

OVERVIEW OF CUTANEOUS LYMPHOMAS

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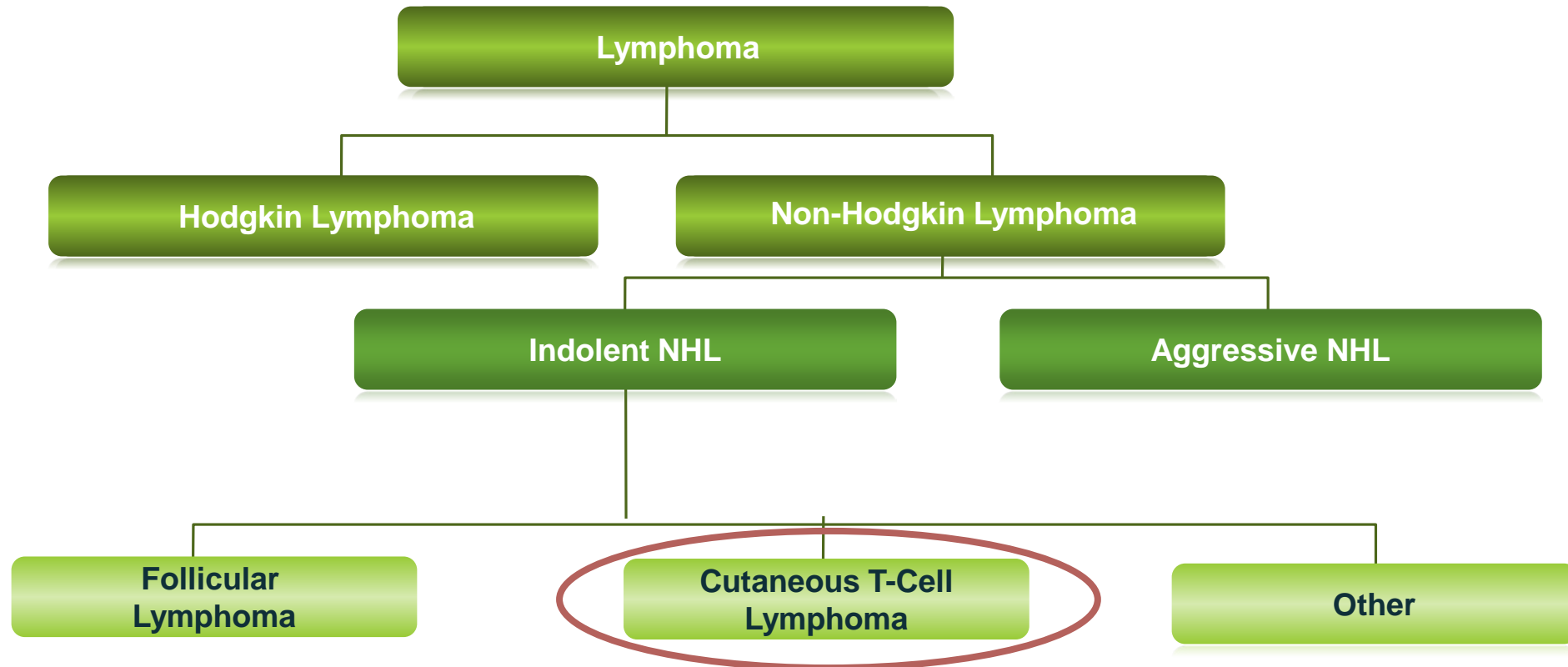
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GOALS

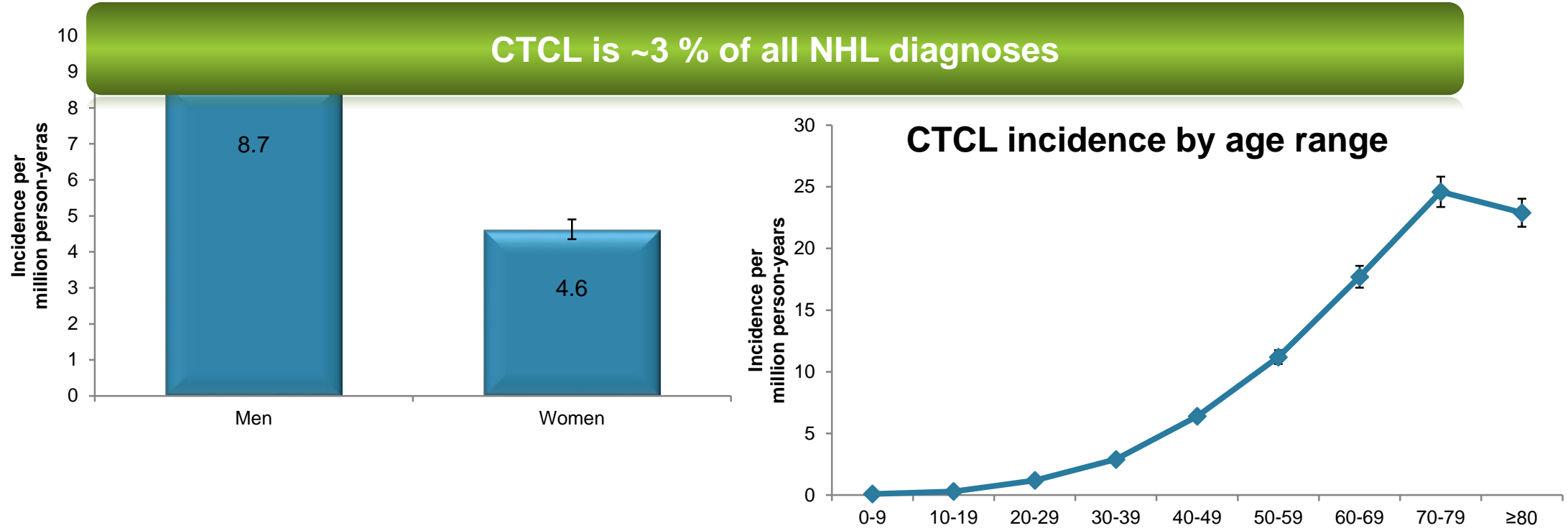
This activity is intended for patients and their families involved in the care of those with Mycosis Fungoides - Cutaneous T Cell Lymphoma (MF-CTCL).

The goal of this activity is to assess and summarize cutaneous lymphomas in clinical practice.

NON-HODGKIN LYMPHOMA (NHL): A HETEROGENEOUS GROUP OF MALIGNANCIES



CTCL REPRESENTS A FRACTION OF ALL NHL DIAGNOSES



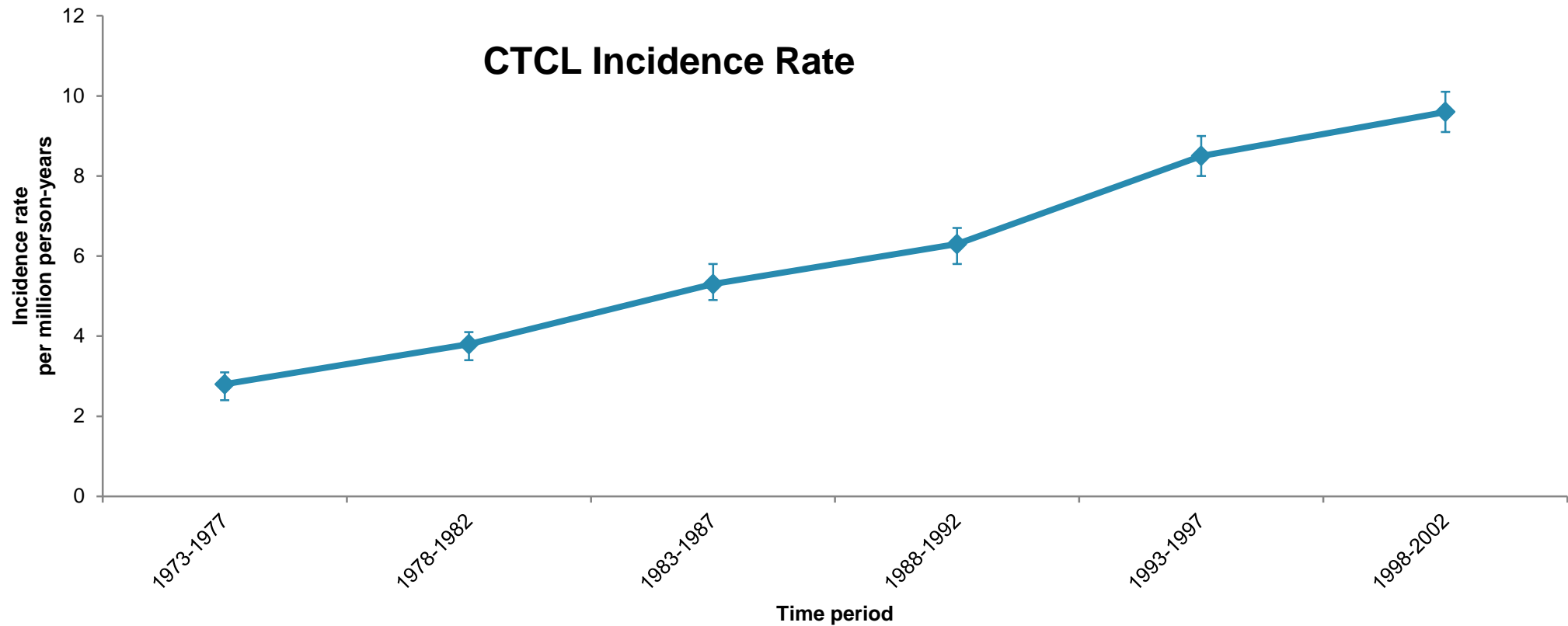
~16,000-20,000 patients with MF in the US

~1,500-3,000 new MF cases diagnosed each year

EPIDEMIOLOGY

- Cutaneous lymphomas represent 3% of all non-Hodgkin lymphomas
- MF is the most common form of CTCL ~ 60% cases
- Incidence: 0.4 per 100,000 inhabitants per year in USA
- Median age: 55-60 years
- Male to Female ratio ~ 2:1
- Majority of patients are Caucasian followed by blacks, Hispanics, and Asians (~70%, 14%, 9%, 7%)

CTCL HAS A SMALL BUT GROWING INCIDENCE



CTCL IN WHO 2008 LYMPHOMA CLASSIFICATIONS

Extranodal- Cutaneous

- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous CD30+ lymphoproliferative disorders
 - Primary cutaneous anaplastic large cell lymphoma
 - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Primary cutaneous $\gamma\delta$ T-cell lymphoma
- Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma
- Primary cutaneous small/medium CD4+ T-cell lymphoma

Mycosis fungoides (60%) and Sézary syndrome (5%) are the most common subtypes of CTCL

CTCL IN WHO 2008 LYMPHOMA CLASSIFICATIONS

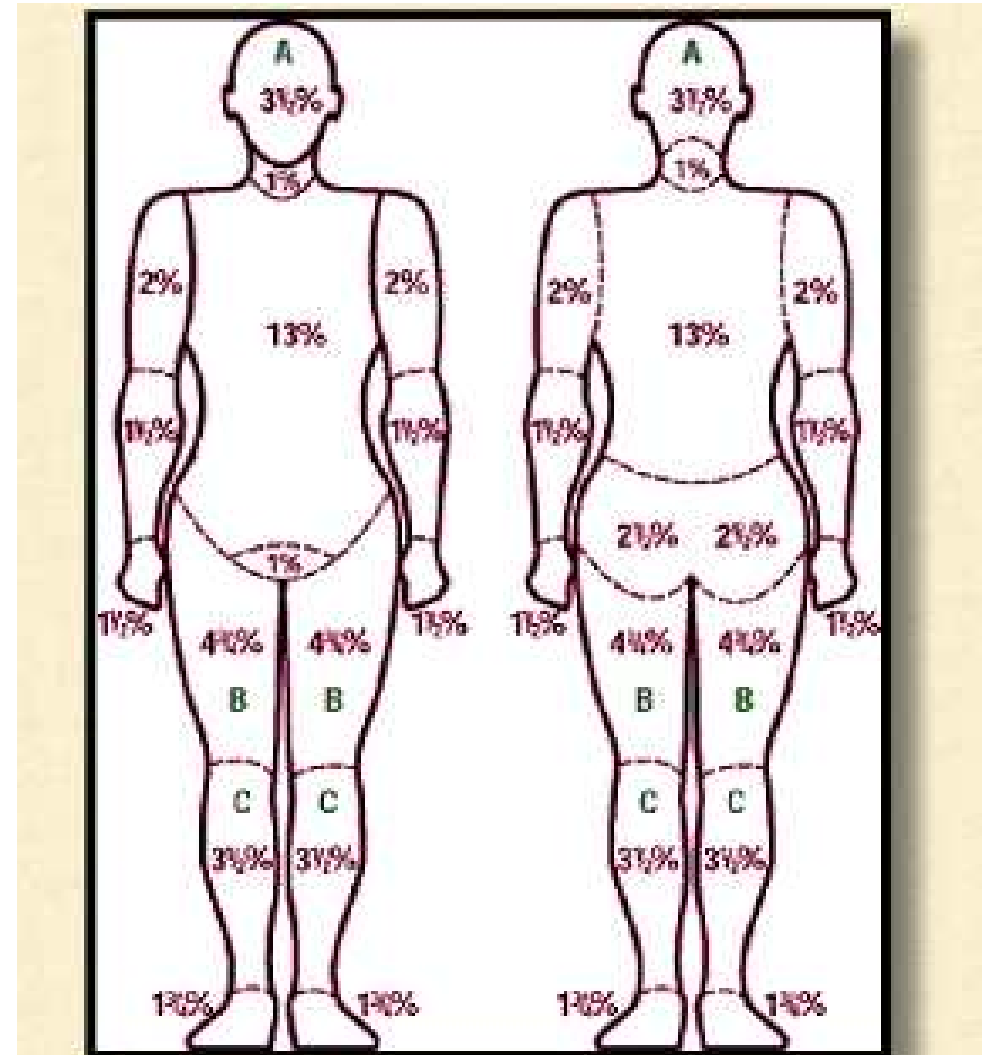
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%TSBA = (TOTAL BODY SURFACE AREA)

- The body is divided into 12 regions with pre-assigned %TSBA based on methodology used to assess burns.
- The extent of skin disease is assessed for each region and quantified by using the patient's palm as the 'ruler' to measure the %TBSA involvement with each region.
 - Patient's palm with 4 fingers, excluding the thumb and measured from wrist to fingertips, is 1% of TBSA.
 - Patient's palm without fingers is 0.05% of TBSA



CTCL – MYCOSIS FUNGOIDES CLINICAL PRESENTATION



Patches, Plaques



Hypopigmented Patches, Plaques

CTCL – MYCOSIS FUNGOIDES CLINICAL PRESENTATION



CLINICAL PHASES OF CTCL – MYCOSIS FUNGOIDES



Patch



Tumor

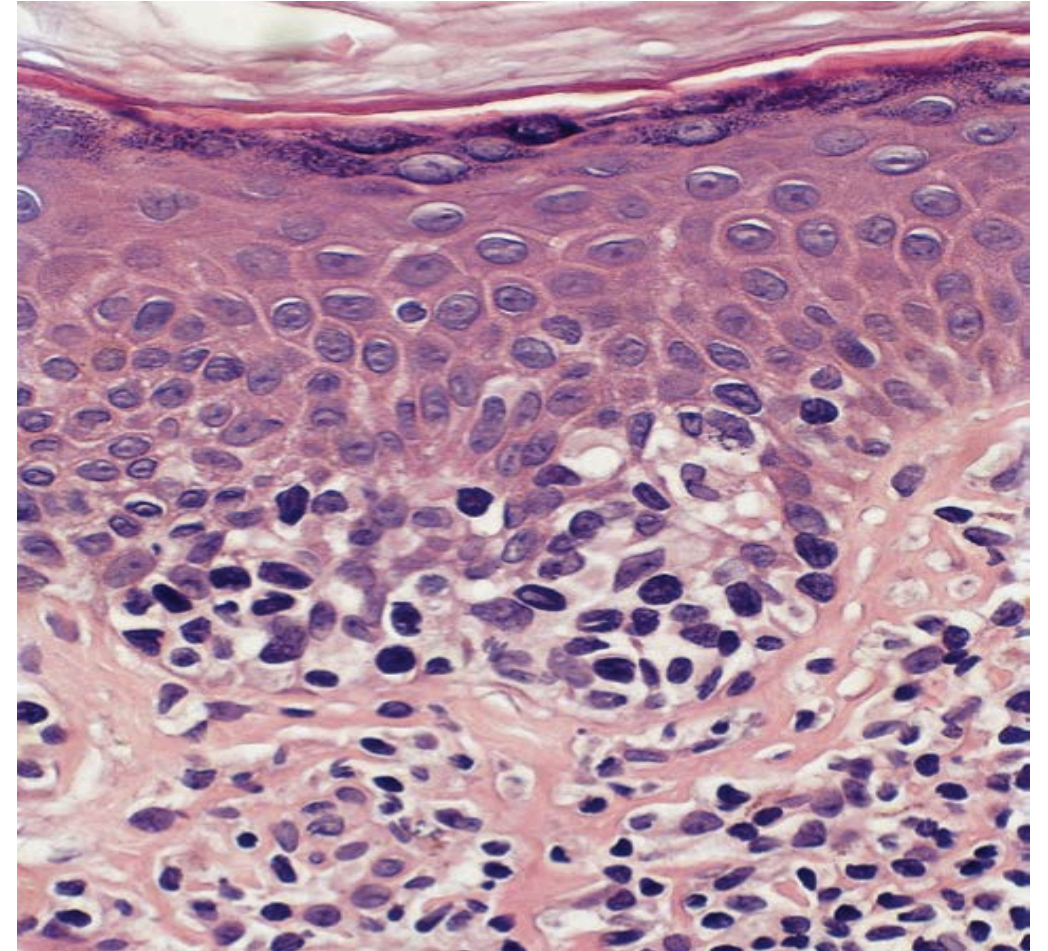
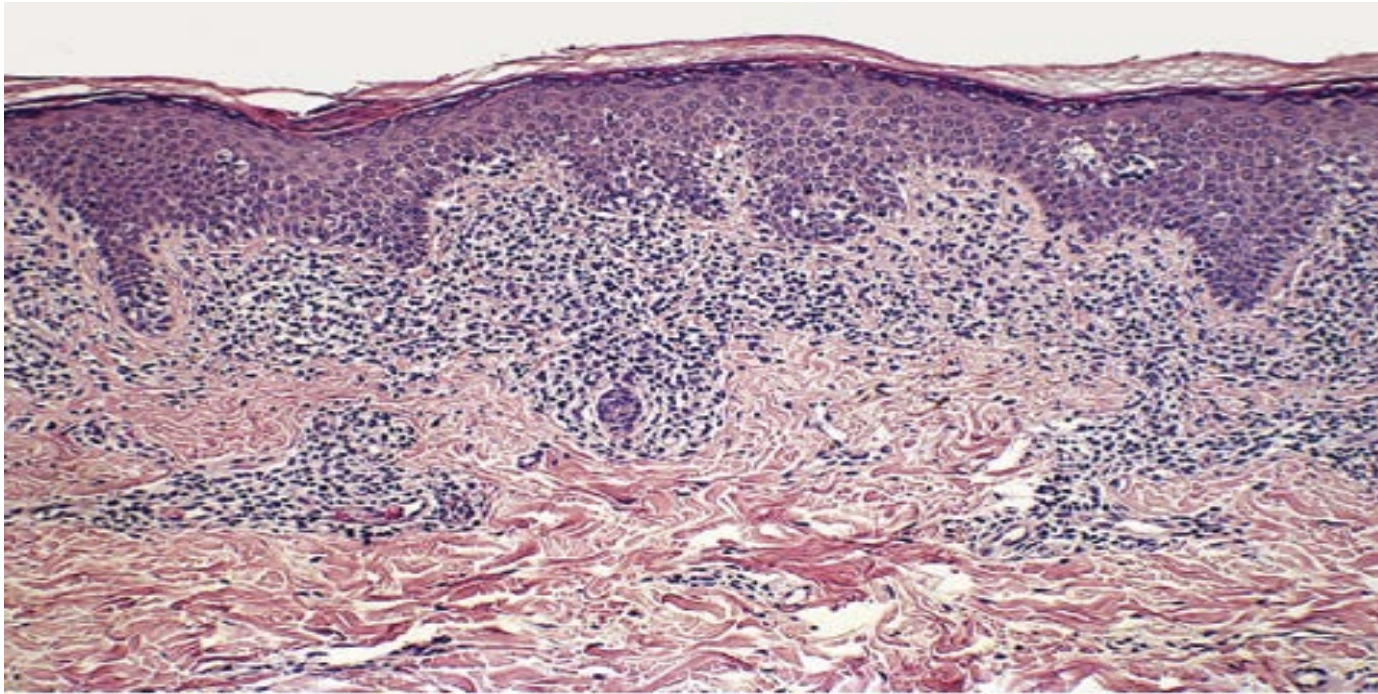


Plaque



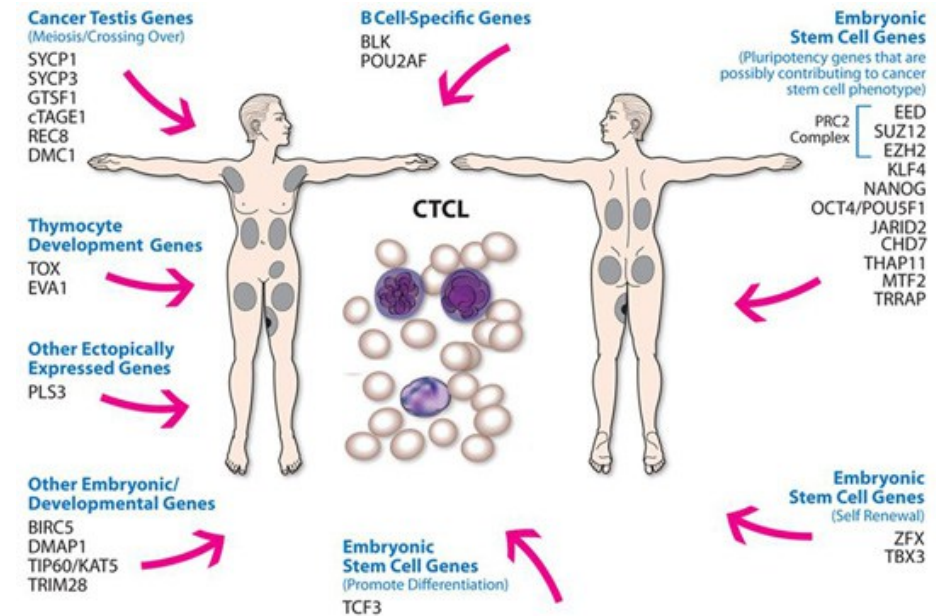
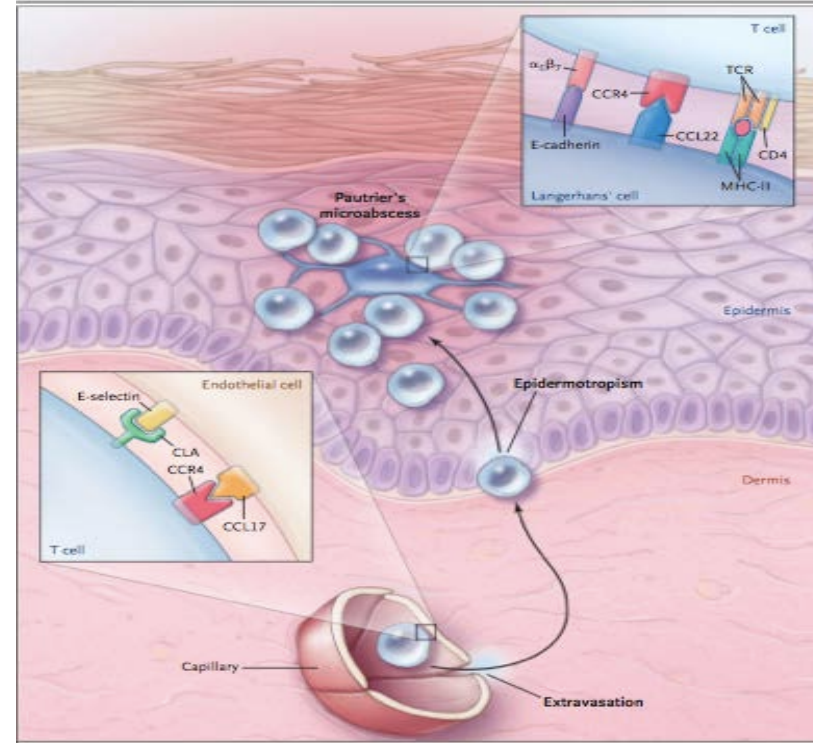
Erythroderma

CTCL PATHOLOGY



PATHOGENESIS

- The pathogenesis involved in the development and progression of MF is not entirely understood



UNKNOWN RISK FACTORS

- Viruses such as EBV and HTLV-1 have no etiologic role in the development of MF as demonstrated in other lymphomas.
- CTCL is rare in post-transplant patients
- No clear link between industrial occupations and the development of MF
- Solar radiation has not been associated as a risk factor for MF
- Atopic patients are not shown to be at increased risk for developing MF

CLINICAL FEATURES

- Years of nonspecific eczematous dermatitis with nonspecific biopsies
- Median duration prior to diagnosis is 4-6 years
- “Classic Presentation”- often pruritic patches or plaques on non-sun exposed areas that slowly progress to tumors
- Hypopigmented lesions: rare but more common in children, adolescents, and darkly pigmented skin
- 30% of patients may presents with tumors or erythroderma
- MF-like presentation described after certain medication ingestions

PEDIATRICS

- Rare
- Low incidence: lack of recognition and hesitation to perform skin biopsies in young children
- Clinical Presentation
 - Thin, atrophic, erythematous patches on the trunk and buttocks are most common
 - Hypopigmentation is a common variant in children
 - Poikiloderma may be present
 - Tumors are uncommon in children

CHALLENGES OF CTCL

- CTCLs are a heterogeneous group of lymphoproliferative disorders
- Management of CTCL is further complicated by the involvement of multiple specialists with differing scope of practice and protocols:
 - Dermatologists
 - Oncologists/Hematologists
 - Pathologists/Dermatopathologists
 - Radiation Oncologists
 - Clinical Investigation Core - Cancer

THE IMPORTANCE OF A TEAM APPROACH

- All patients with a new diagnosis of CTCL should be reviewed initially by a multidisciplinary team
- The diagnosis, staging and management plan should be collaborative
- Central review of pathology and the use of accredited laboratories for immunophenotypic and molecular studies is desirable
- Patient management should be shared between dermatologists and cancer centers, or a specialists

DIAGNOSIS

ESSENTIAL:

- Biopsy of suspicious skin sites
- Dermatopathology review of slides

USEFUL UNDER CERTAIN CIRCUMSTANCES:

- Immunohistochemical studies of skin biopsy^a (CD2, CD3, CD4, CD5, CD7, CD8, CD26)
- Molecular study for T-cell receptor (TCR) gene rearrangements (assessment of clonality) of skin biopsy;^a PCR methods
- Assessment of peripheral blood for Sezary cells (in cases where skin is not diagnostic, especially T4) including Sezary cell prep, flow cytometry and PCR for TCR gene rearrangement
- Biopsy of suspicious lymph nodes

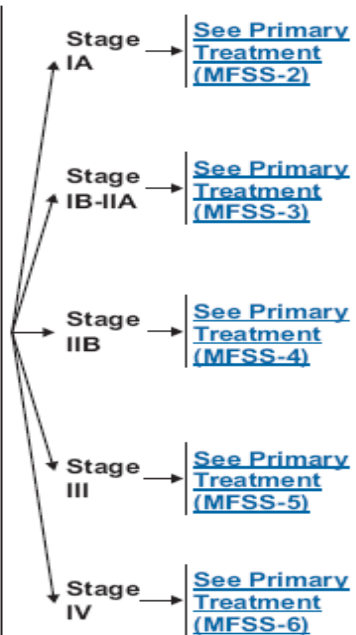
WORKUP^b

ESSENTIAL:

- Complete physical examination
 - Examination of entire skin: assessment of %BSA (palm plus digits ≈ 1%BSA) and type of skin lesion (patch/plaque, tumor, erythroderma)
 - Palpation of lymph node regions
 - Palpation of organomegaly/masses
- Laboratory studies:^c
 - CBC with Sezary screen (manual slide review, "Sezary cell prep")
 - Sezary flow cytometric study (optional for T1); CD3, CD4, CD7, CD8, CD26 to assess for expanded CD4+ cells with increased CD4/CD8 ratio or with abnormal immunophenotype including loss of CD7 or CD26
 - TCR gene rearrangement of peripheral blood lymphocytes if Sezary Syndrome suspected
- Comprehensive metabolic panel
- LDH
- Imaging studies
 - Chest x-ray (in T1 or limited T2 where there is no indication of palpable adenopathy or blood involvement chest x-ray may be the only imaging study)
 - Neck/chest/abdominal/pelvic contrast-enhanced CT or integrated whole body PET/CT (≥ T2, large cell transformed or follicular MF, or with palpable adenopathy or abnormal laboratory studies)
 - Biopsy of suspicious lymph nodes (recommend assessment of clonality for all but particularly NCI LN 2-3) or suspected extracutaneous sites

USEFUL IN SELECTED CASES:^d

- Bone marrow biopsy (not required for staging but used to document visceral disease in those suspected to have marrow involvement including B2 blood involvement and in patients with unexplained hematologic abnormality)



^aPimpinelli N, Olsen EA, Santucci M, et al., for the International Society for Cutaneous Lymphoma. Defining early mycosis fungoides. *J Am Acad Dermatol* 2005;53:1053-1063

^bSee Revisions to the Staging and Classification of Mycosis Fungoides and Sézary Syndrome: A Proposal of the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC). Now in press in *Blood* 2007. Available as First Edition Paper, prepublished online May 31, 2007.

^cSezary syndrome (B2) defined by Sezary cell count ≥ 1,000/mL (Sezary cell prep) or expanded CD4+ cells with CD4/CD8 ratio ≥ 10, CD4+/CD7- ≥ 40%, or CD4+/CD26- ≥ 30% of lymphs in the presence of a positive clonal TCR gene rearrangement.

^dAdditional studies for related therapy: additional immunohistochemical studies - CD25, CD30 (targeted therapies), thyroid function studies (bexarotene therapy), lipid panel (systemic retinoid therapy).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.