

# Overview of Cutaneous Lymphomas

## Diagnosis, Staging, and Prognosis

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# Agenda

- Overview of cutaneous T and B- cell lymphomas
  - Diagnosis, Staging, Prognosis
- Multidisciplinary care model

FEELING SICK



HAIR LOSS



Fig. 1

CHEMOTHERAPY

# Cutaneous lymphoma stats

- Classified as NHLs by WHO
- Skin is #2 most common site of involvement by extranodal NHL
- Overall incidence approx 1:100,000
- CTCL more common than CBCL



McKee et al.: Pathology of the Skin with Clinical

# Cutaneous T Cell Lymphoma (CTCL)

# WHO-EORTC classification of primary cutaneous lymphomas

## Cutaneous T-cell and NK-cell lymphomas

Mycosis fungoides

MF variants and subtypes

Folliculotropic MF

Pagetoid reticulosis

Granulomatous slack skin

Sézary syndrome

Primary cutaneous CD30+ lymphoproliferative disorders

Primary cutaneous anaplastic large cell lymphoma

Lymphomatoid papulosis

Subcutaneous panniculitis-like T-cell lymphoma\*

Adult T-cell leukemia/lymphoma

Extranodal NK/T-cell lymphoma, nasal type

Primary cutaneous peripheral T-cell lymphoma, unspecified

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)

Cutaneous  $\gamma/\delta$  T-cell lymphoma (provisional)

Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)

# WHO-EORTC classification of primary cutaneous lymphomas

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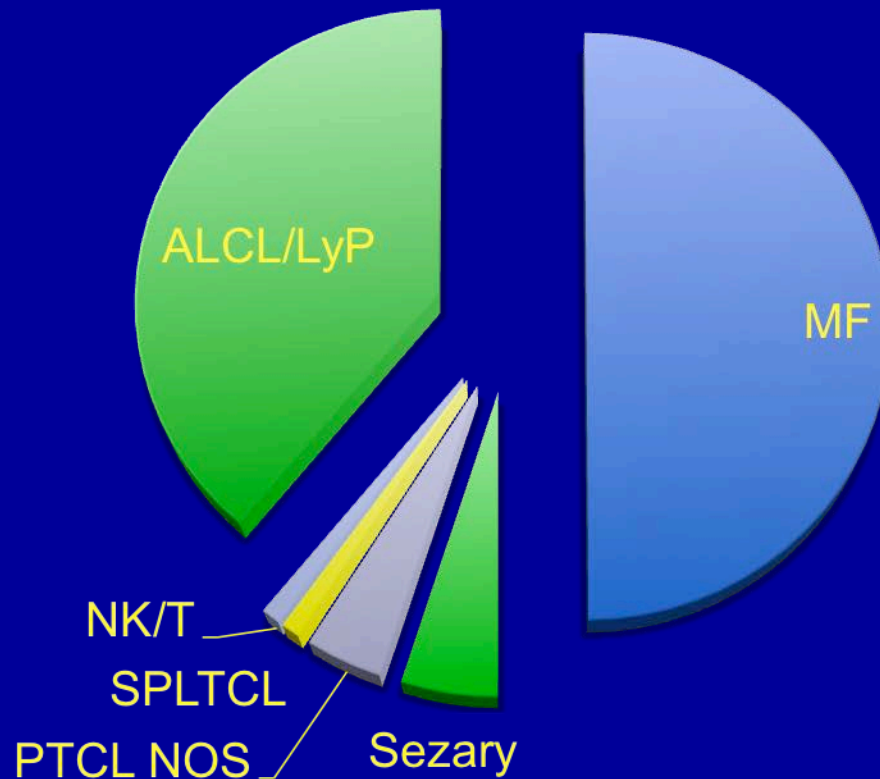
Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)

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# Epidemiology

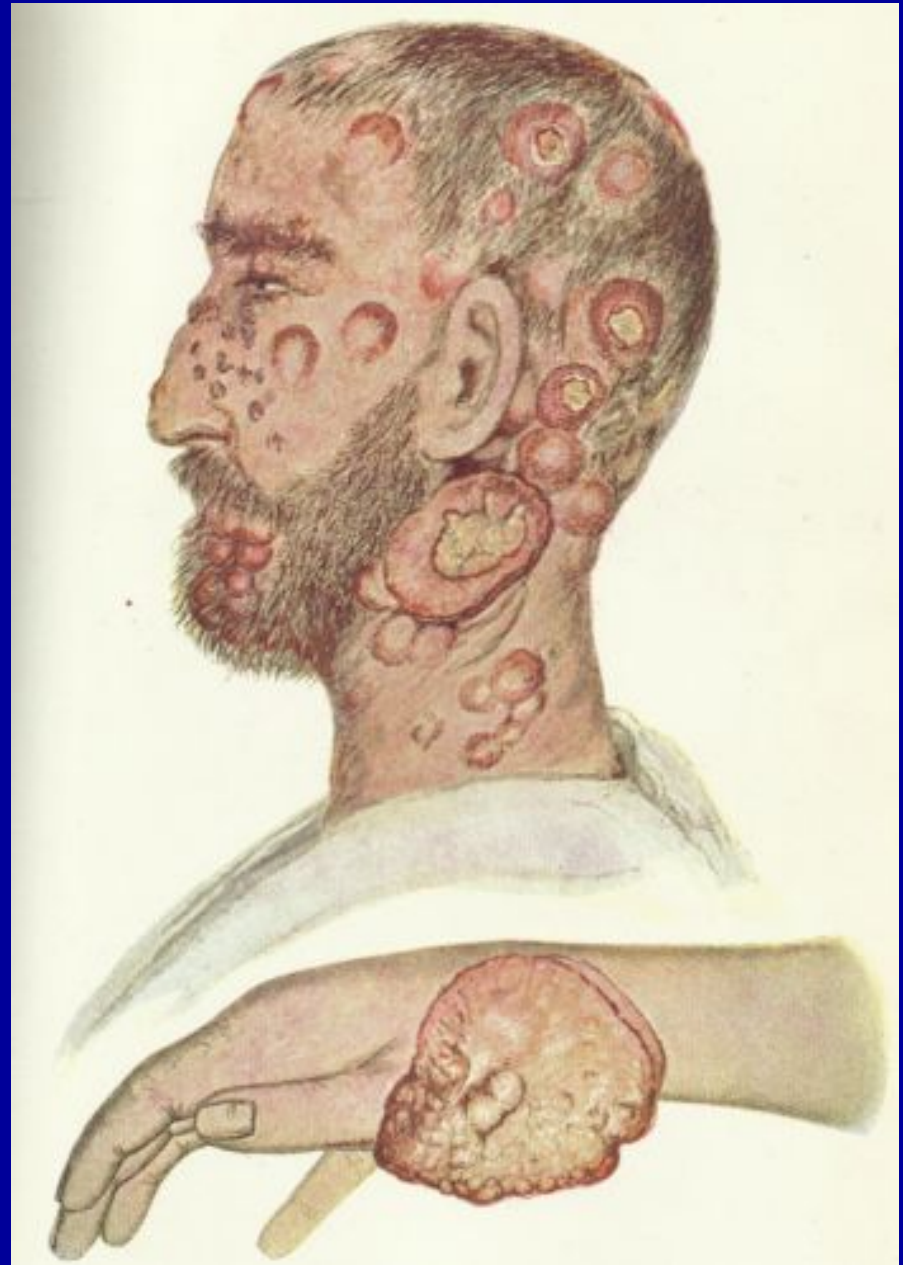
## Cutaneous T cell lymphomas





# Mycosis Fungoides

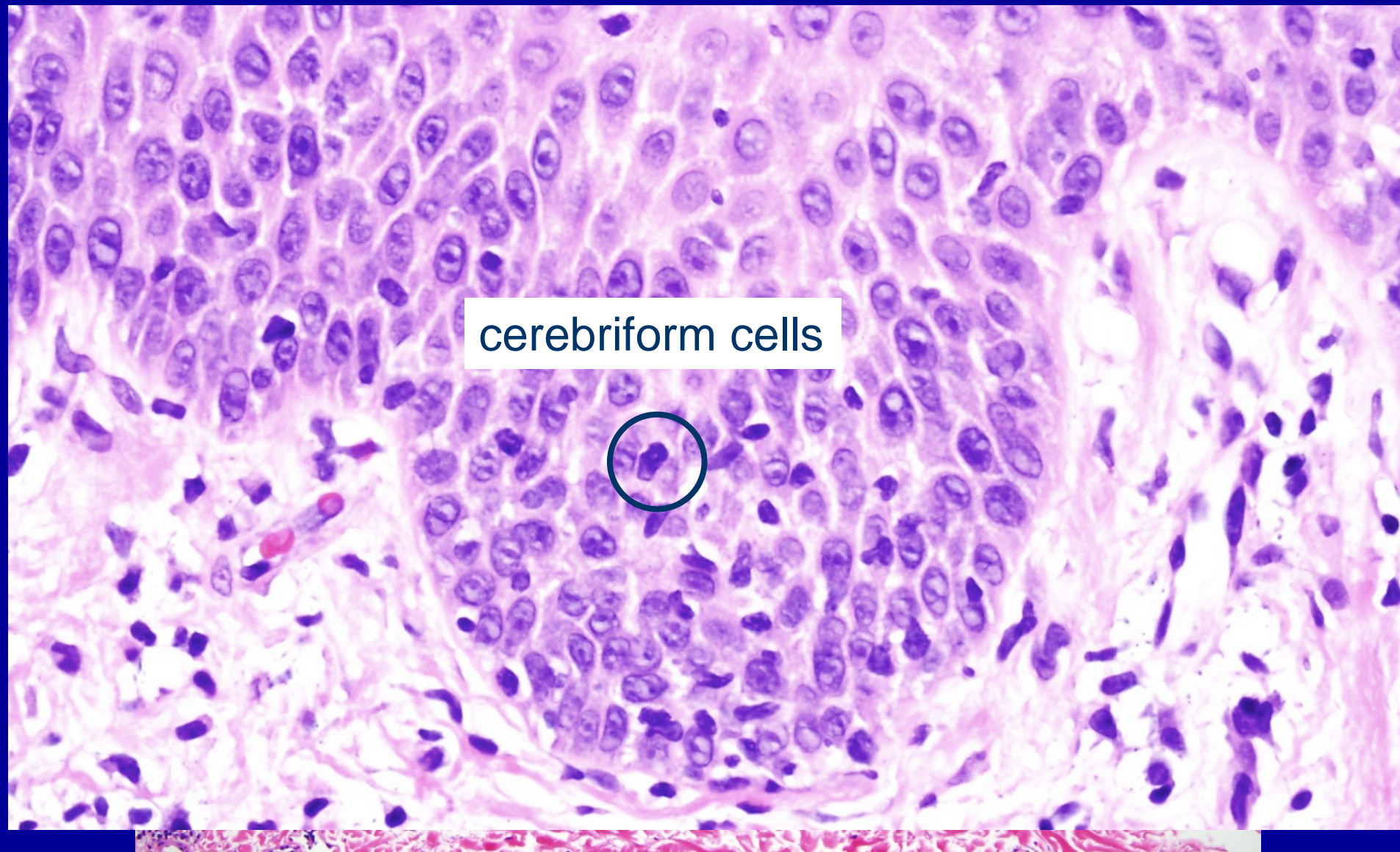
=Disease caused by fungus +  
Resembling fungus



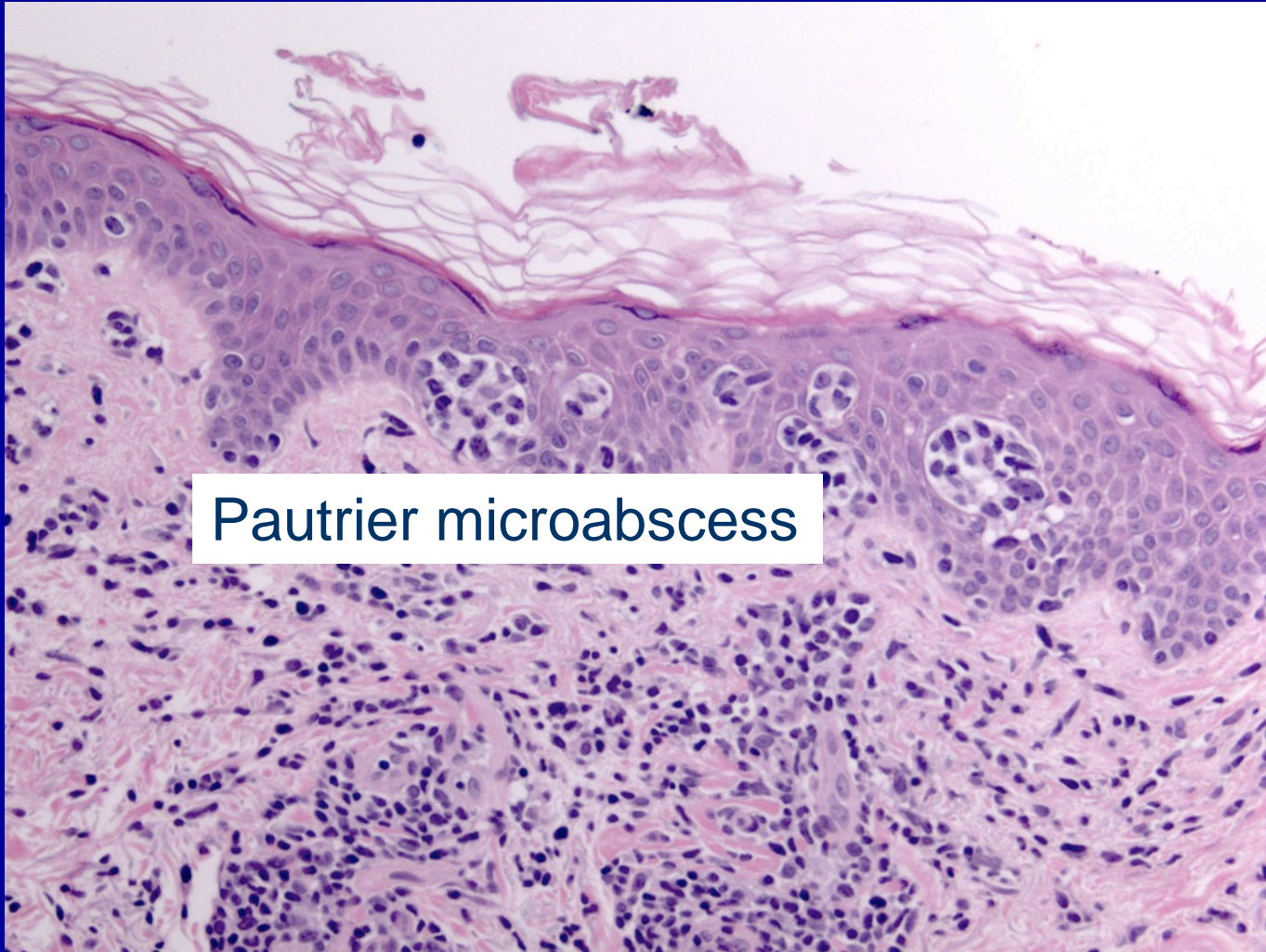




# MF under the microscope

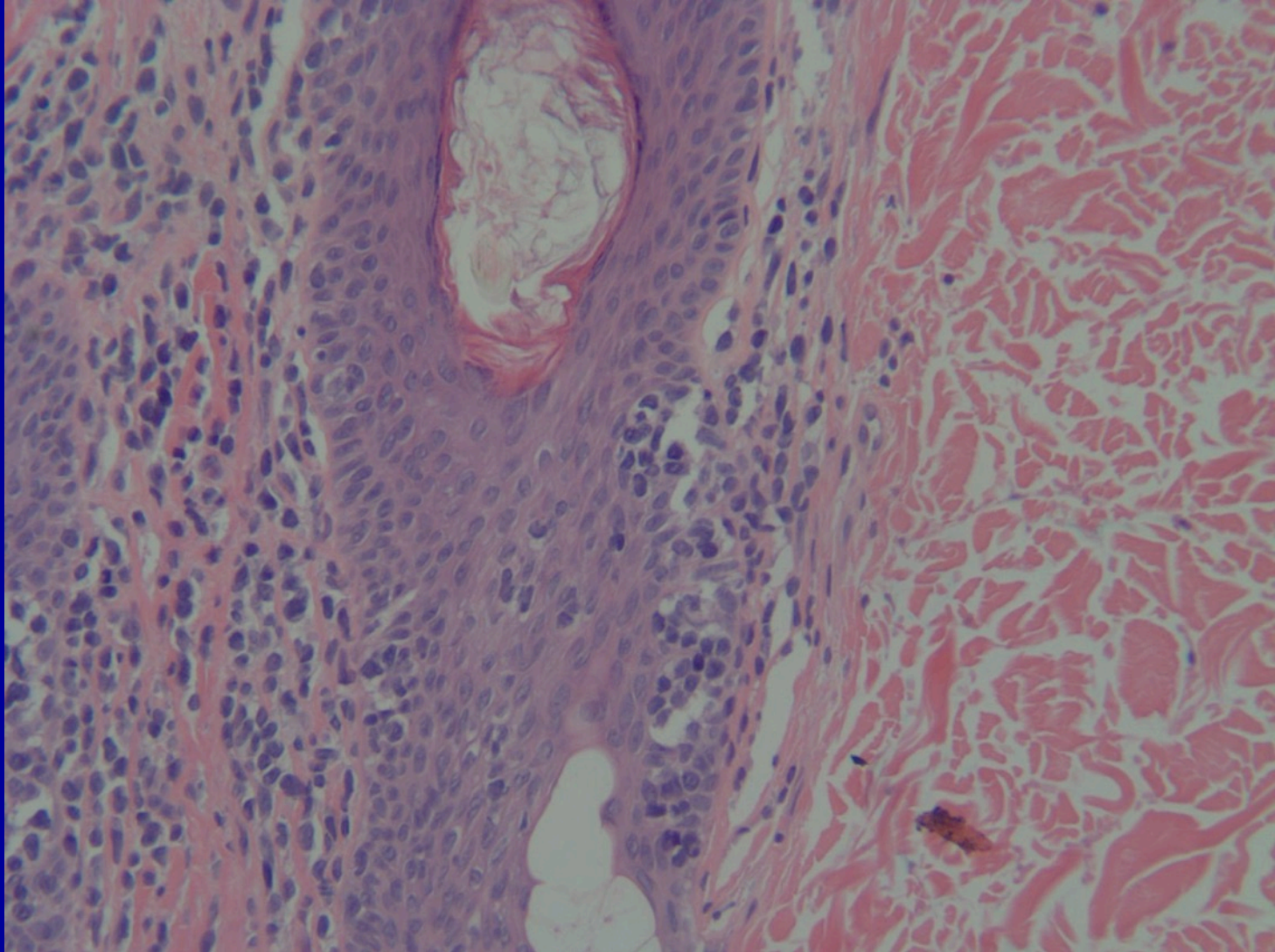


# Epidermotropism

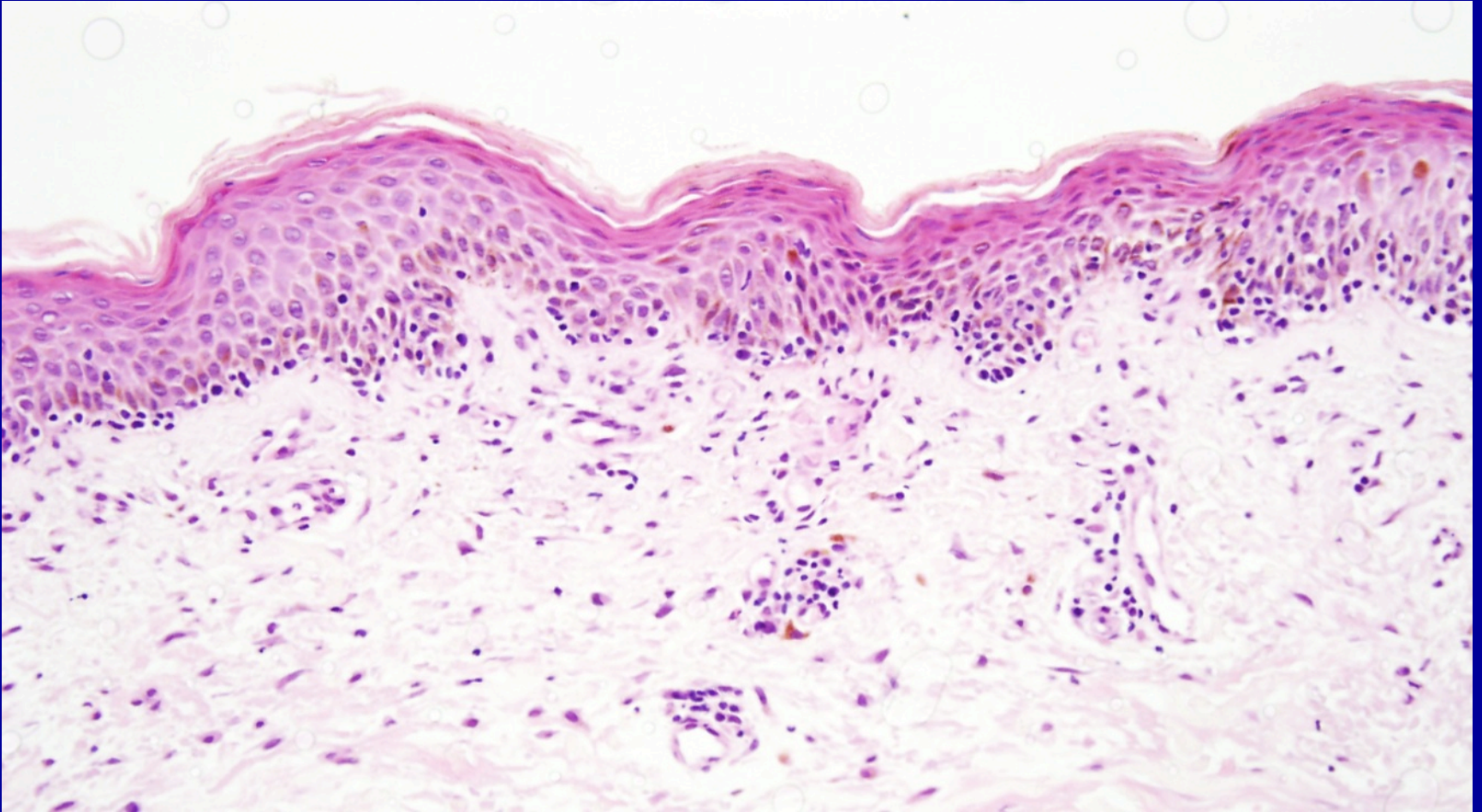


Pautrier microabscess

# Folliculotropism



# “Tagging”



# CTCL staging

- TNMB system (unique to CTCL)
  - T: extent of skin involvement
    - T1 <10%
    - T2 >10%
    - T3 tumors
    - T4 erythroderma
  - N: nodal involvement
    - Clinical or histologic
  - M: visceral involvement
  - B: blood involvement



# CTCL staging

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
II	1,2	0	0	0,1
IIB	3	0-2	0	0,1
III	4	0-2	0	0,1
IIIA	4	0-2	0	0,1
IIIB	4	0-2	0	0,1
IVA1	1-4	0-2	0	2
IVA2	1-4	3	0	0,1
IVB	1-4	0-3	1	0,1

**Early**

**Advanced**

**Tumors**

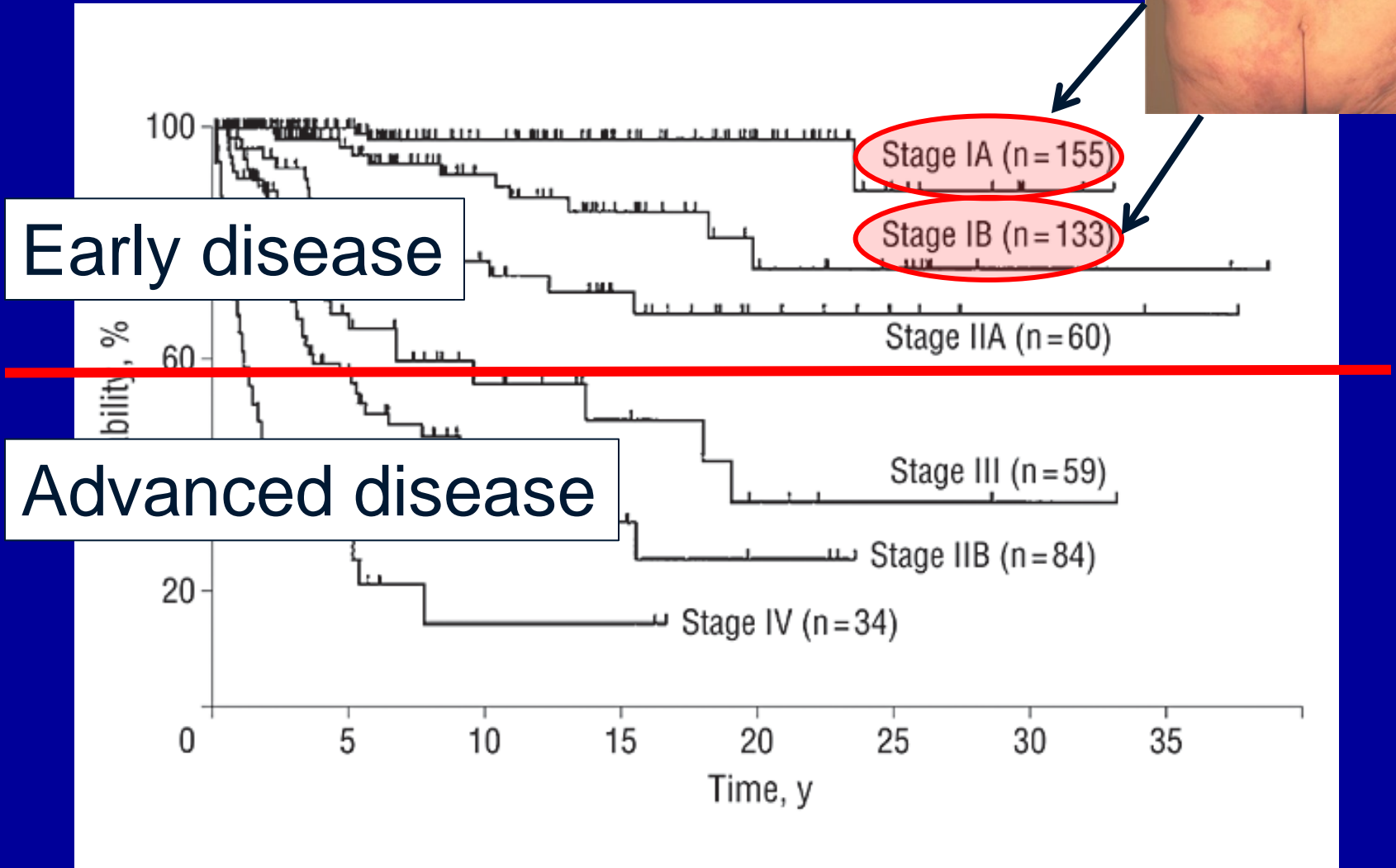
**Erythroderma**

**Blood involvement**

**Nodal involvement**

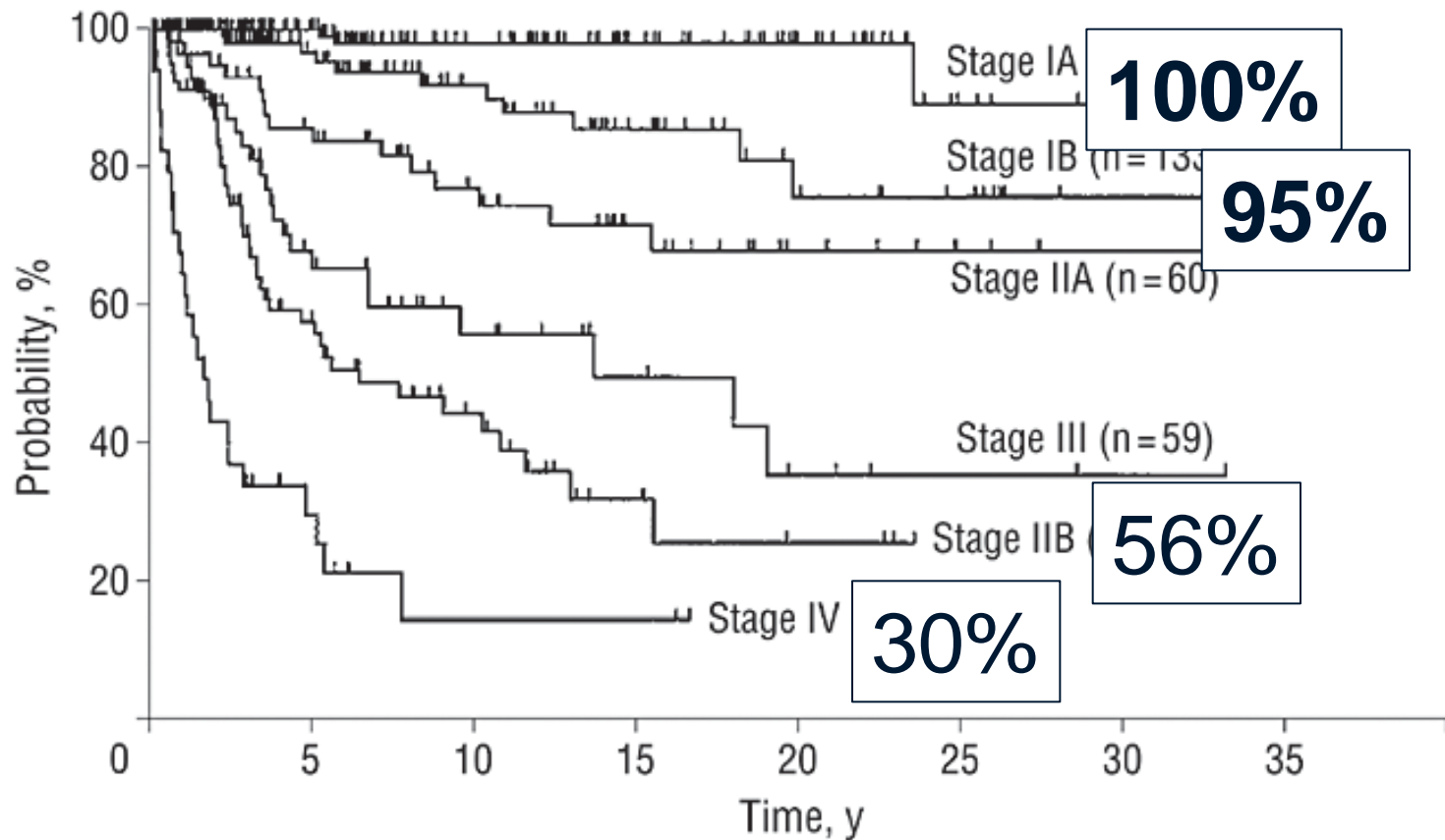
# Prognosis of CTCL/MF

**Actuarial disease-specific survival of 525 patients with mycosis fungoides and Sezary syndrome according to their clinical stage at diagnosis**

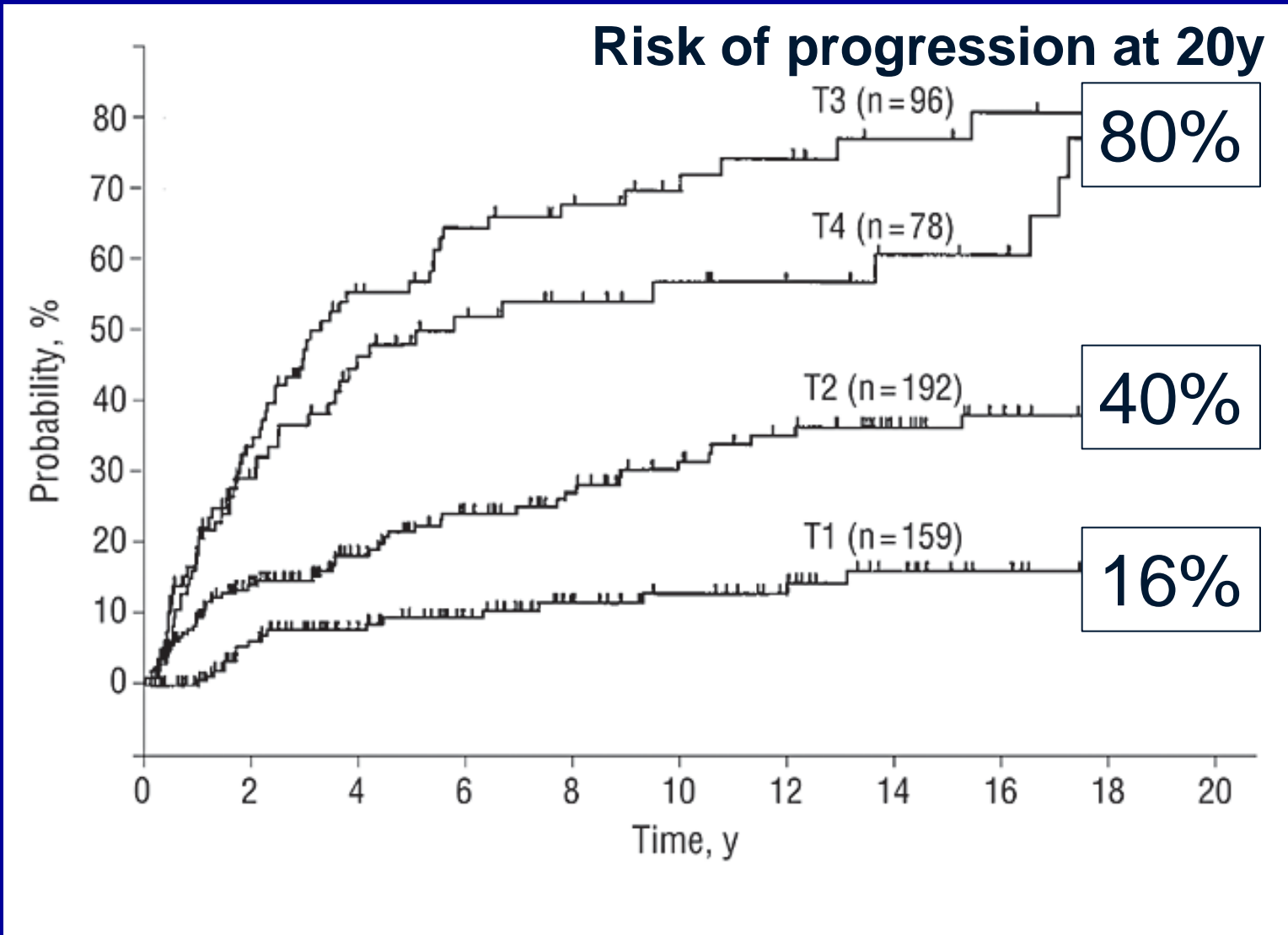


# Actuarial disease-specific survival of 525 patients with mycosis fungoides and Sezary syndrome according to their clinical stage at diagnosis (stages IA-IV)

## 5 year survival



# Risk for disease progression with MF/Sezary syndrome according to T classification at diagnosis



# Primary Cutaneous B Cell Lymphoma (CBCL)

# WHO-EORTC classification (2008)

## Cutaneous B-cell lymphomas

Primary cutaneous marginal zone B-cell lymphoma

Primary cutaneous follicle center lymphoma

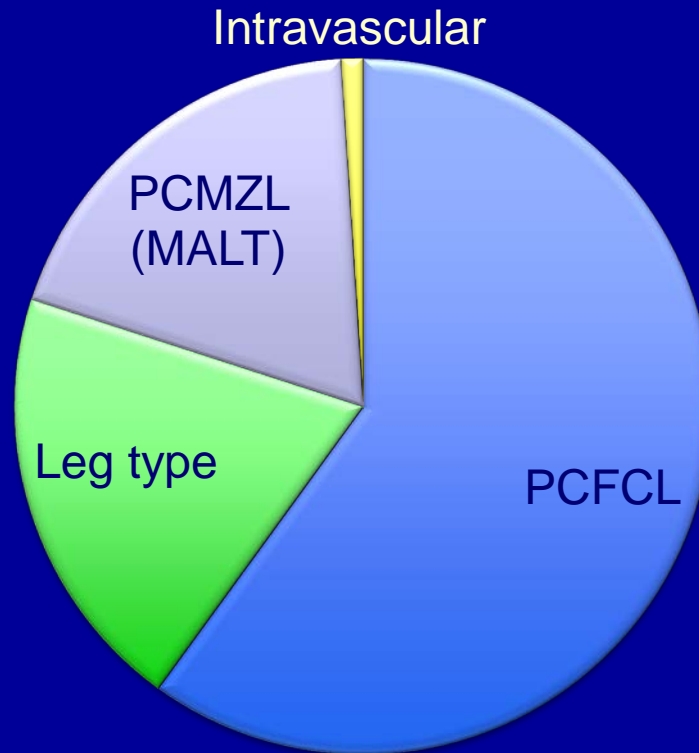
Primary cutaneous diffuse large B-cell lymphoma, leg type

Primary cutaneous diffuse large B-cell lymphoma, other

Intravascular large B-cell lymphoma

# Epidemiology

## Primary Cutaneous B Cell Lymphomas





# Practical classification of CBCCLs

## Indolent

- PCMZL
- PCFCL

## Intermediate

- DLBCL-leg type

# Clinical Features of CBCL



# Follicle center lymphoma

- Adults, 60s
- Head and neck – esp. scalp
- Solitary/grouped papulonodules, plaques



Image courtesy of Ellen Kim, MD

# Marginal Zone Lymphoma

- Younger population
- Frequently solitary or few
- UE, Trunk, Head



# DLBCL: leg type

- Elderly (70s)
- Nodules, tumors
- Leg (but doesn't have to be)

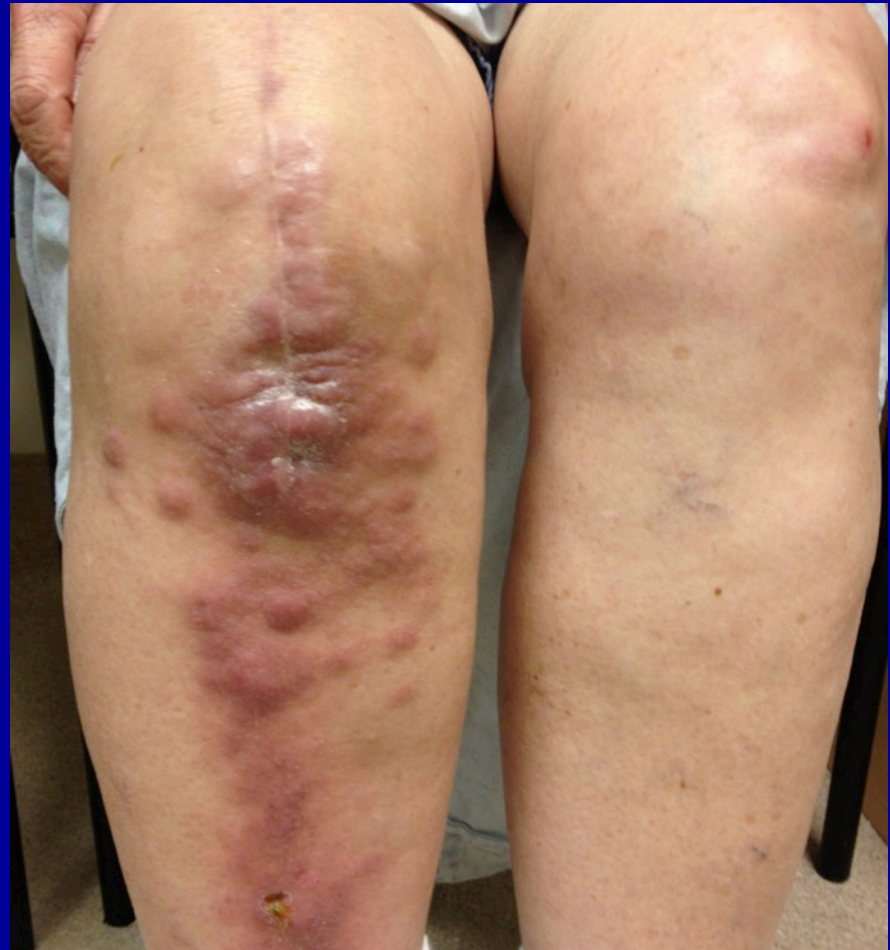


Image courtesy of Ellen Kim, MD

# Prognosis of CBCL

## Indolent types

- 95-99% 5 yr survival

## Intermediate (leg) type

- 70% 5 yr survival

# Diagnosing Cutaneous Lymphomas

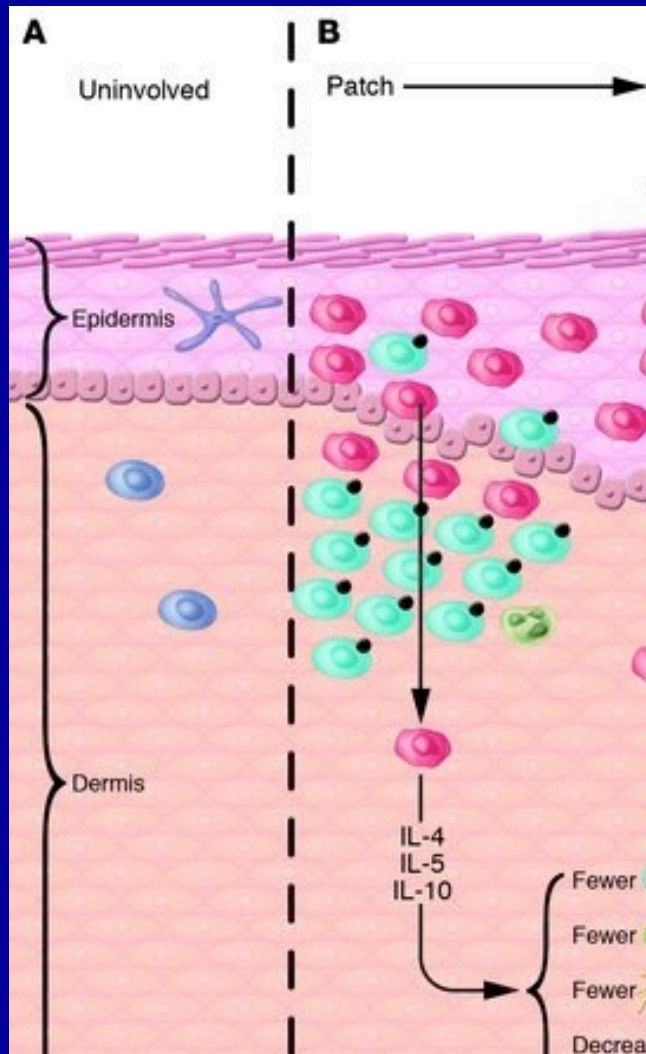
# Tools to Diagnose Cutaneous Lymphoma

- History
- Physical exam
- Skin biopsy (often multiple!)
- Blood tests
- Imaging (CT scans or PET/CT)
- Bone marrow, lymph node biopsy





Why is it so hard to diagnose  
early disease?



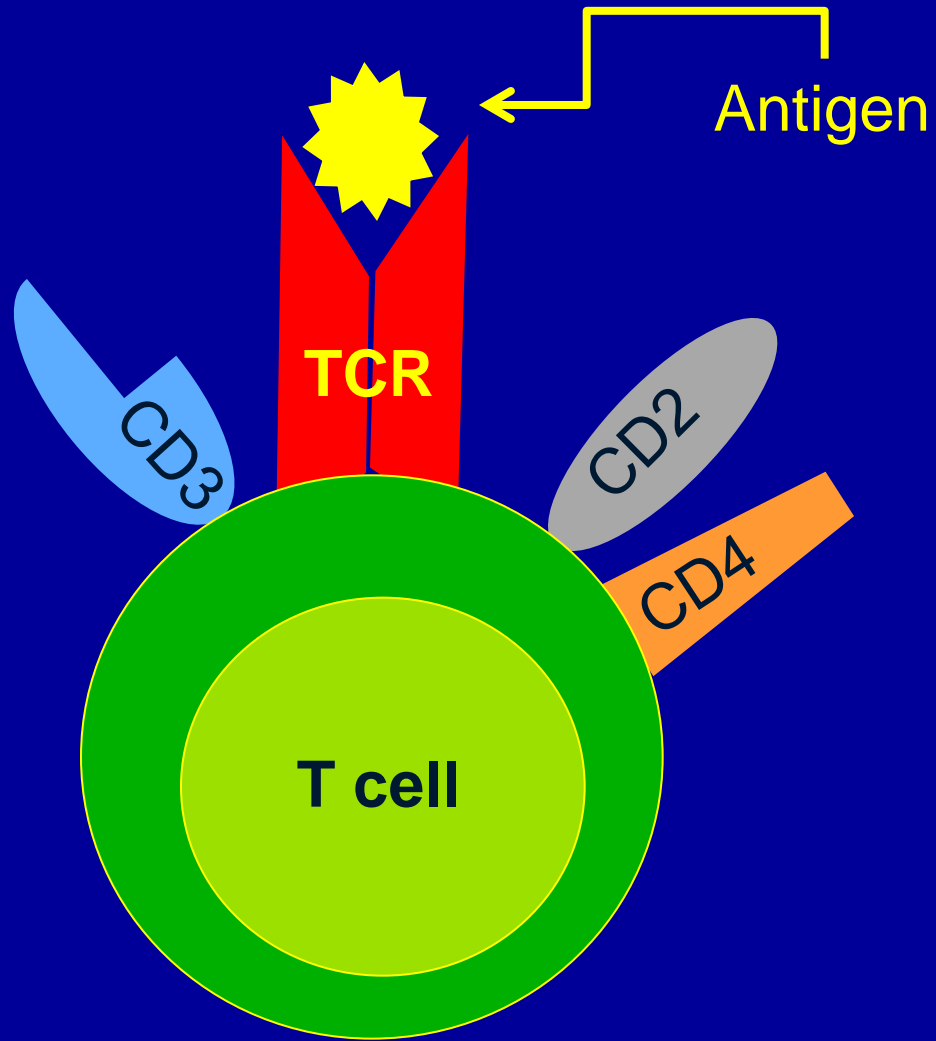
Adapted from Kim et al, *J Clin Invest.* 2005; 115:798



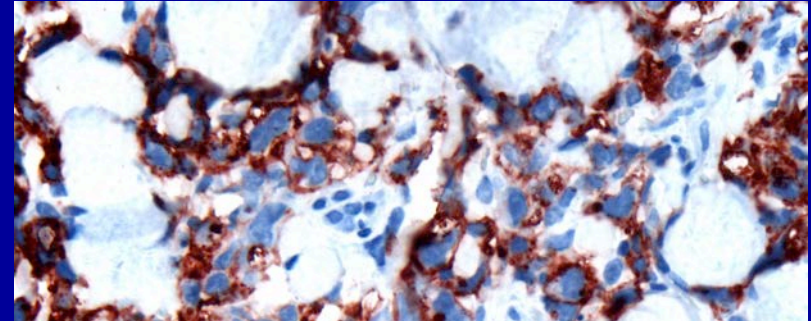
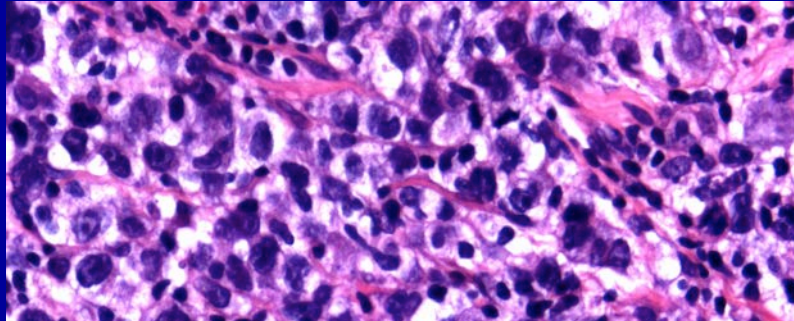
- **Clinical (max 2 points)**
  - Persistent patches/plaques
    - Non sun-exposed sites, variably sized, poikiloderma
- **Histopathologic (max 2 points)**
  - Superficial lymphoid infiltrate
    - Epidermotropic and not spongiotic, atypia
- **Molecular studies (1 point)**
  - Clonal gene rearrangement study
- **Immunopathology (1 point)**
  - >50% T cells, loss of CD7, epidermal/dermal discordance

# Special studies used to diagnosis cutaneous lymphoma

- Immunohistochemical stains or “markers”
- Molecular (DNA based) studies
  - Gene rearrangement or “clonality”
  - Flow cytometry

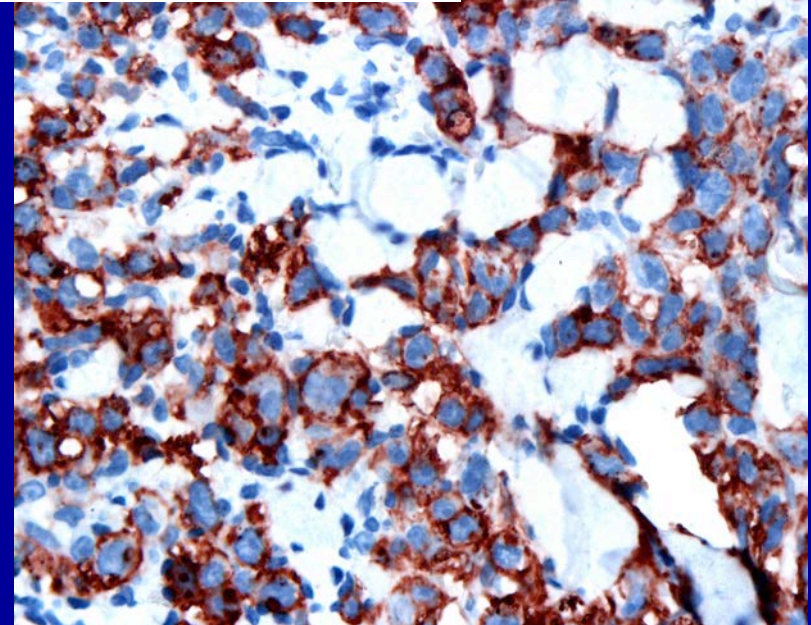
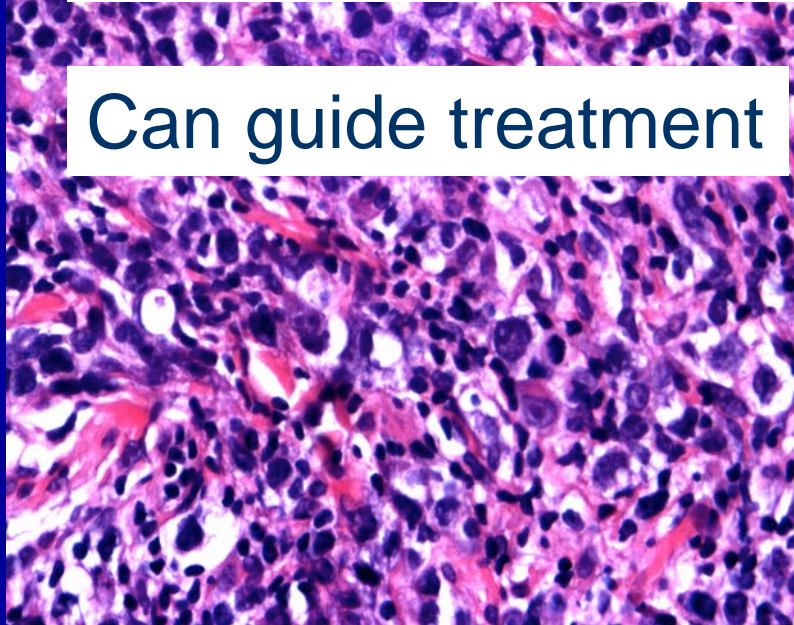


# Immunohistochemical Stains - “Markers”



Help identify what type of lymphoma

Can guide treatment

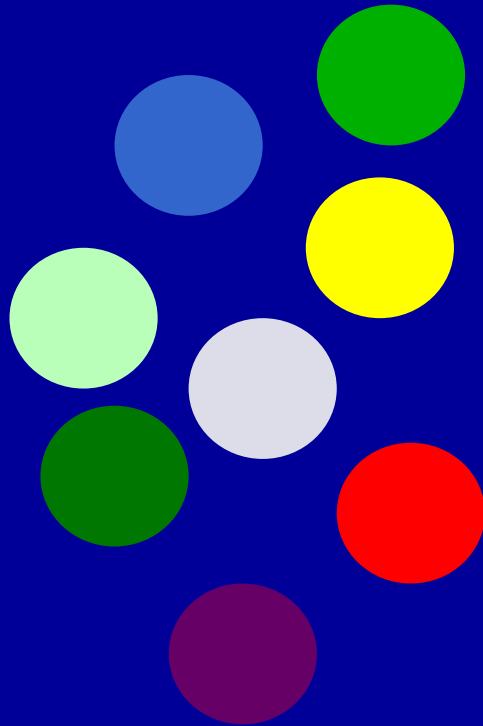


# Molecular studies in the diagnosis of cutaneous lymphoma

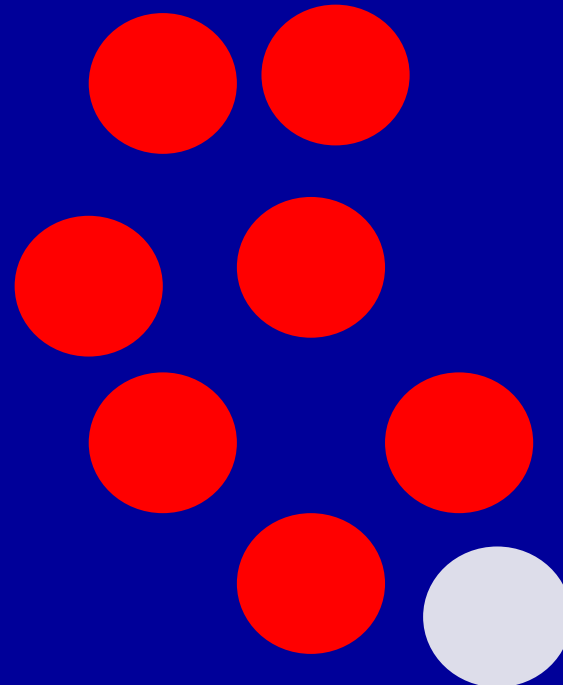
- Gene rearrangement or “clonality” studies
- Flow cytometry

# Gene rearrangement (clonality) studies

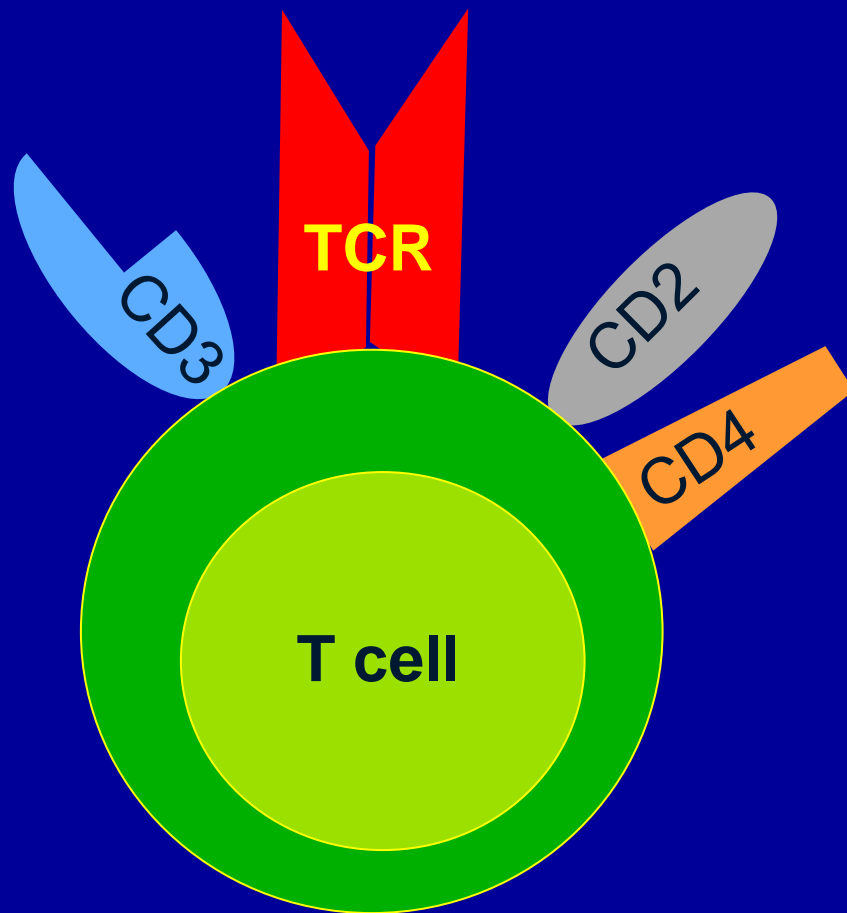
Polyclonal B or T cells



Monoclonal B or T cells







## INTERPRETATION

Skin, right hip (28 February 2012): POSITIVE for a clonal T cell population (see comment).

## COMMENT

A T cell clone was present in a polyclonal background. Although these results could support a diagnosis of cutaneous T cell lymphoma, T cell clones can also be observed in some reactive conditions. Clinical and histological correlation is required.

## CLINICAL

57 year old male with history of rash/exanthema.

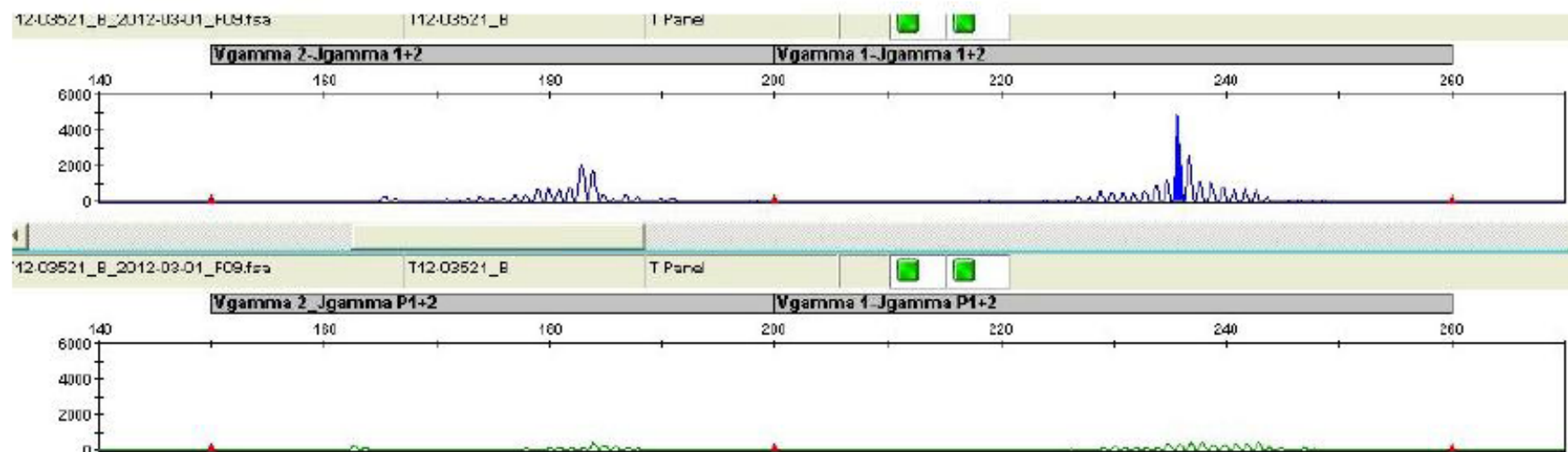
## RESULTS

### Test Performed

### Result

### *TCRG*

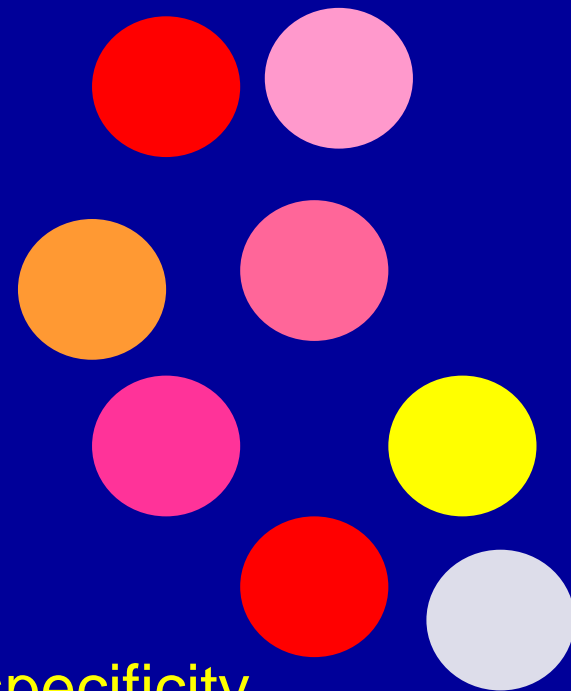
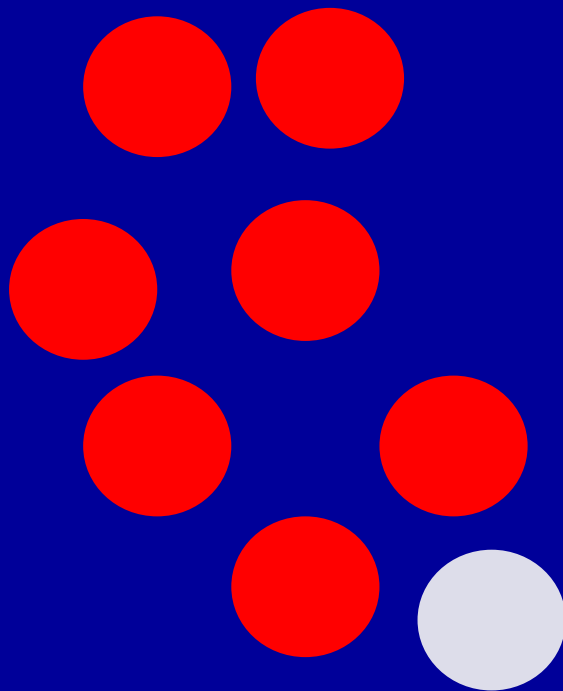
Positive [V $\gamma$ I:J $\gamma$ 1/2 (235.66)]



# High throughput sequencing

Traditional clonality studies

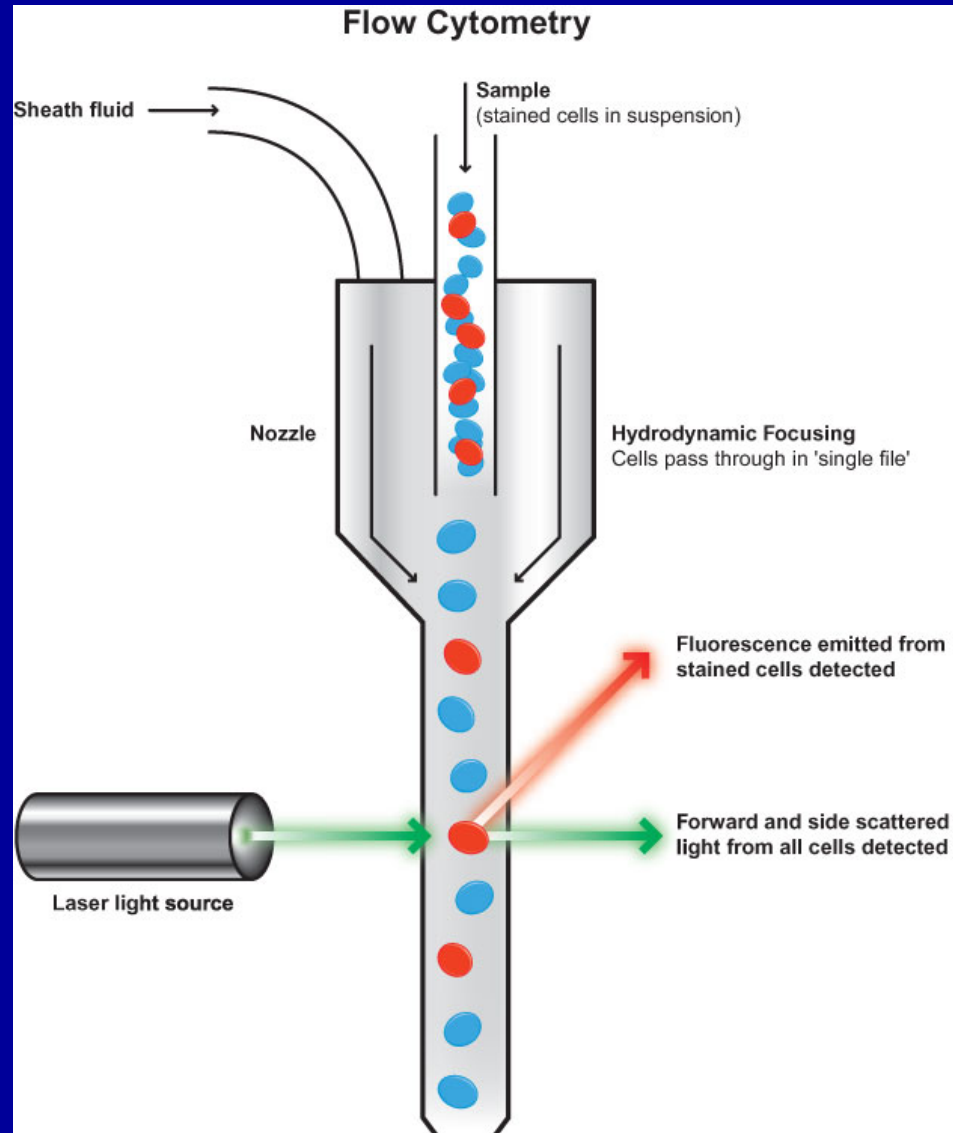
High throughput sequencing



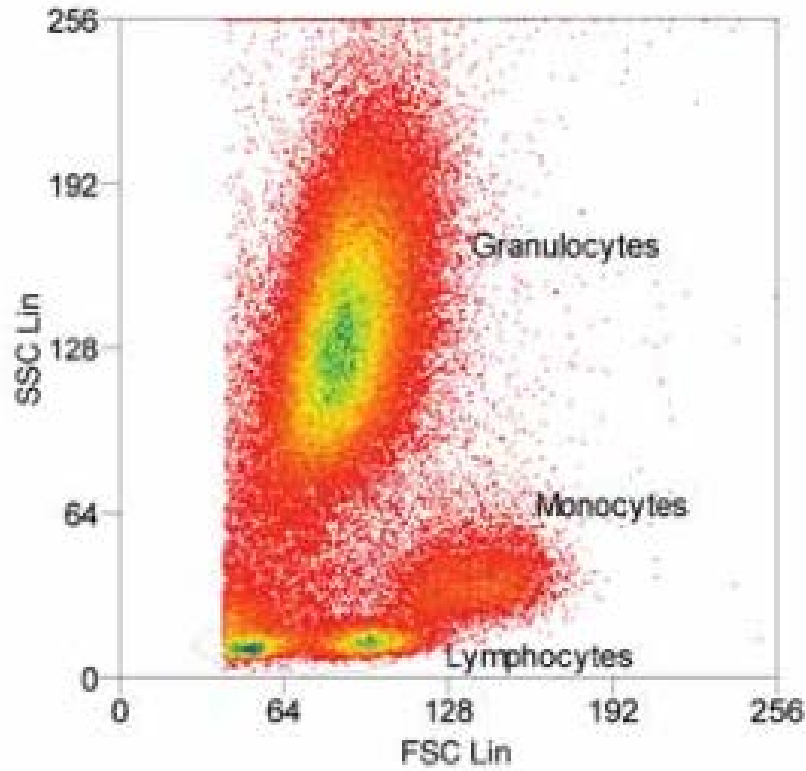
Higher specificity  
Higher sensitivity

# Flow cytometry

- Skin
- Blood
- Other tissue



Density plot



Contour diagram

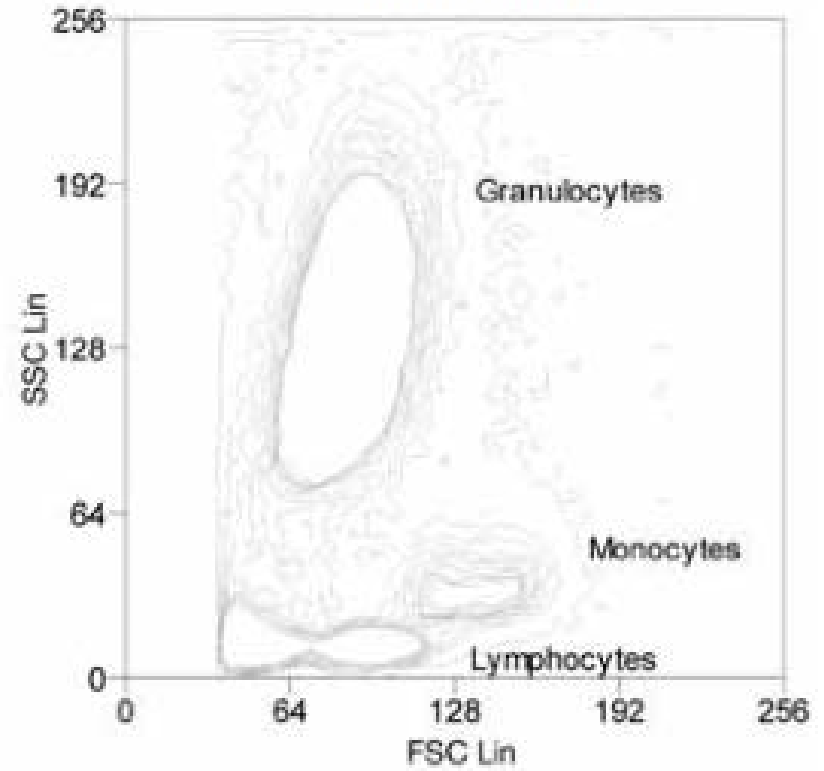


FIGURE 9

Analysis of lysed whole blood using FSC/SSC

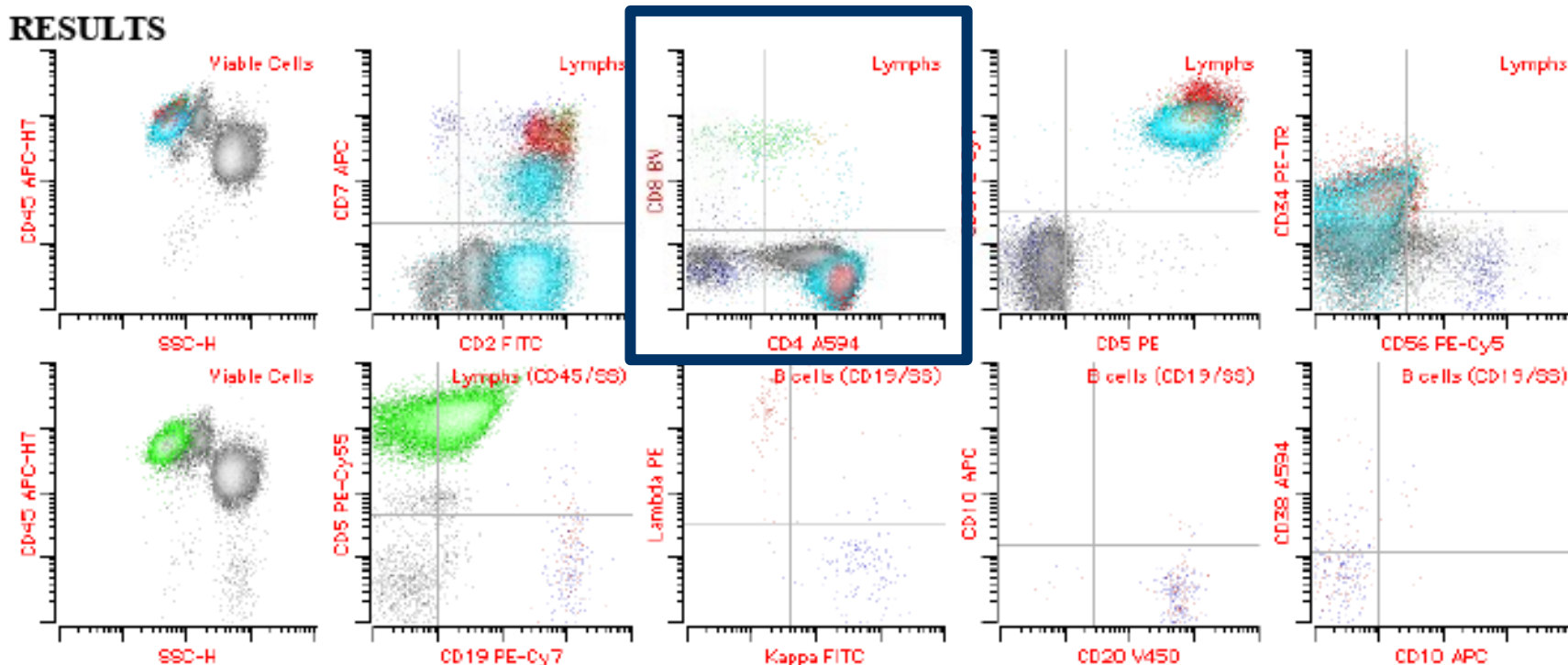
## COMMENT

Flow cytometry reveals an abnormal T cell population having abnormal expression of CD3 (slightly decreased), and CD7 (low to absent) with normal expression of CD2, CD4, CD5, and CD45 without CD8, CD30, CD34, or CD56. The immunophenotype of the abnormal T cell population is consistent with involvement by a T cell lymphoproliferative disorder but is not specific. Although not diagnostic in isolation, this finding could support a diagnosis of Sezary syndrome in the appropriate clinical and morphologic context. Molecular studies to attempt identification of a clonal T cell population could be performed, if desired. The abnormal population represents 22.8% of the total white cells. Clinical and morphologic correlation will be required for definitive diagnosis and for classification.

## CLINICAL

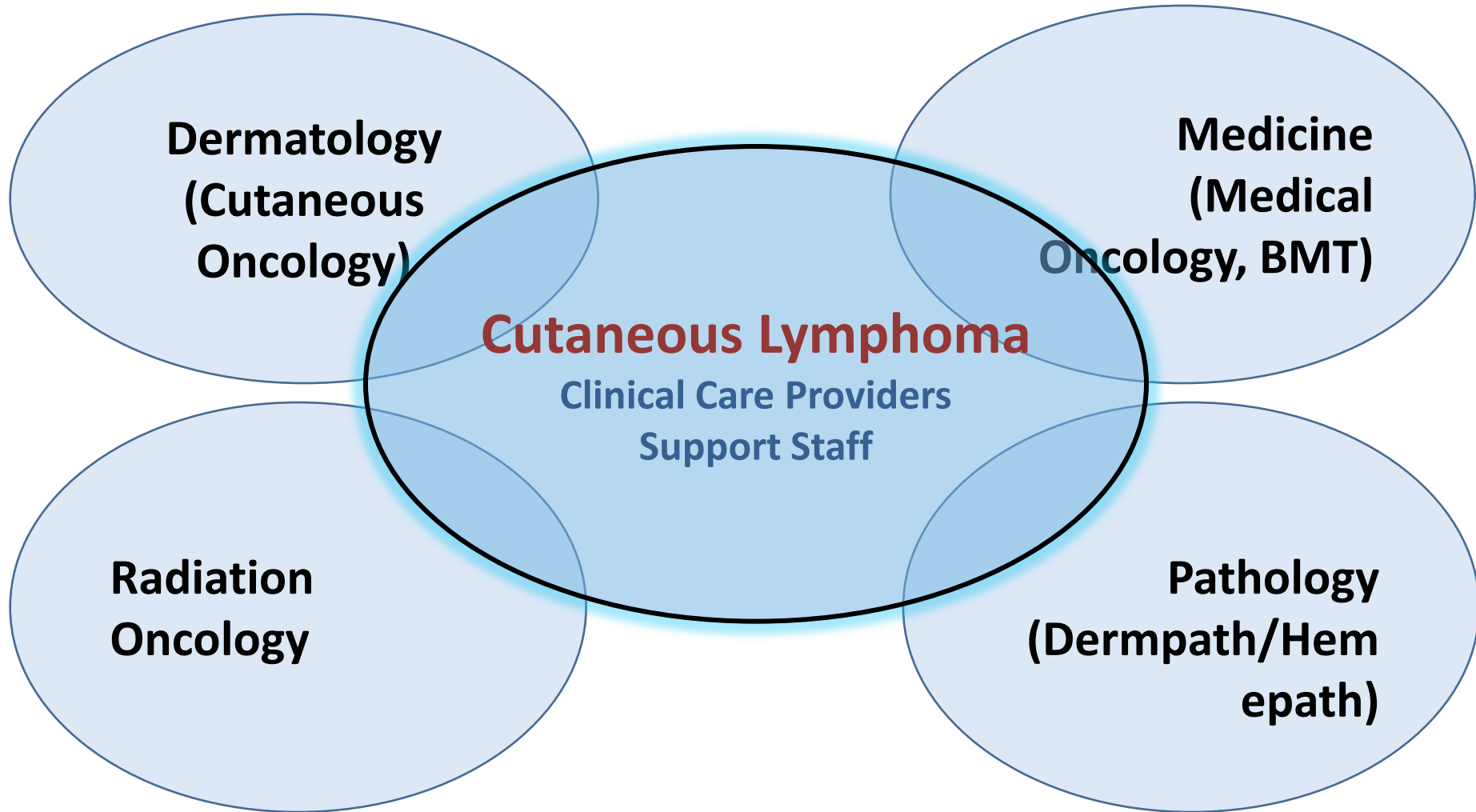
69 year old female with chronic erythroderma.

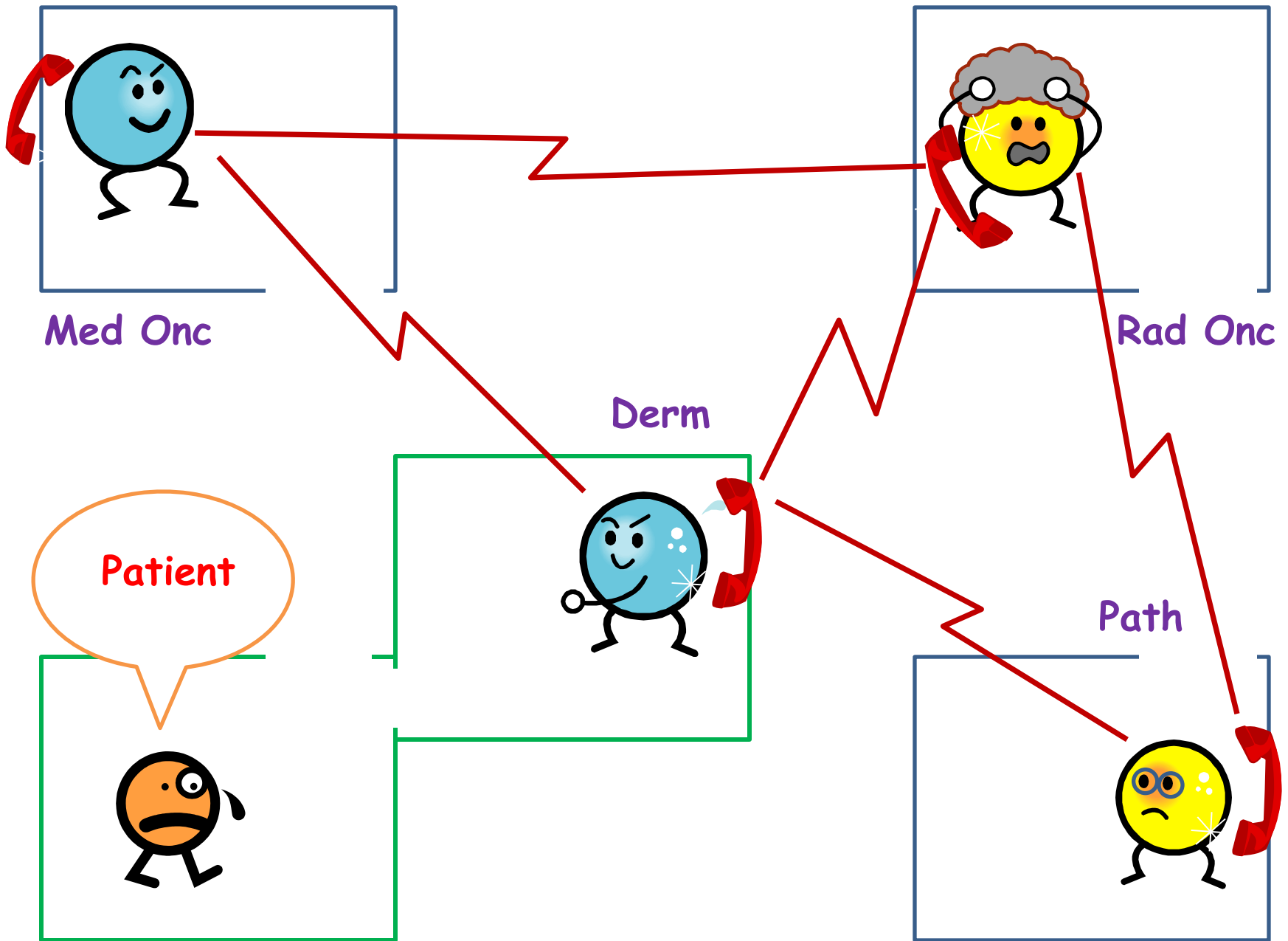
## RESULTS



Immunophenotyping by flow cytometry after lysis of the erythroid cells reveals that the white blood cells consist of 28.8 % lymphocytes, 7.8 % monocytes, and 62.6 % granulocytes. The lymphocytes consist of 0.97 % B cells (CD19+), 97.4 % T cells (CD3+) having a CD4:CD8 ratio of 50.5, and 1.6 % NK cells (CD3-, CD7+).

# *Teamwork & Synergy in Clinical Care*





Med Onc

Rad Onc

Derm

Patient

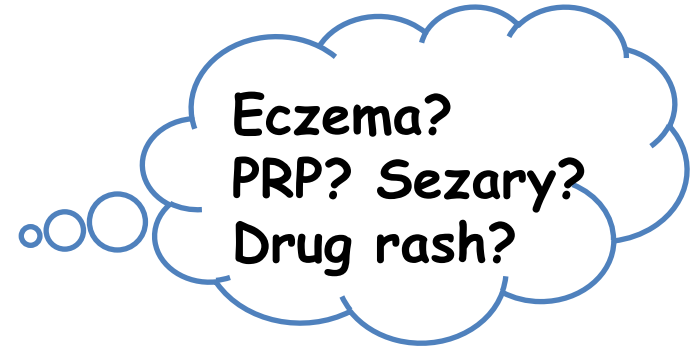
Path

*Separate physical space (separate clinics)*

Courtesy Youn Kim MD



Patient



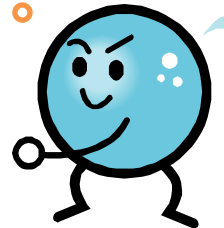
Med Onc



Path



Derm



Rad Onc



*Path joins clinicians (ideal clinical-path correlation)*

Courtesy Youn Kim MD

