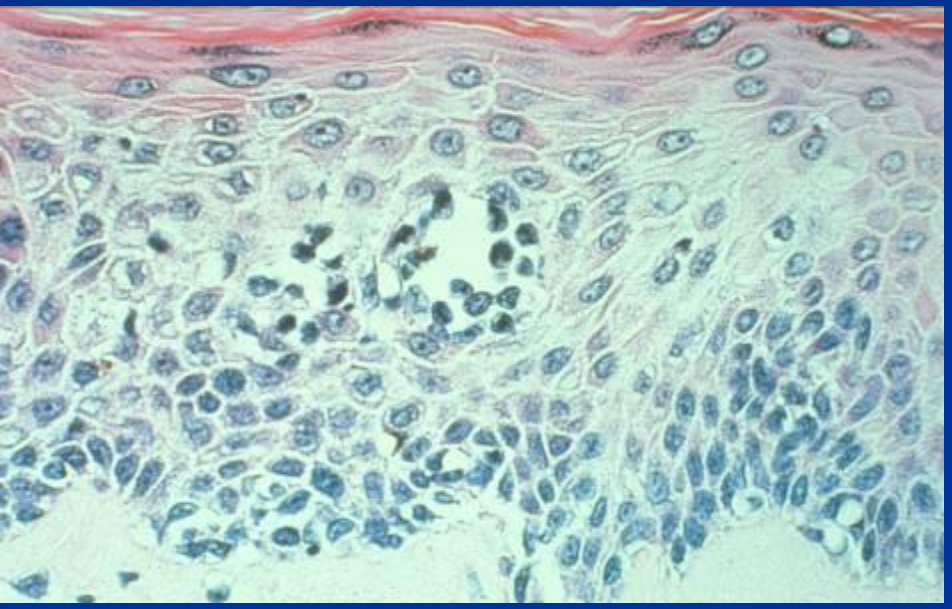


Morphology

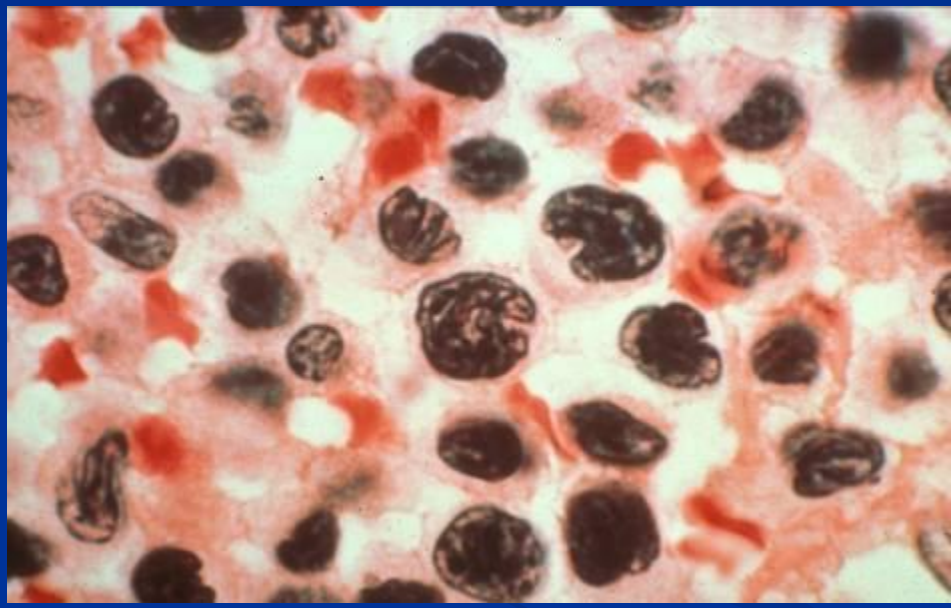
- Pautrier microabcesses
  - Only seen in a proportion of cases
  - Highly characteristic



Mycosis Fungoides

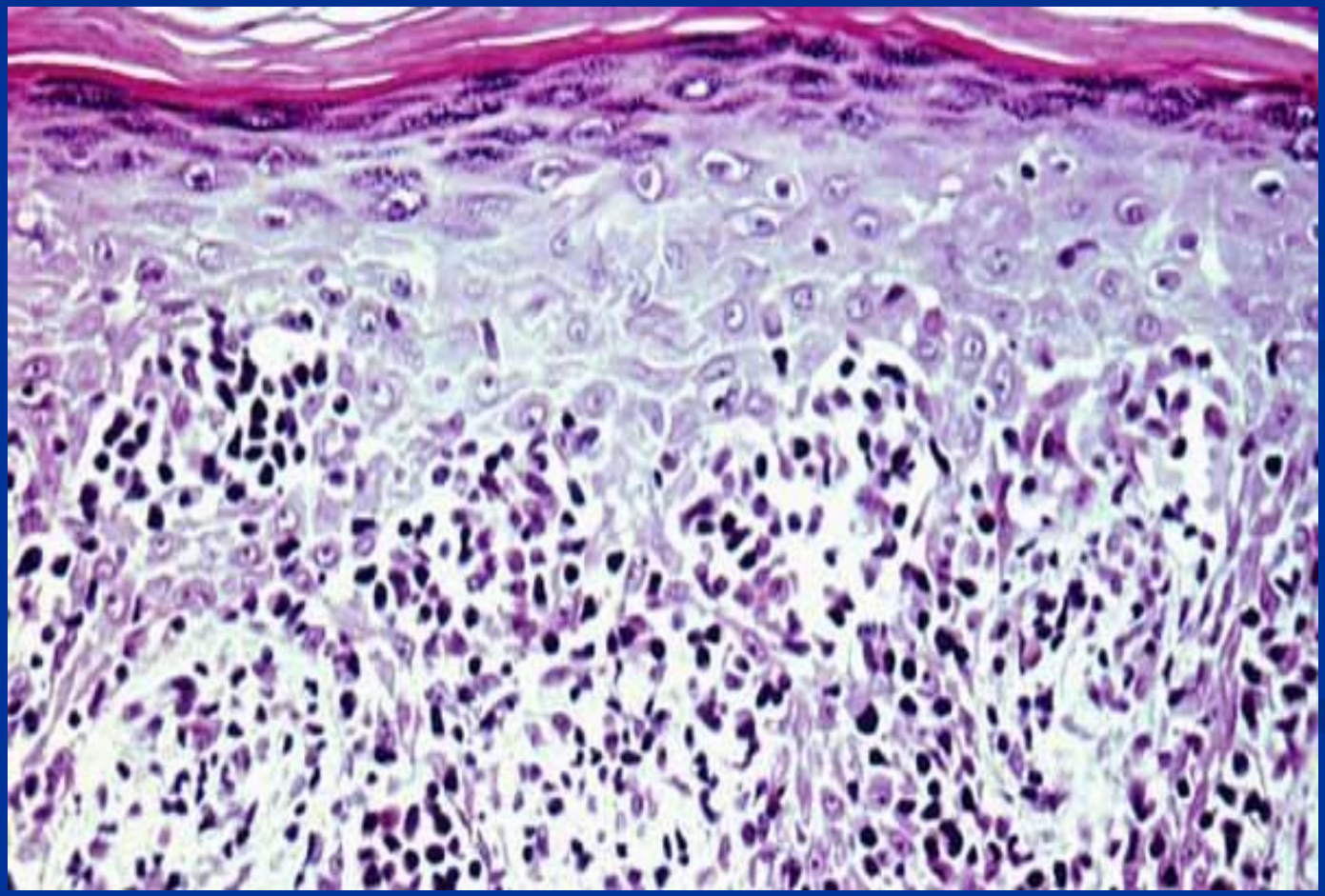


Epidermis with Pautrier microabscess



Atypical lymphoid cells

Mycosis Fungoides
Pautrier Microabscesses



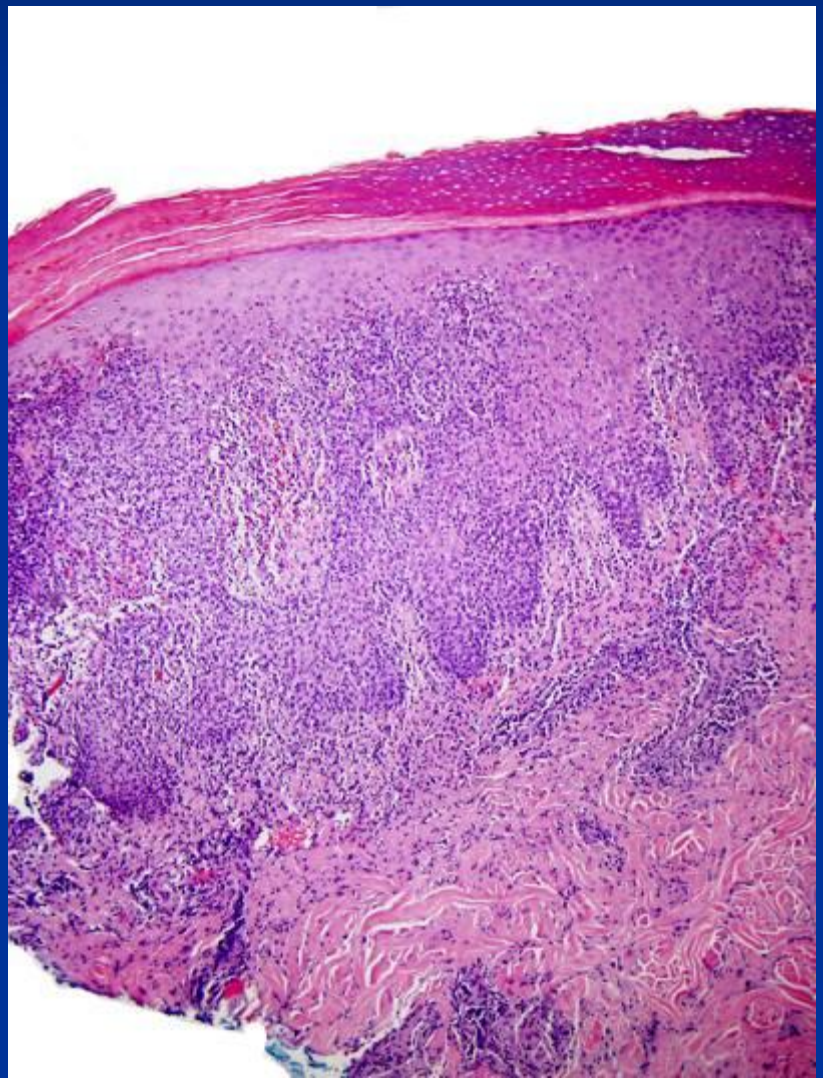
Morphology

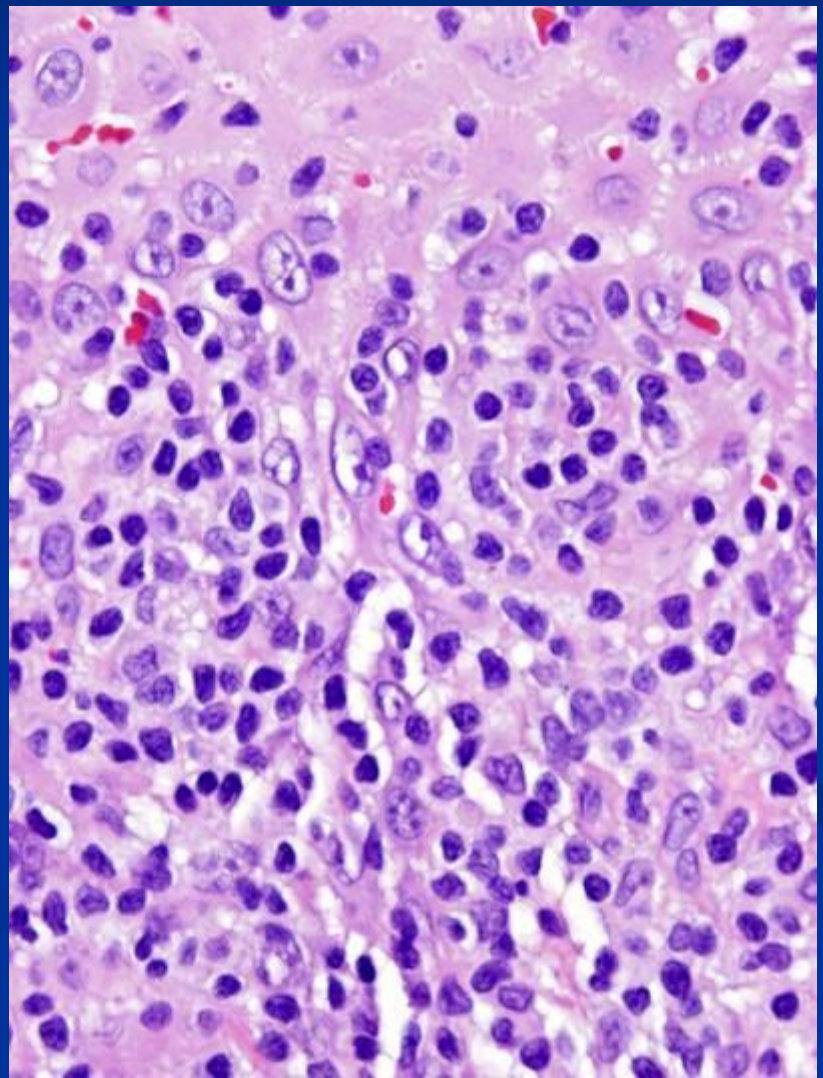
- Dermal infiltrates
  - Patchy
  - Band-like
  - Diffuse
  - Often associated with inflammatory infiltrate of small lymphocytes and eosinophils

Morphology

- Patch
  - Sparse infiltrate of lymphocytes spread along the papillary dermis
  - Only slight cytological atypia

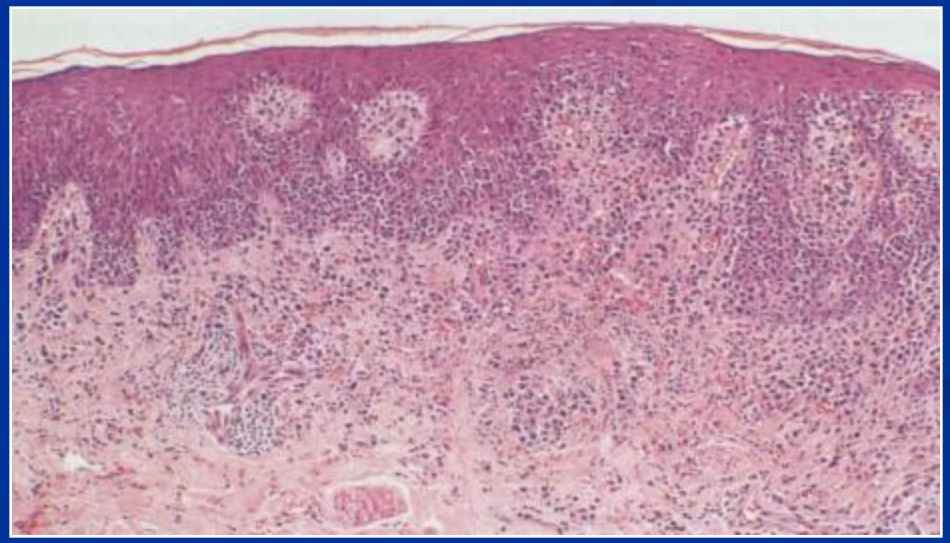
Mycosis Fungoides





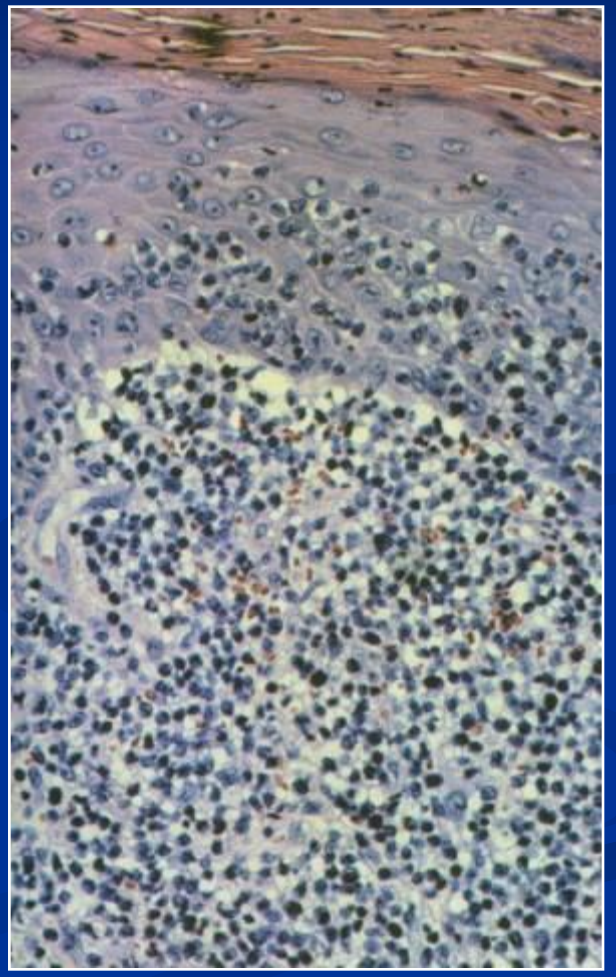
Morphology

- Plaque
  - More dense infiltrate of atypical lymphocytes that can extend around the adnexae
  - Atypical lymphocytes are more common
    - 10-30 μm in diameter
    - Prominent nuclear convolutions (cerebriform)



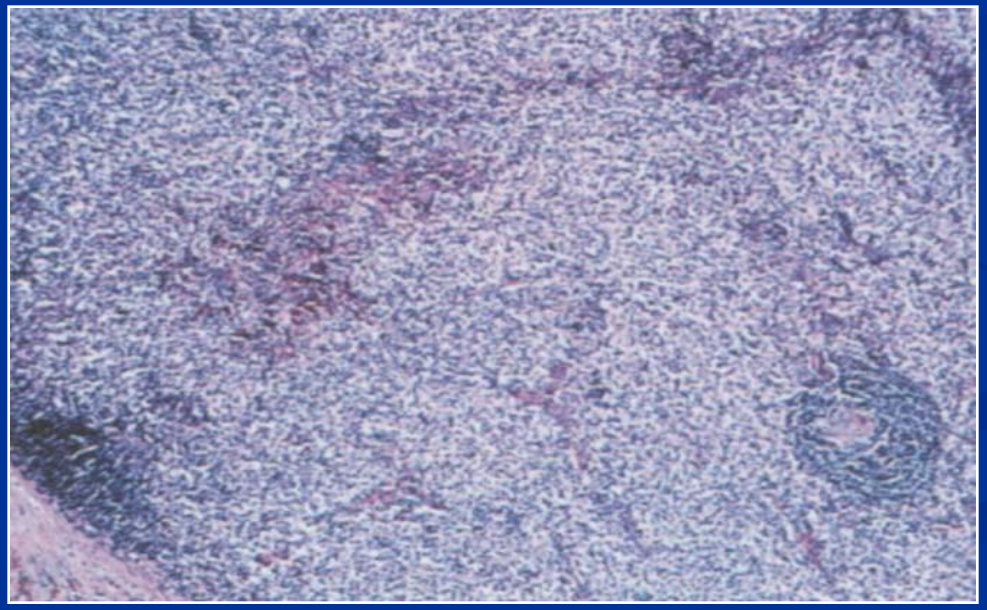
Morphology

- Tumor
  - Involvement of entire dermis +/- subcutis
  - Infiltrate of larger atypical lymphocytes



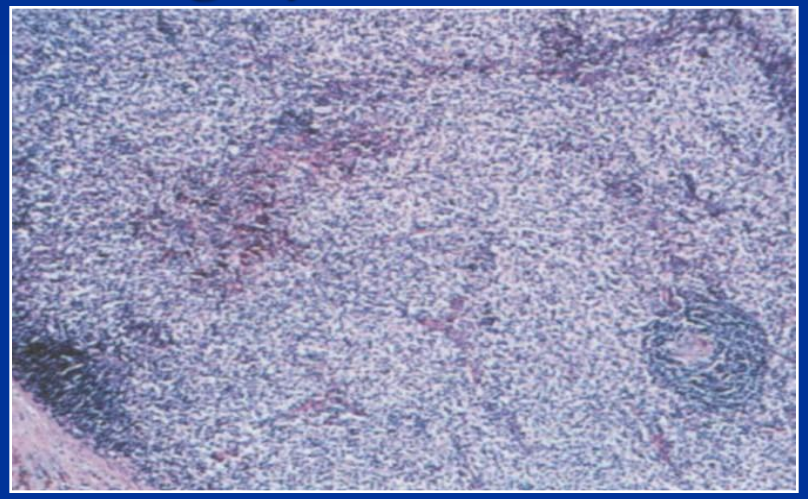
Morphology

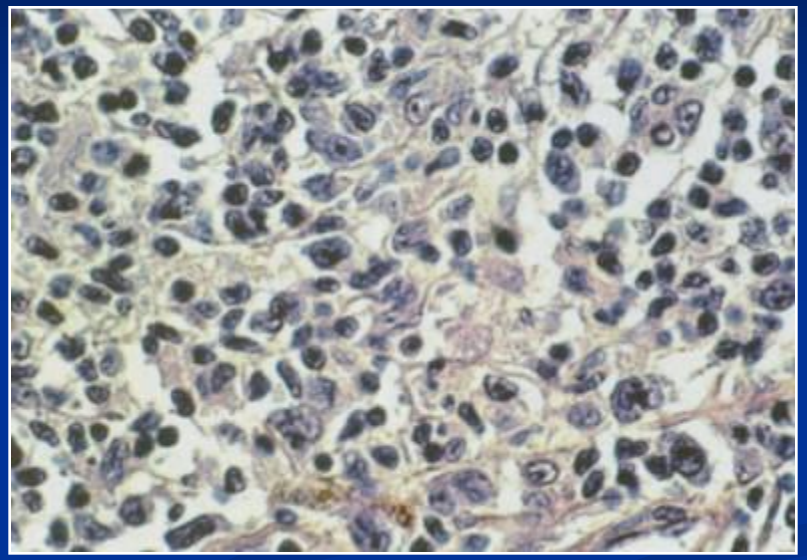
- LN involvement
  - Dermatopathic lymphadenopathy
    - Paracortical expansion due to the presence of large number of histiocytes and interdigitating cells

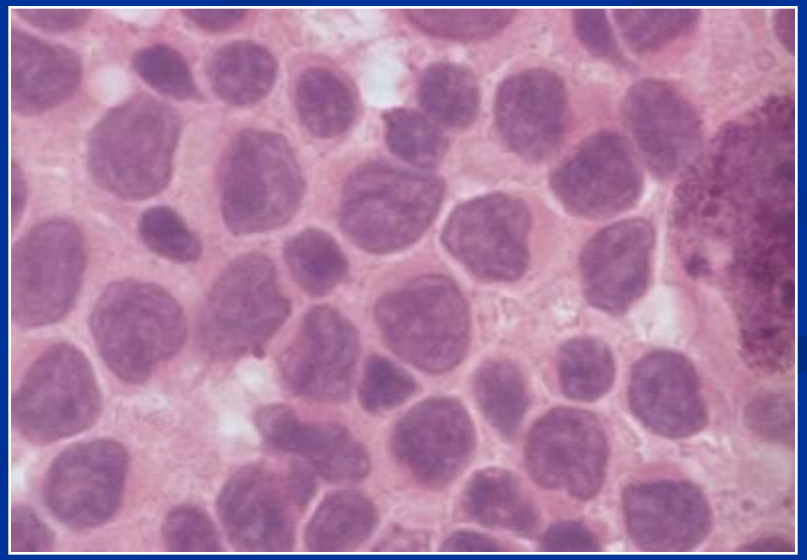


Morphology

- LN involvement, category II







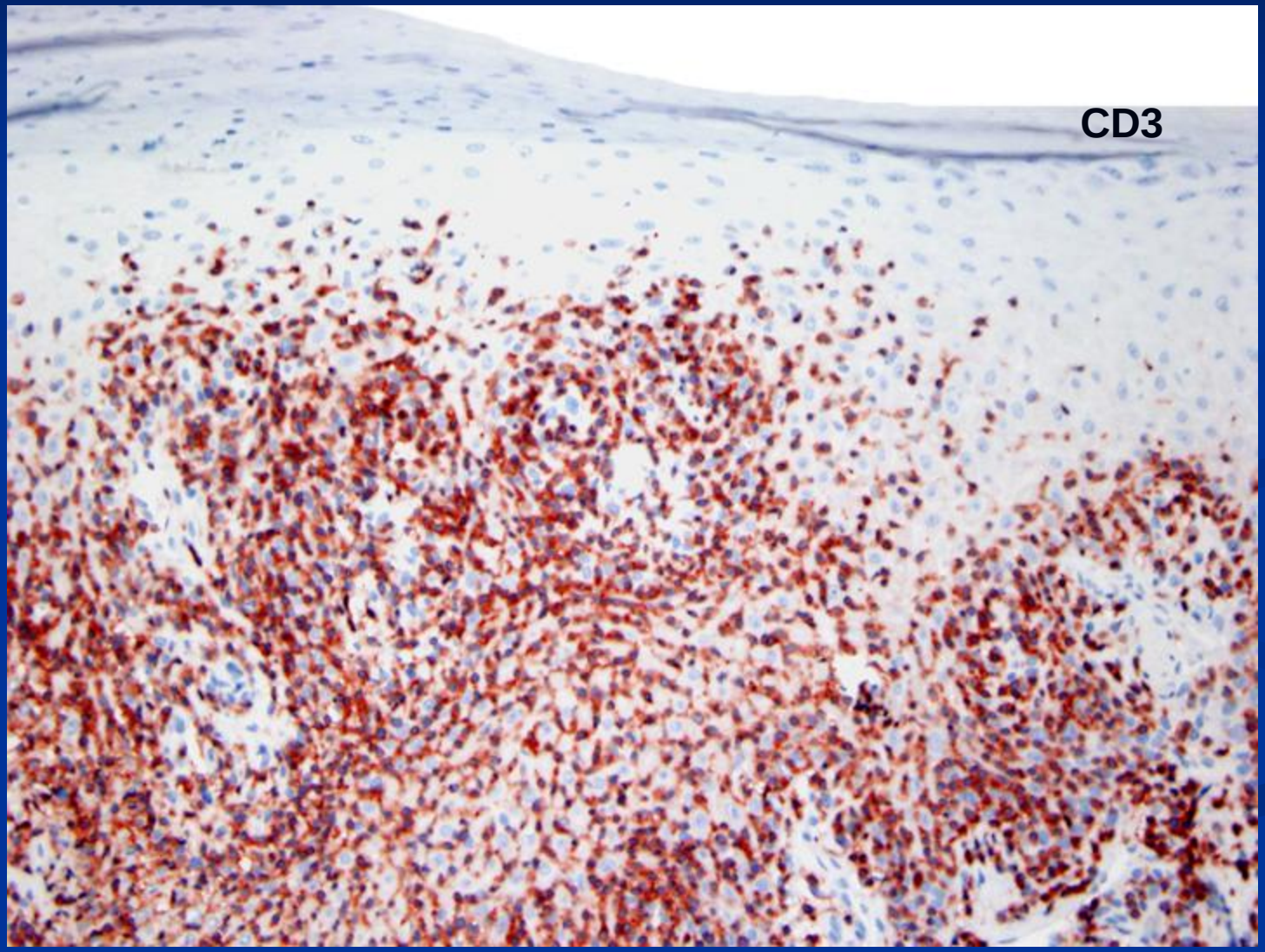
Morphology

- LN involvement
  - Clonal T-cells present in
    - Majority of category II and III lesions
    - Occasionally in category I lesions
  - Presence of clonal T-cells may be associated with unfavorable outcome

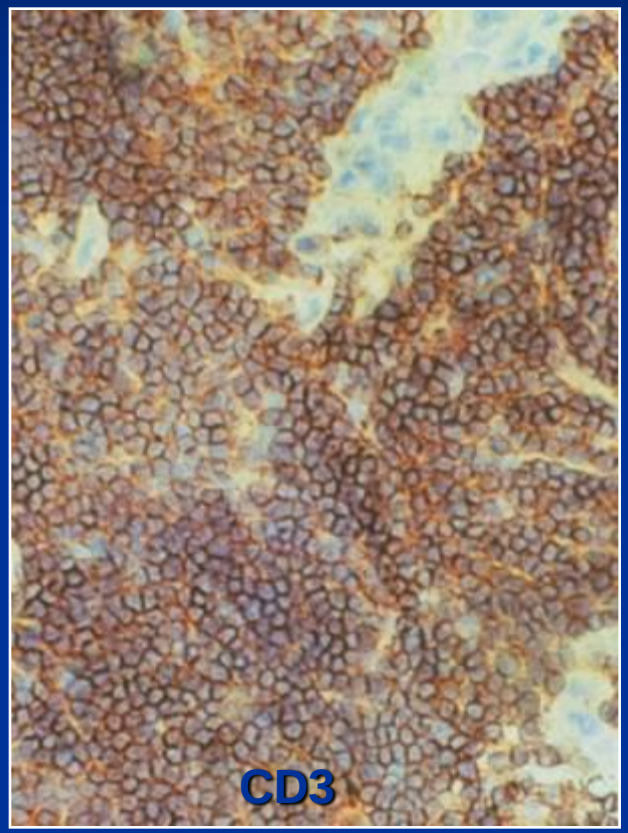
Immunophenotype

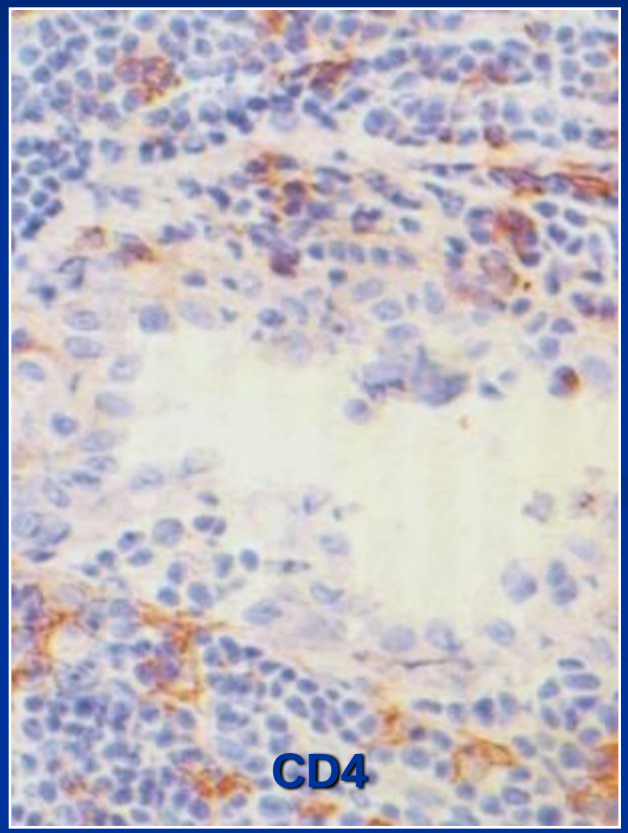
- CD2/3/4/5 and TCRβ positive
- HECA antigen (associated with lymphocyte homing to skin) positive in most cases
- CD7/8 negative
- Cytotoxic granule associated proteins negative in early patch/plaque lesions

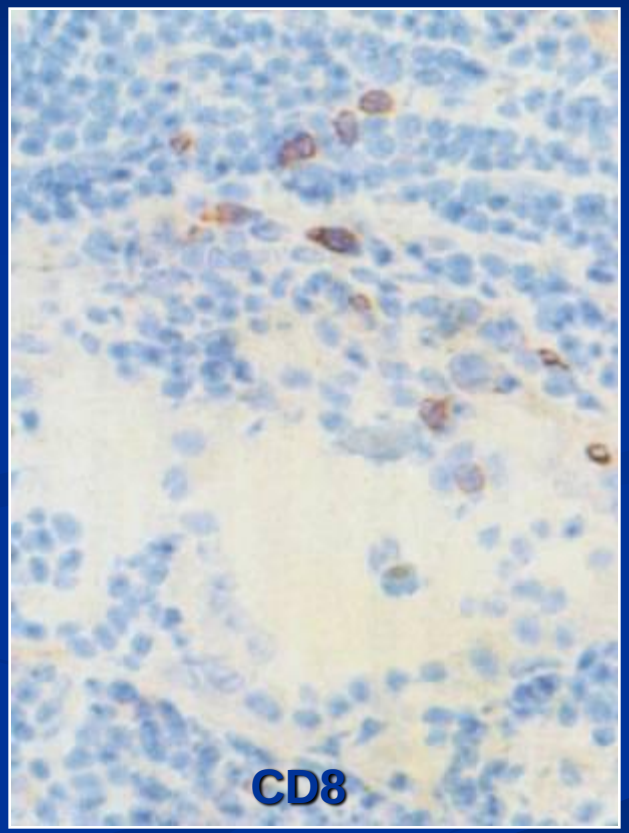
Mycosis Fungoides



Immunophenotype







CD4 negative
(most cases positive)

Genetics

- TCR clonally rearranged
- Inactivation of CDK2A/p16 and PTEN identified in two studies
- Complex karyotypes present in many patients (particularly in advanced stages)
- No specific chromosomal abnormality identified

Prognosis

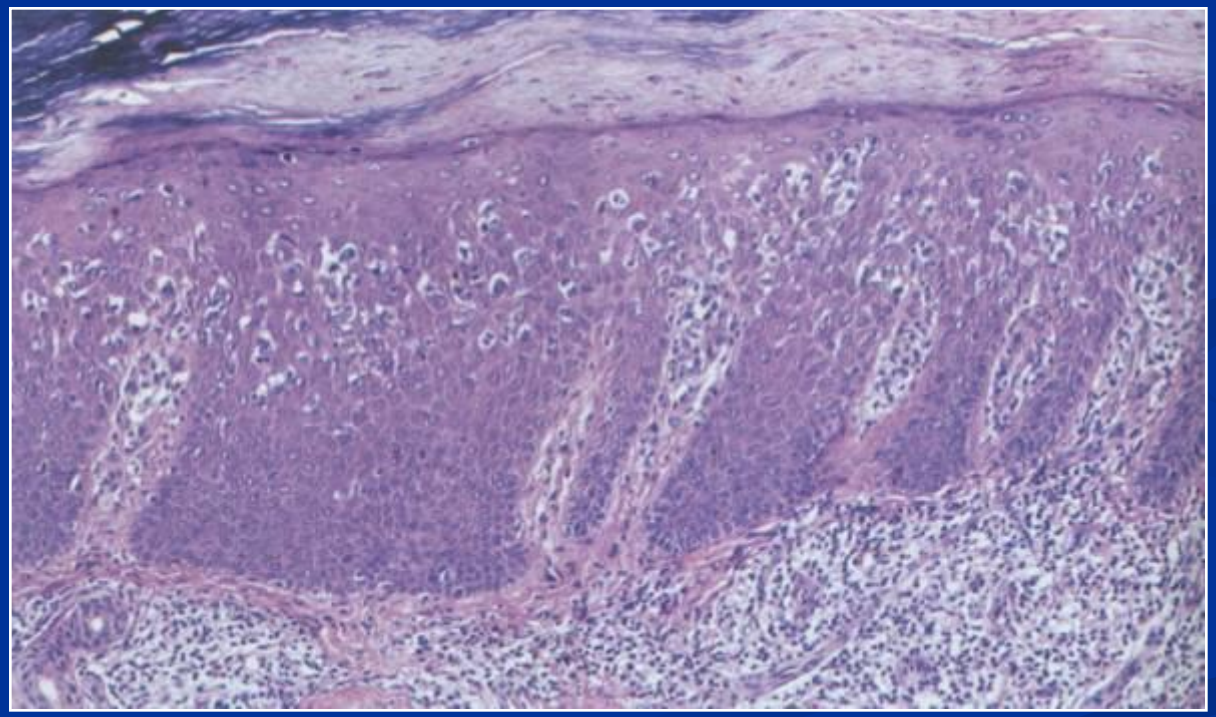
- Most important prognostic factor is clinical stage
- Limited disease
  - Excellent prognosis
  - Survival similar to general population
- Advanced stages: poor prognosis, especially with
    - Skin tumors
    - Extracutaneous dissemination

Prognosis

- Other adverse prognostic indicators
  - Age > 60 years
  - Elevated LDH
  - Transformation to a large T-cell lymphoma

MF Variants

- Pagetoid reticulosis
  - Infiltrate is strictly epidermal



MF Variants

- Pagetoid reticulosis
  - Distinguish between
    - Woringer-Kolopp disease (localized skin lesions)
    - Ketron-Goodman disease (multiple skin lesions

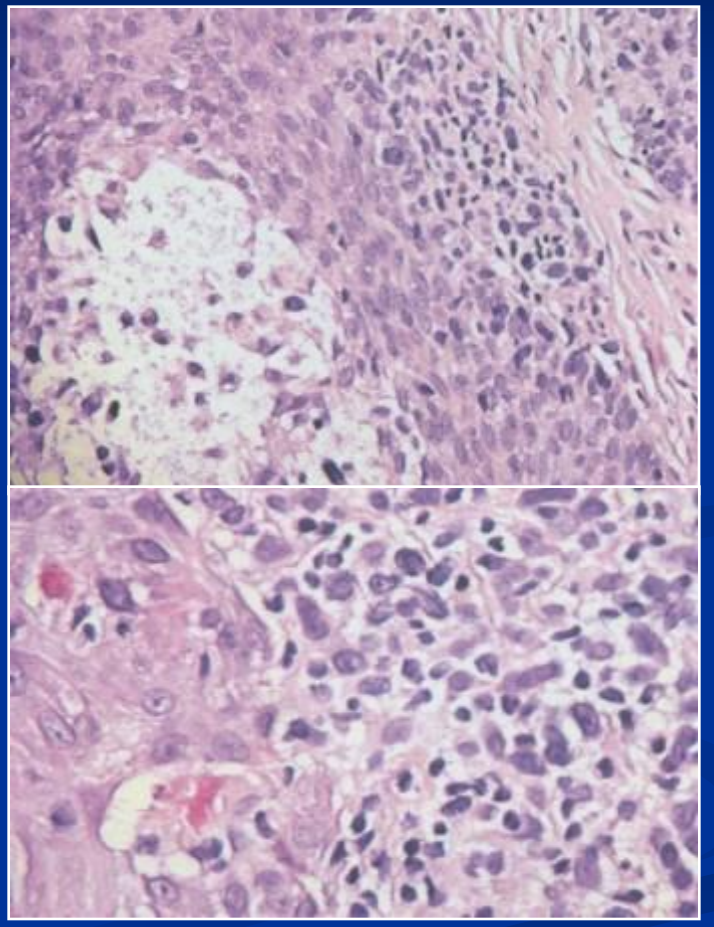
      [It is generally recommended that the designation be restricted to the localized variants which have an excellent prognosis]

MF Variants

- Pagetoid reticulosis
  - Cerebriform neoplastic T-cells
  - Often CD30 positive
  - CD4+/CD8- or CD4-/CD8+ or CD4-/CD8-
  - TCR rearrangement in some cases

MF Variants

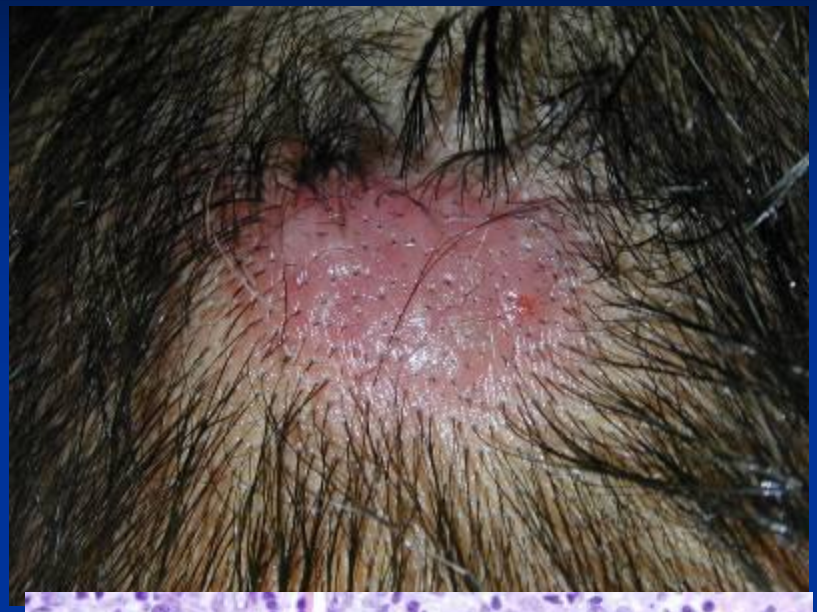
- MF-associated follicular mucinosis
  - Rare
  - Follicular (rather than epidermal) infiltrates of cerebriform T-cells
  - Mucinous degeneration of hair follicles

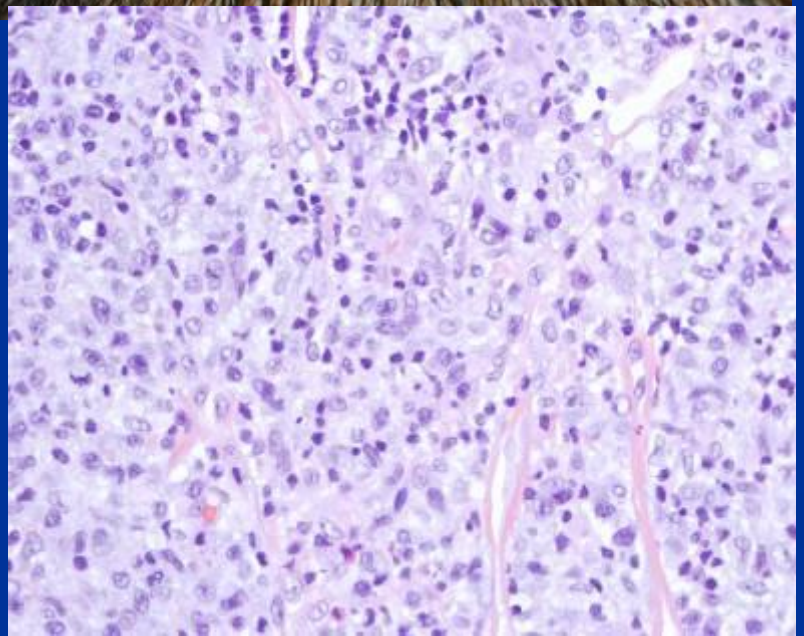


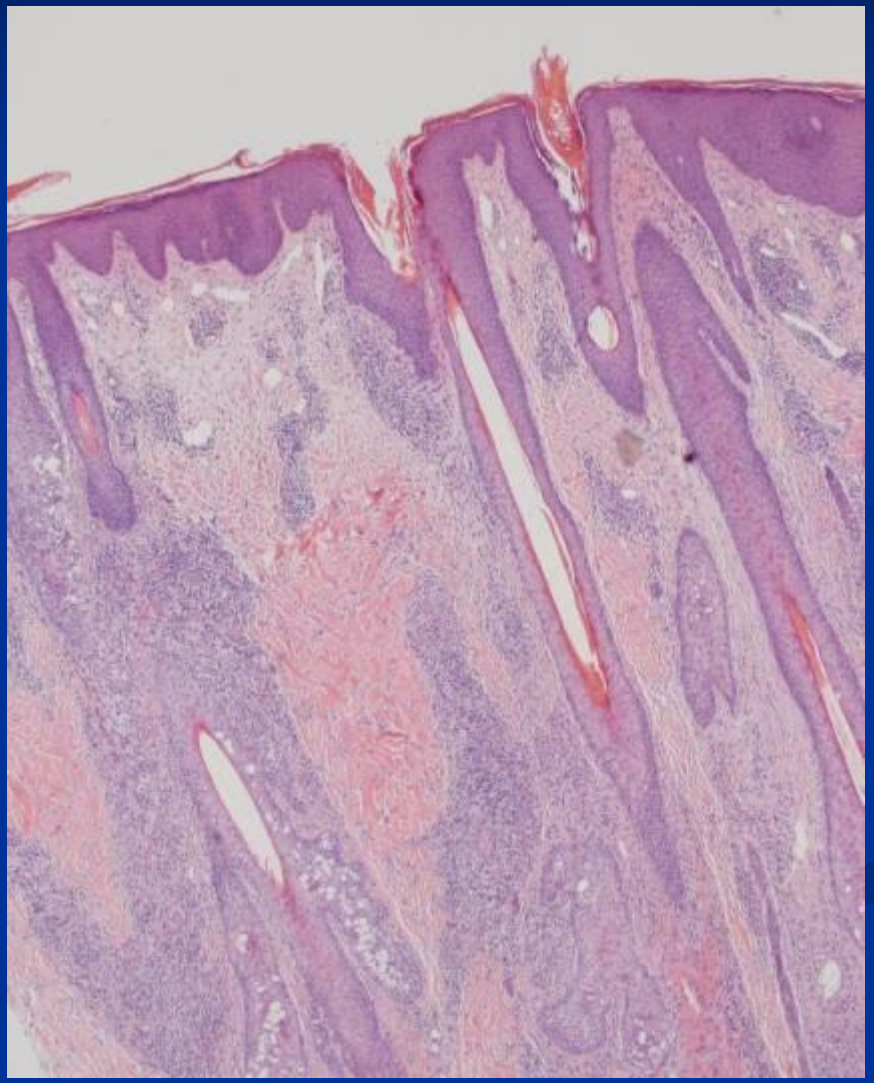
MF Variants

- MF-associated follicular mucinosis
  - Head and neck
  - TCR clonal rearrangement in most cases
  - Indolent (but slightly less favorable prognosis than MF)

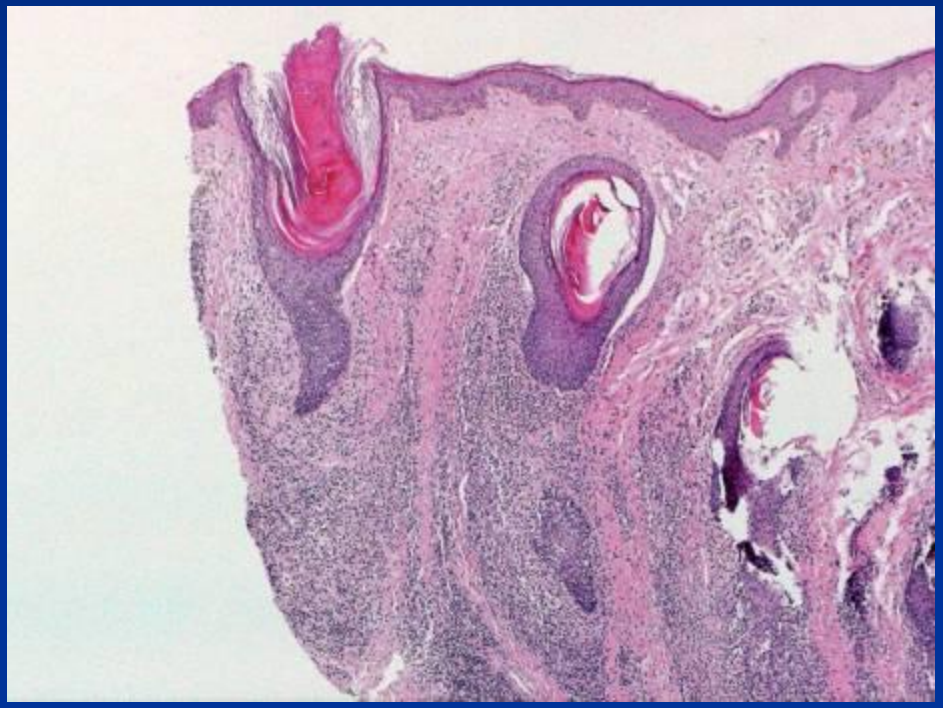
Mycosis Fungoides-associated Follicular Mucinosis

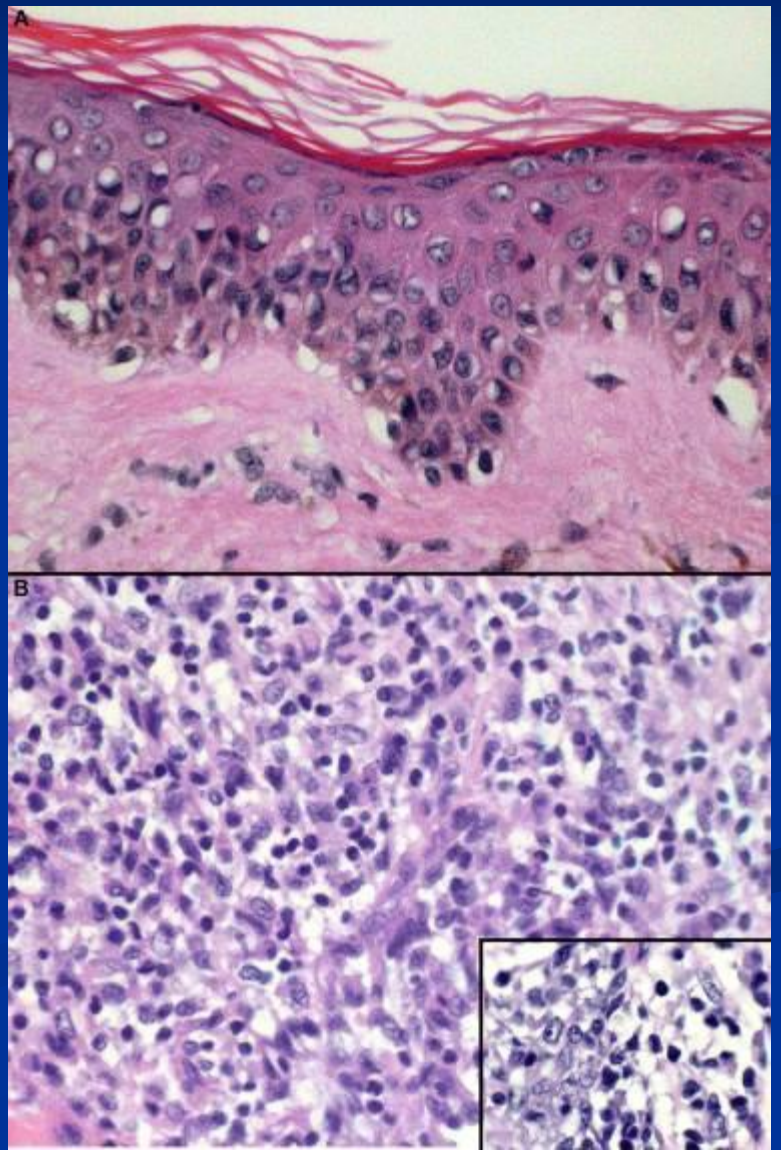






Mycosis Fungoides-Associated Follicular Mucinosis

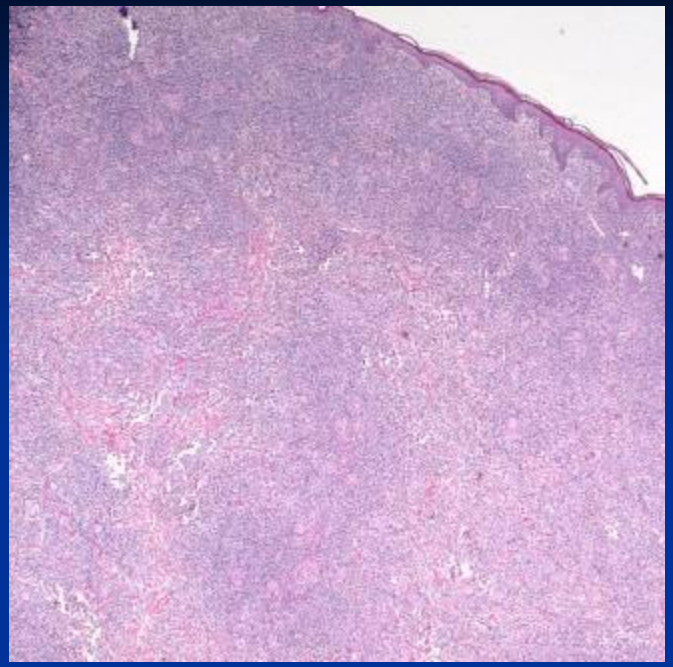


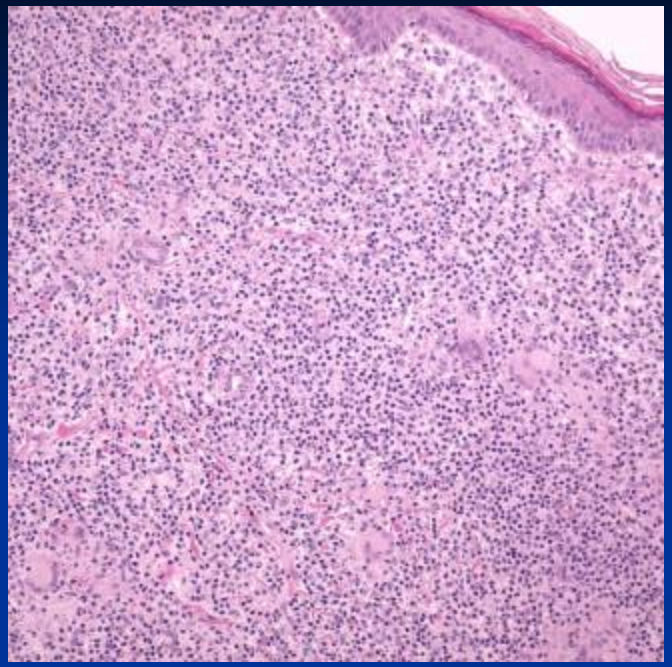


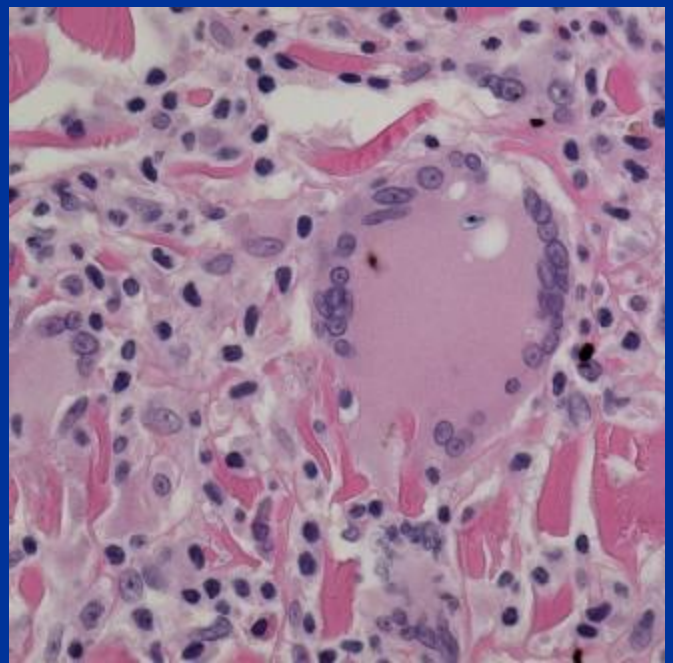
Mycosis Fungoides
Granulomatous Slack Skin Disease

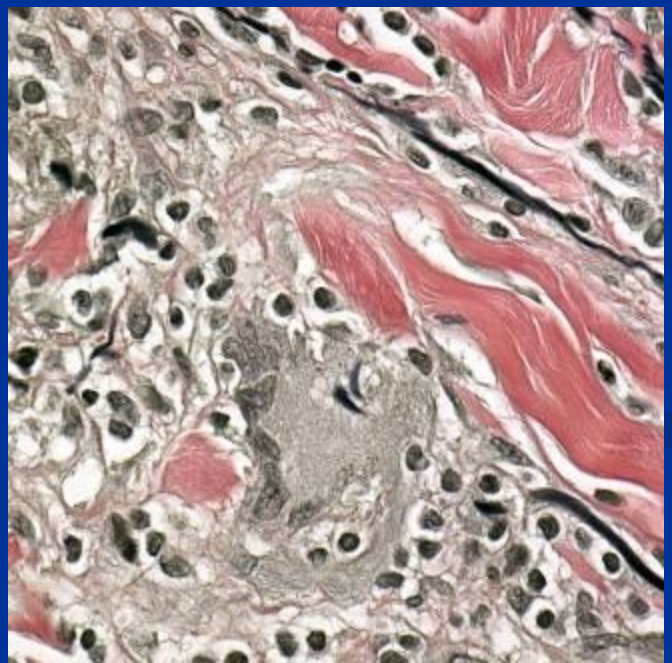
- May be seen with other types of lymphoma (e.g., Hodgkin) and may be separate entity
- Slowly developing folds of atrophic skin
- Preferentially involves axillae or groin
- Granulomatous infiltrate with atypical T lymphocytes, macrophages, multinucleated giant cells
- Elastophagocytosis

Granulomatous Slack Skin Disease









Sézary Syndrome

Definition

- Generalized mature T-cell lymphoma
- Characterized by
  - Erythroderma
  - Lymphadenopathy
  - Neoplastic T-lymphocytes in PB (cerebriform)
- MF variant, but behavior is much more aggressive

Epidemiology

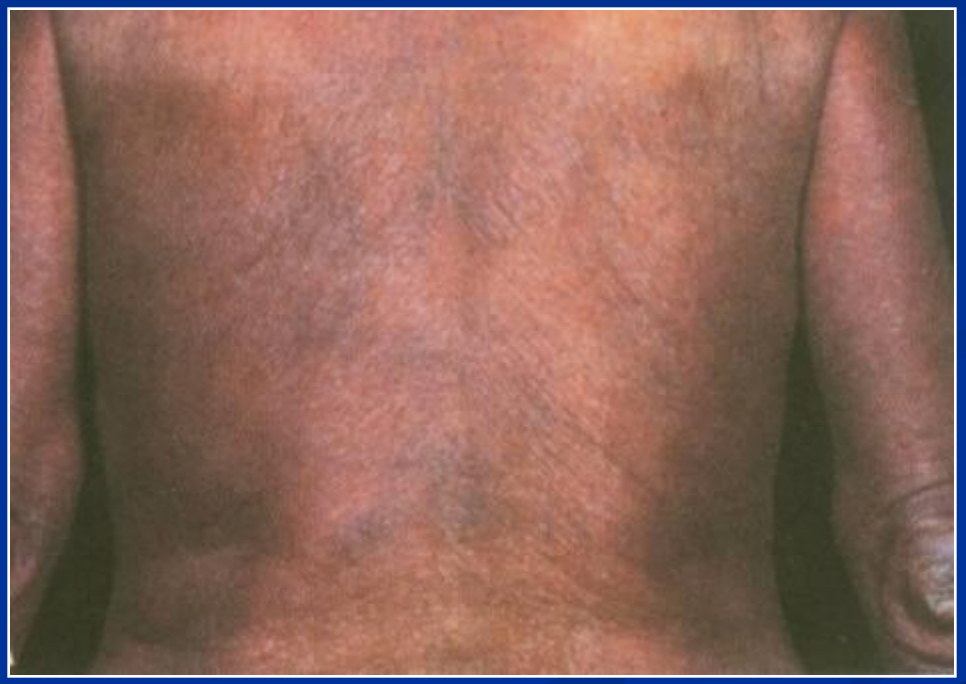
- Rare
- Exclusively in adults

Sites of involvement

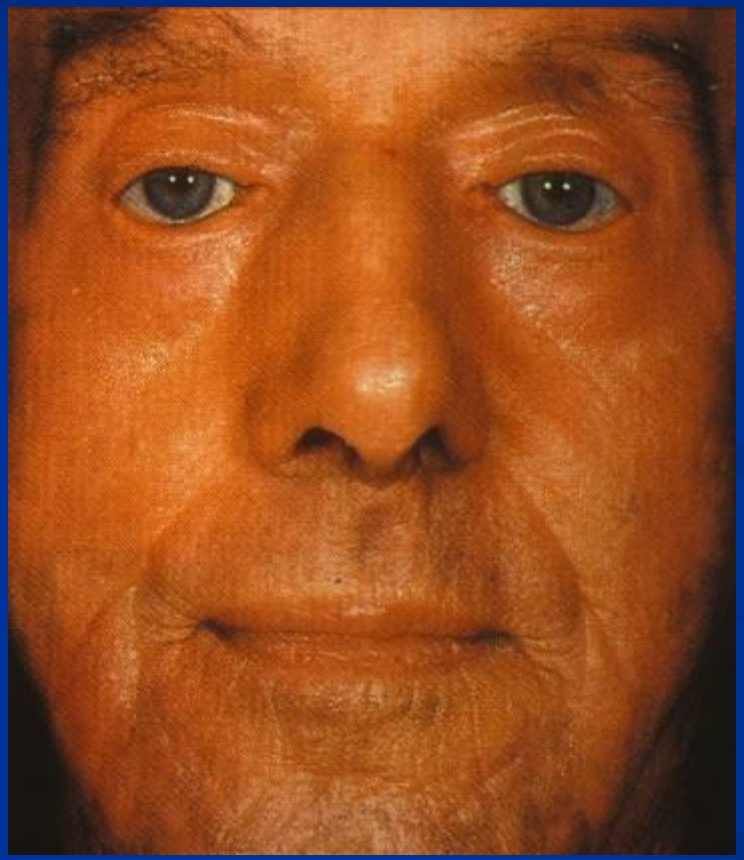
- Generalized disease with involvement of
  - Skin
  - LN
  - PB
  - Visceral organs, in the terminal stages
- BM often spared

Clinical features

- Patients present with
  - Erythroderma
  - Generalized lymphadenopathy
  - Pruritis
  - Alopecia
  - Palmar or plantar hyperkeratosis
  - onychodystrophy

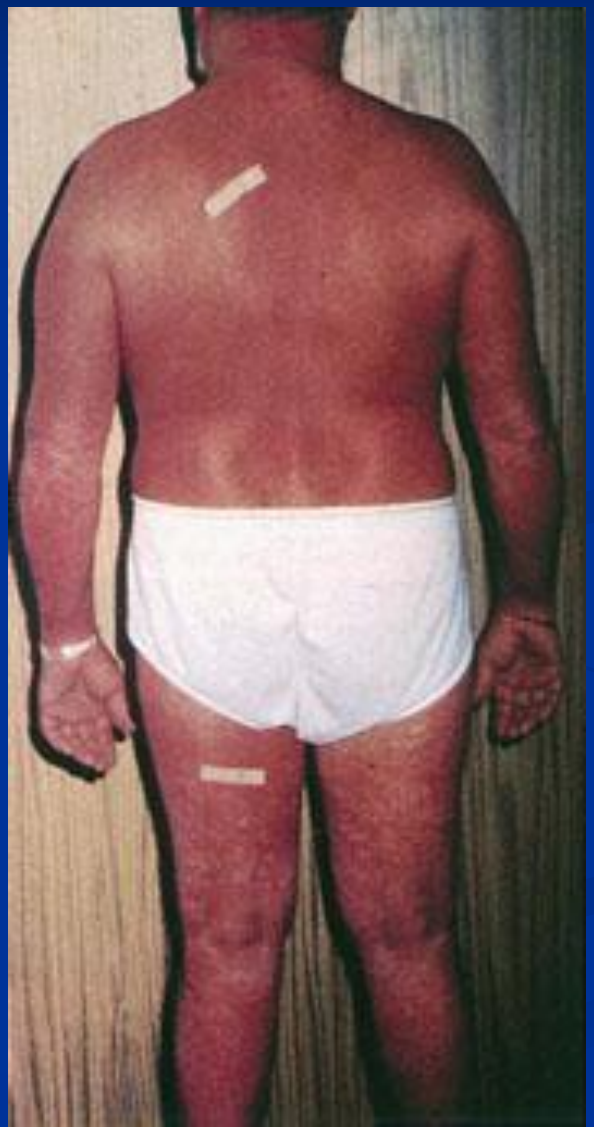


Sezary Syndrome



Diffuse erythroderma

Sezary Syndrome
Diffuse Erythroderma



Etiology

- Unknown pathogenesis
- Association with HTLV-1 is controversial

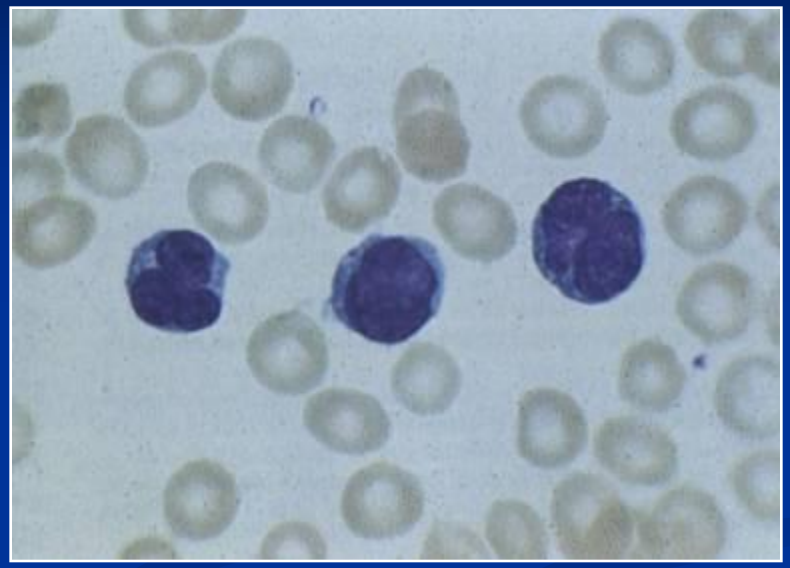
Morphology

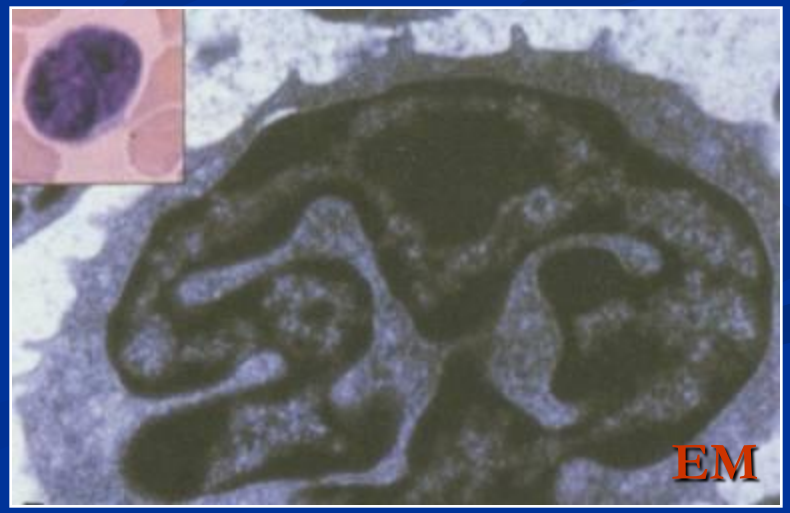
- Skin lesions are similar to MF with dermal and epidermal infiltrates of cerebriform T-lymphocytes

- LN
  - Effaced architecture
  - Paracortical or diffuse infiltrates
  - With or without changes of dermatopathic lymphadenopathy

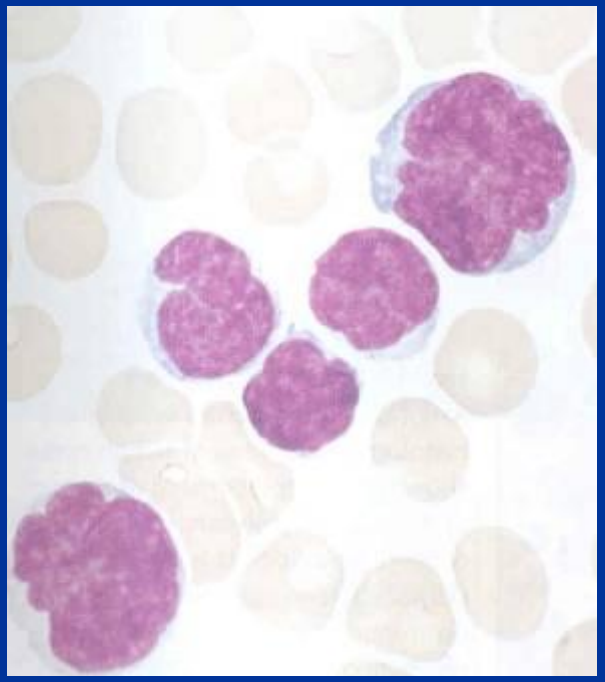
Morphology

- Neoplastic cells in PB
  - Markedly convoluted nuclei
  - Predominantly small (Lutzner cells), or large (classical Sézary cells), or mixture of both





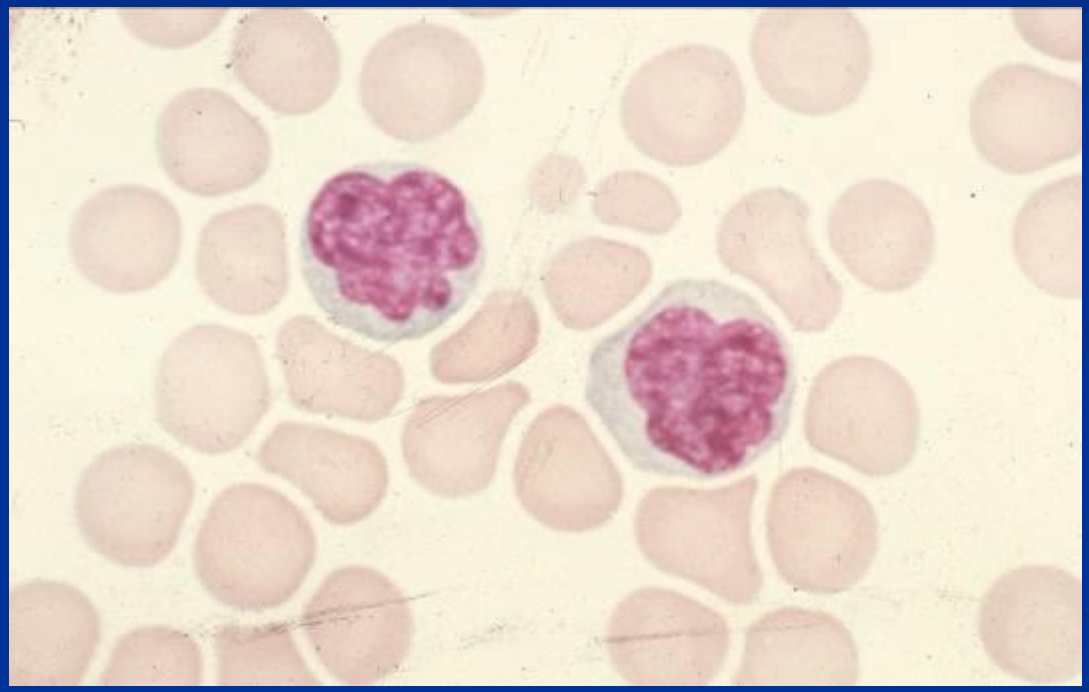
Sezary syndrome



Cells with convoluted nuclei

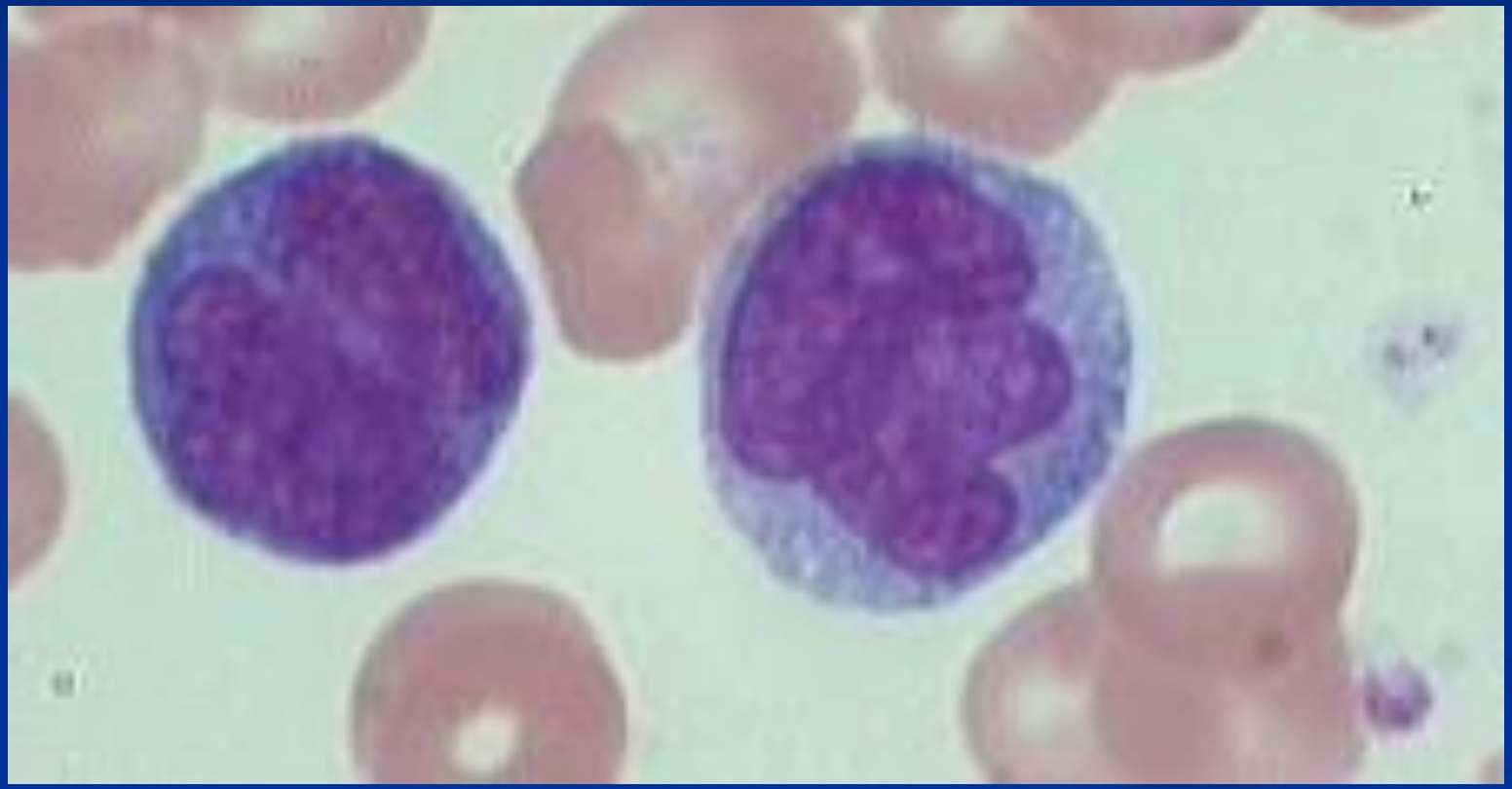
Cebebriform nuclei (EM)

Sezary Syndrome



Sezary cells in peripheral blood

Sezary Syndrome



Morphology

- Neoplastic cells in PB
  - No consensus on degree of lymphocytosis
  - Most studies require ≥1000 Sézary cells per mm^3

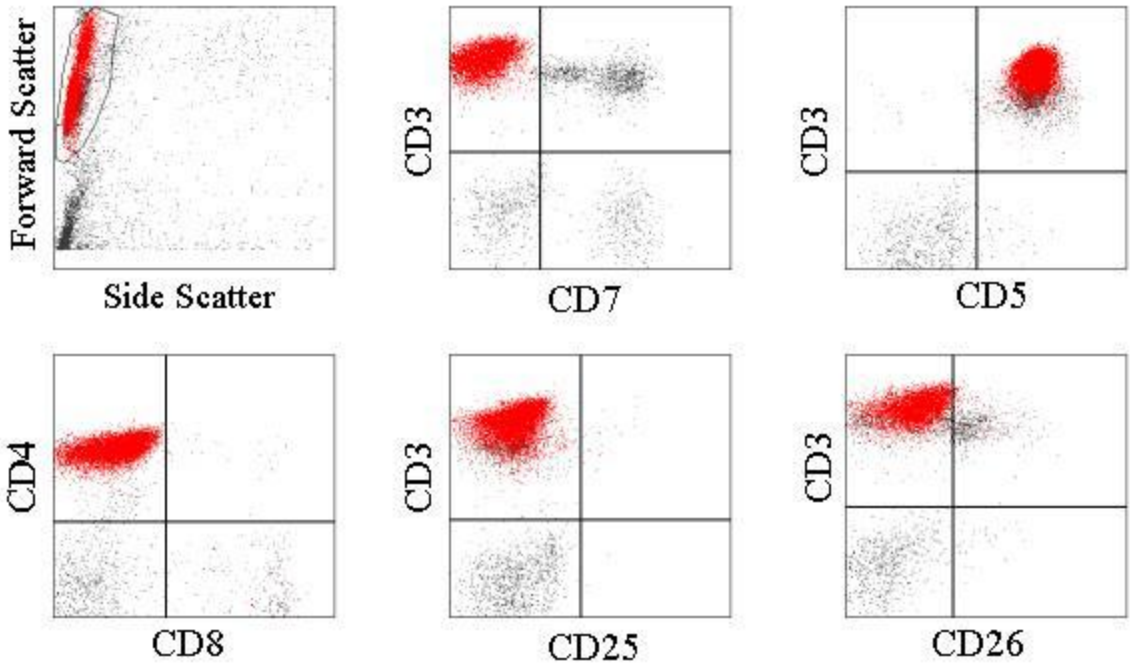
Morphology

- BM infiltrates
  - Sparse
  - interstitial

Immunophenotype

- CD2/3/5 and TCRβ positive
- CD4 positive in most cases
  - Elevated CD4/CD8 ratio
  - Increased proportion of CD4(+)/CD7(-) T cells
- CD8 expression is rare
- Aberrant T-cell phenotypes are common

Sezary Syndrome: Flow Cytometry



Genetics

- TCR clonally rearranged
- Complex karyotypes present in many patients
- No specific cytogenetic abnormality identified

Prognosis

- Aggressive disease
  - 10-20% 5 year survival rate
- May transform to a large T-cell lymphoma as a terminal event