Mature T-Cell and NK-Cell Neoplasms: Introduction

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- Neoplasms derived from mature or post-thymic T cells or NK-cells

Mature T-Cell and NK-Cell Neoplasms: Introduction

- Incidence: 12% of all Non Hodgkin Lymphomas
- Most common:

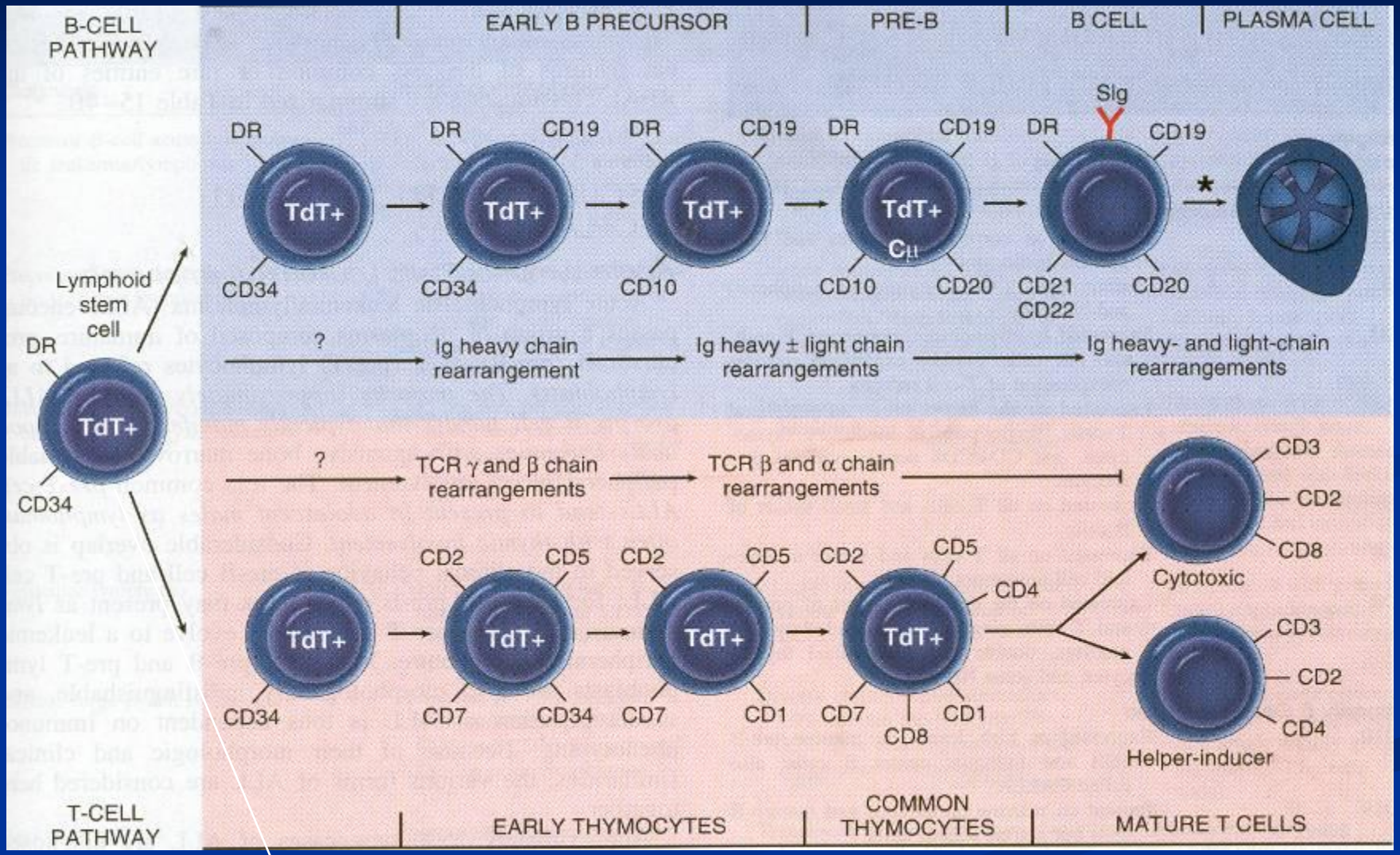
  Peripheral T-Cell Lymphoma (NOS): 3.7%

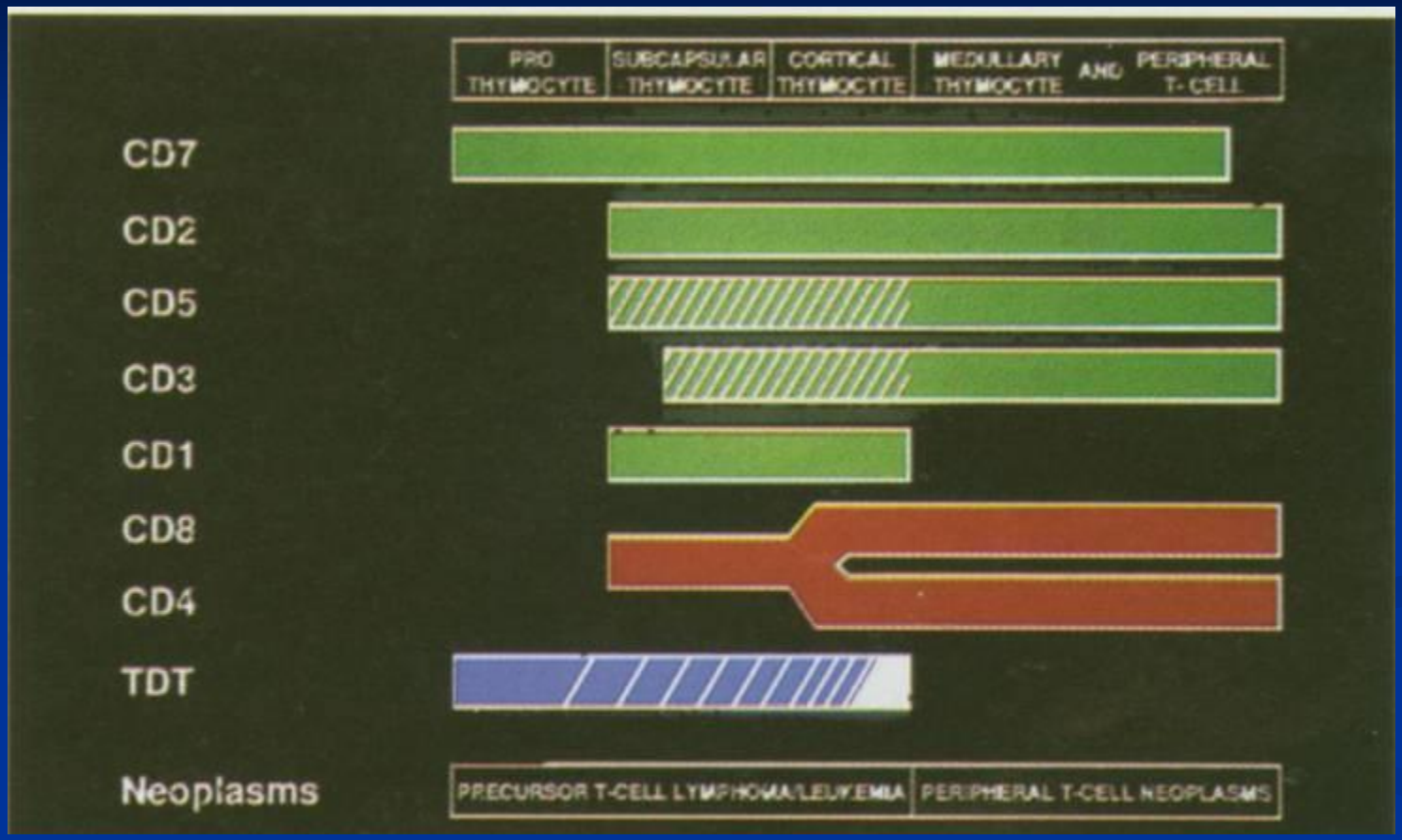
  ALCL: 2.4%
- More common in Asia

Epidemiology

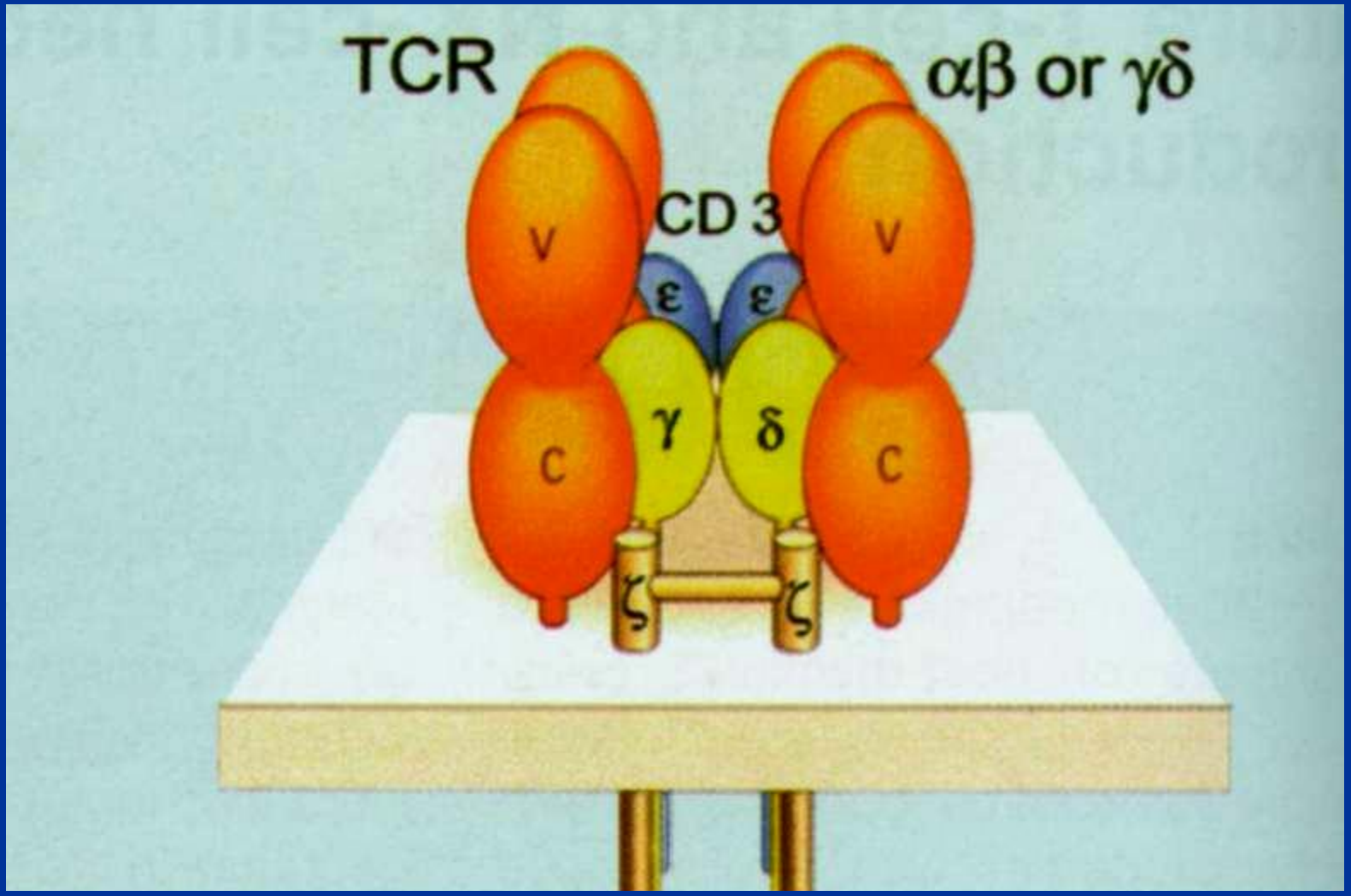
- HTLV-1 infection: in southwestern SW Japan, seropositivity 8-10%; life time risk 6.9% for men and 2.9% for women
- Caribbean basin: HTLV-1, blacks
- Nasal type NK/T cell lymphoma and aggressive NK/T cell leukemia higher in Asia
- Higher in native Americans in North and South America (linkage to Asians)

Pathophysiology:





T cell differentiation scheme



T cell receptor complexed with CD3

T-Cells

- Two major classes of T-cells: αβ T-cells and γδ-T cells
- αβ and γδ chains composed of V and C portions.
- β and δ chains also contain D portion.
- All chains contain J portions
- Both associated with CD3 (γ, δ, and ε chains)
- Each chain ~45 kDa

αβ T-cells

- Two major subtypes
- CD4+ cells and CD8+ cells
- Cytokine secreting

αβ T-cells

- CD4+ cells (2 types)
- Th1 cells (secrete IL-2, IFN-γ)
- Provide help to other T-cells and macrophages

αβ T-cells

- Th2 cells (secrete IL-4, 5, 6, 10)
- Provide help to B-cells in production of antibodies

γδ T-Cells

- Less than 5% of T-cells
- More primitive response - first line of defense against bacteria; mucosal immunity
- Restricted distribution: splenic red pulp and GI epithelium
- Not MHC restricted

NK cells

- NK cells do not have complete TCR complex but express ε chain of CD3 in cytoplasm
- Express CD2, CD7, CD8, CD56, CD57
- CD16+ (less positive in other T-cells)
- Cytotoxic proteins (perforin, granzyme B, T-cell Intracellular Antigen (TIA-1)

Multiparameter Approach for Lymphoma Classification

- Morphology
- Immunophenotype
- Genetics
- Clinical features

Mature T-Cell and NK-Cell Neoplasms: Introduction

- Specific genetic abnormalities not identified for many
- Exception ALCL with t(2;5)

Mature T-Cell and NK-Cell Neoplasms: Introduction

- Poor prognosis

T-Cell Prolymphocytic Leukemia

T-Cell Prolymphocytic Leukemia

Synonyms

- Lukes: "Knobby" type of T-cell leukemia
- Kiel: T-prolymphocytic leukemia/T-cell lymphocytic leukemia
- REAL: T-cell prolymphocytic leukemia/T-cell /T-cell CLL

T-Cell Prolymphocytic Leukemia

- Aggressive T-cell Leukemia
- Small to medium sized prolymphocytes
- Mature post-thymic T-cell phenotype
- Bone marrow, peripheral blood, lymph nodes, liver, spleen, skin
- Rare
- 2% of cases of small lymphocytic leukemia in adults over 30 years

T-Cell Prolymphocytic Leukemia

Clinical features:

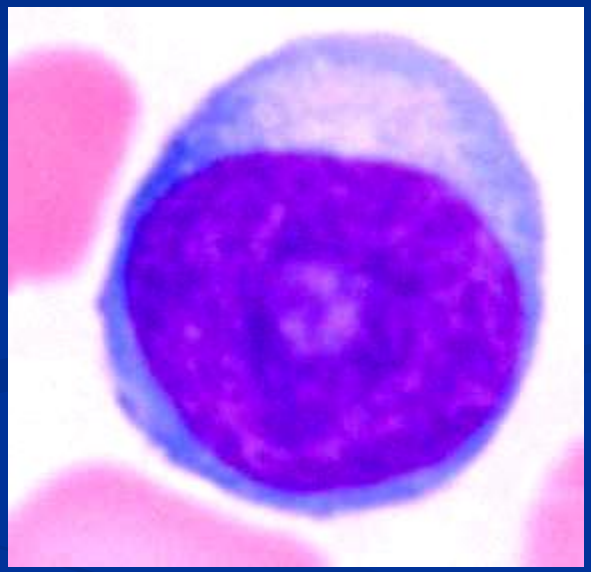
- Hepatosplenomegaly
- Lymphadenopathy
- Skin infiltration (but not erythroderma) 20%
- Anemia
- Thrombocytopenia
- Lymphocytosis (>100 x 10^9/L)

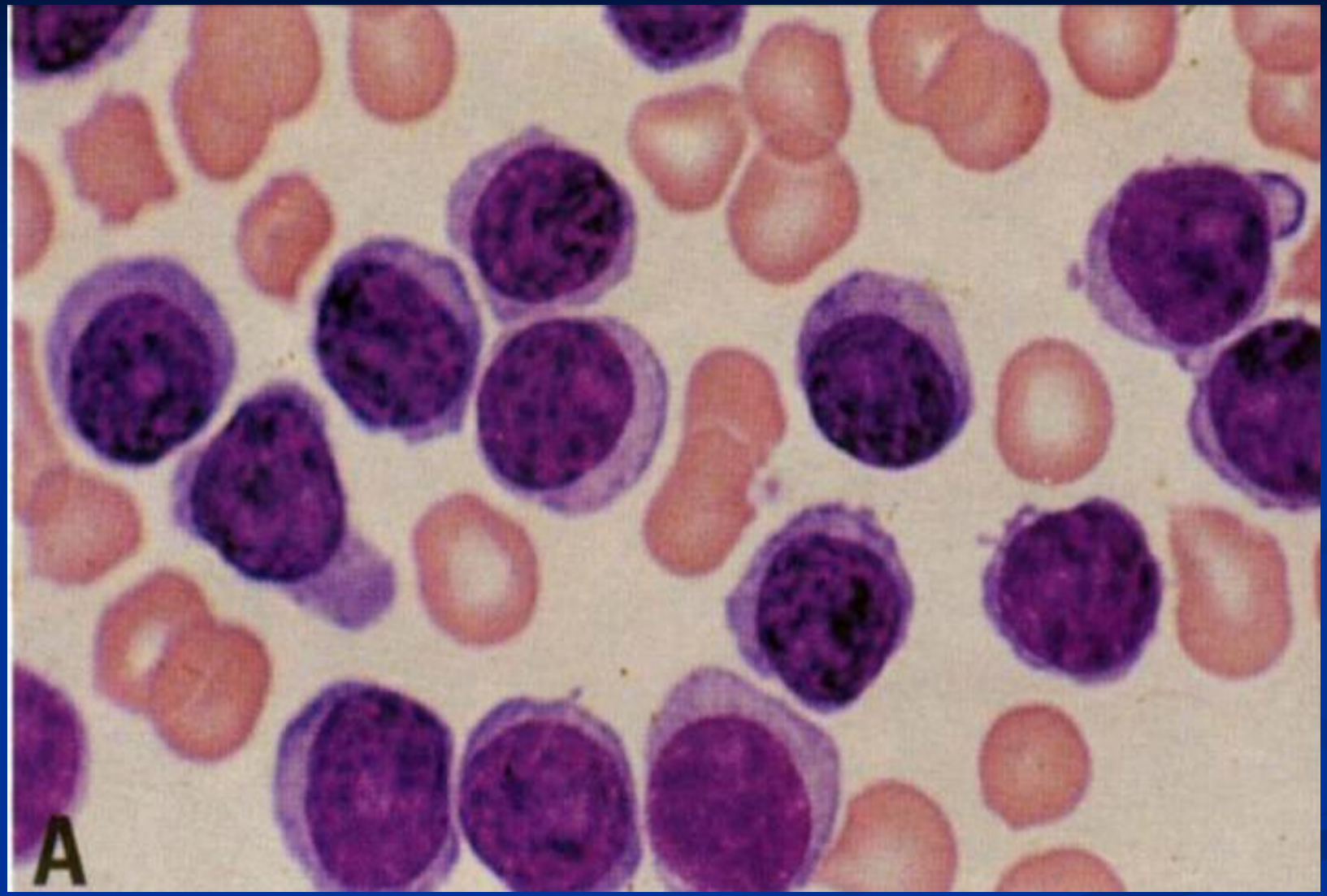
T-Cell Prolymphocytic Leukemia

- Normal serum Ig, no M
- Negative for antibodies against HTLV-1 in serum

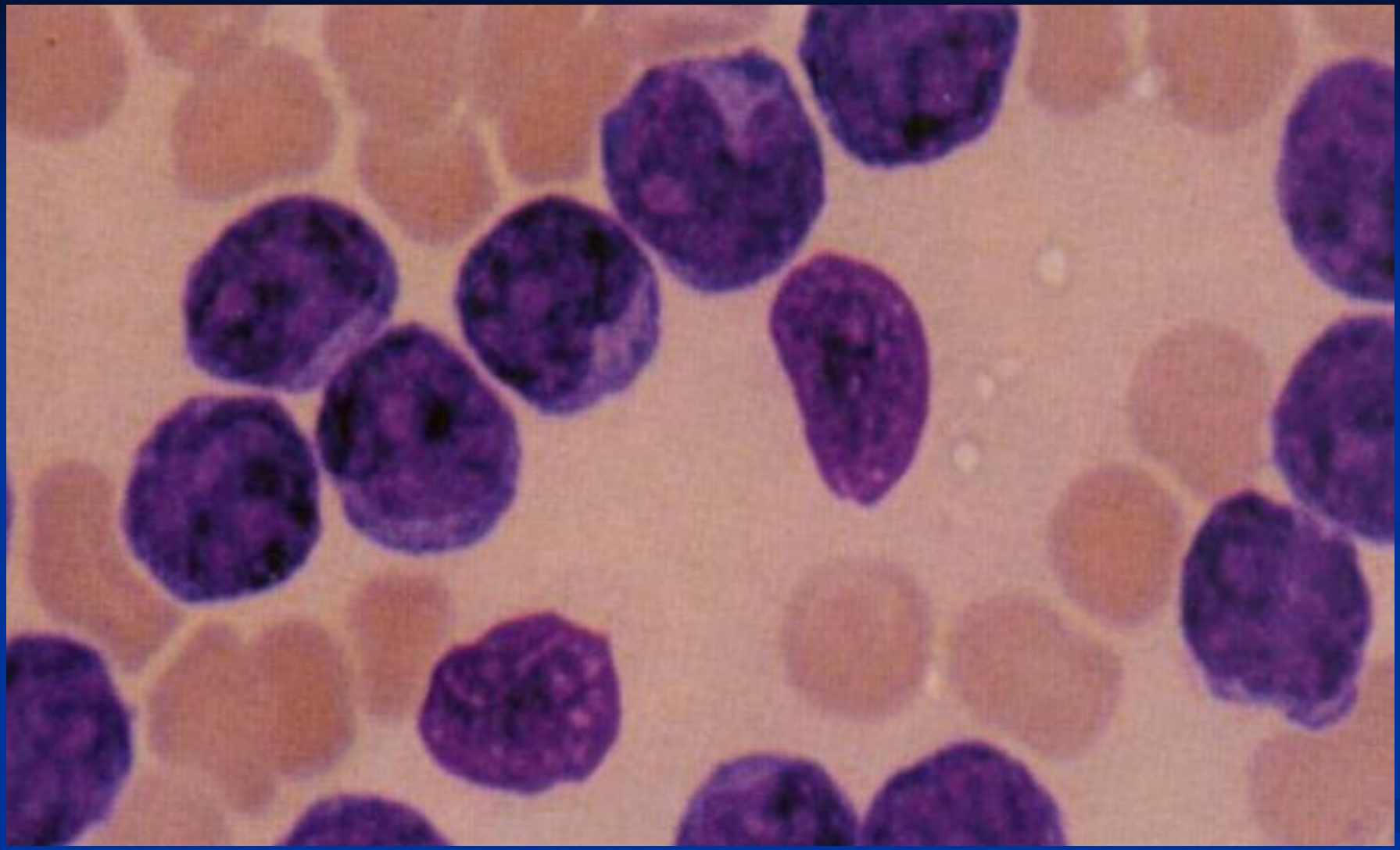
T-Cell Prolymphocytic Leukemia

- Diagnosis on peripheral blood smears
- Small to medium sized lymphocytes
- Non-granular basophilic cytoplasm
- Round, oval or irregular nuclei
- Visible nucleolus
- Cytoplasmic protrusions, or blebs

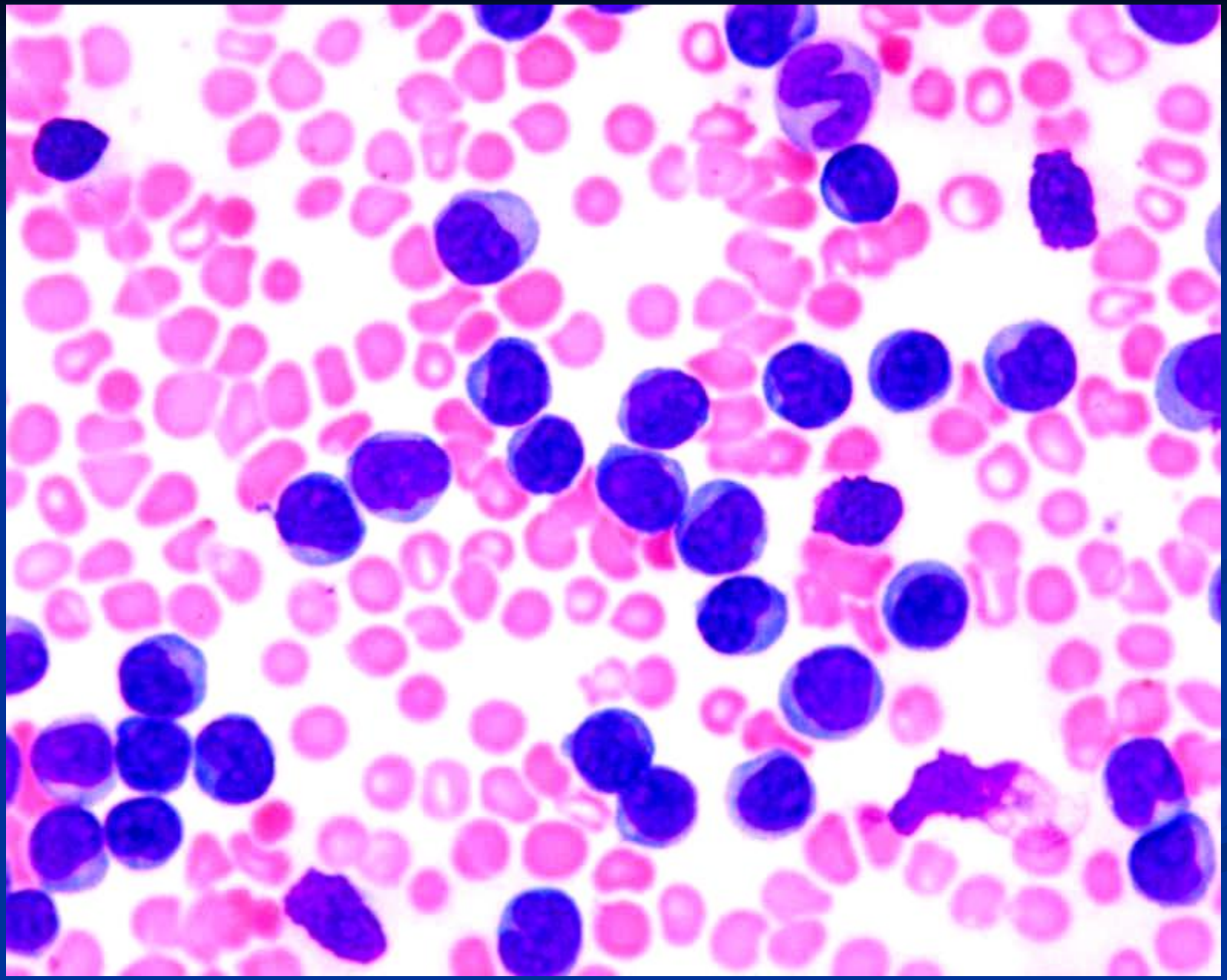


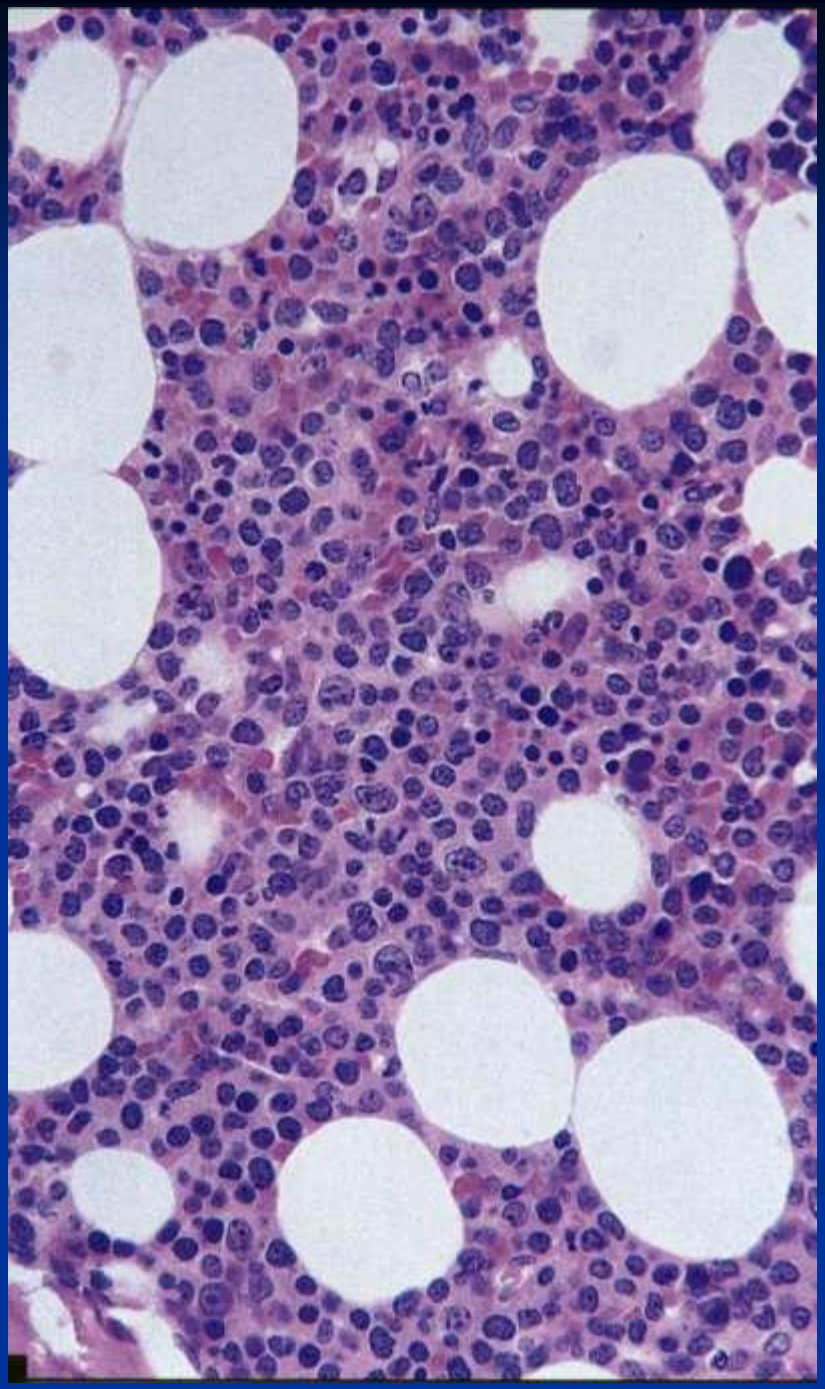


PB smear



PB smear





Bone marrow

T-Cell PLL Variants

- Small cell variant (20-25%)
- Nucleolus not prominent

T-Cell PLL Variants

- Sezary-cell like (cerebriform) variant (5%)

T-Cell PLL

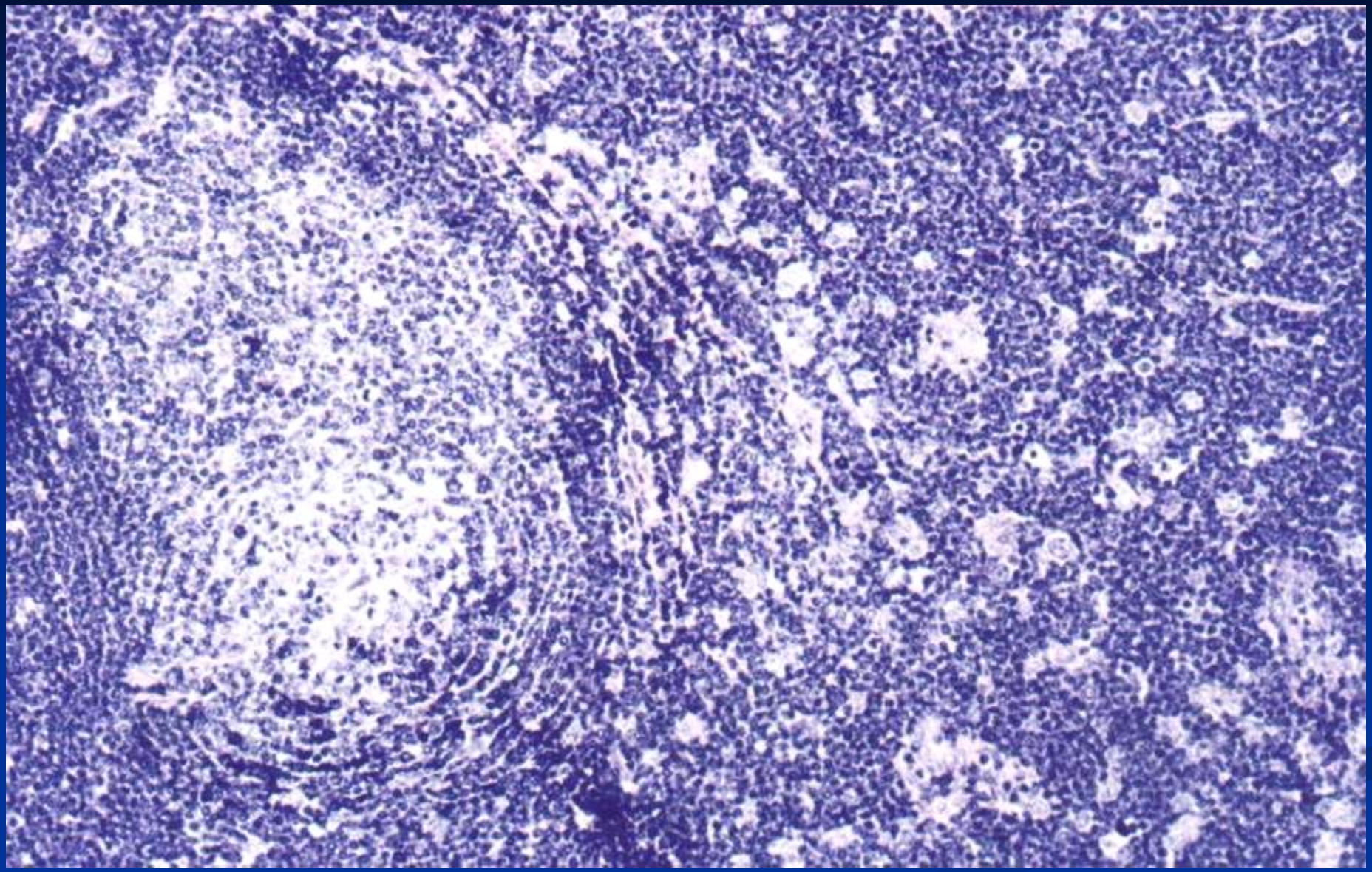
- Strong staining with alpha-naphthyl acetate esterase
- Dot-like staining in Golgi region

T-Cell PLL

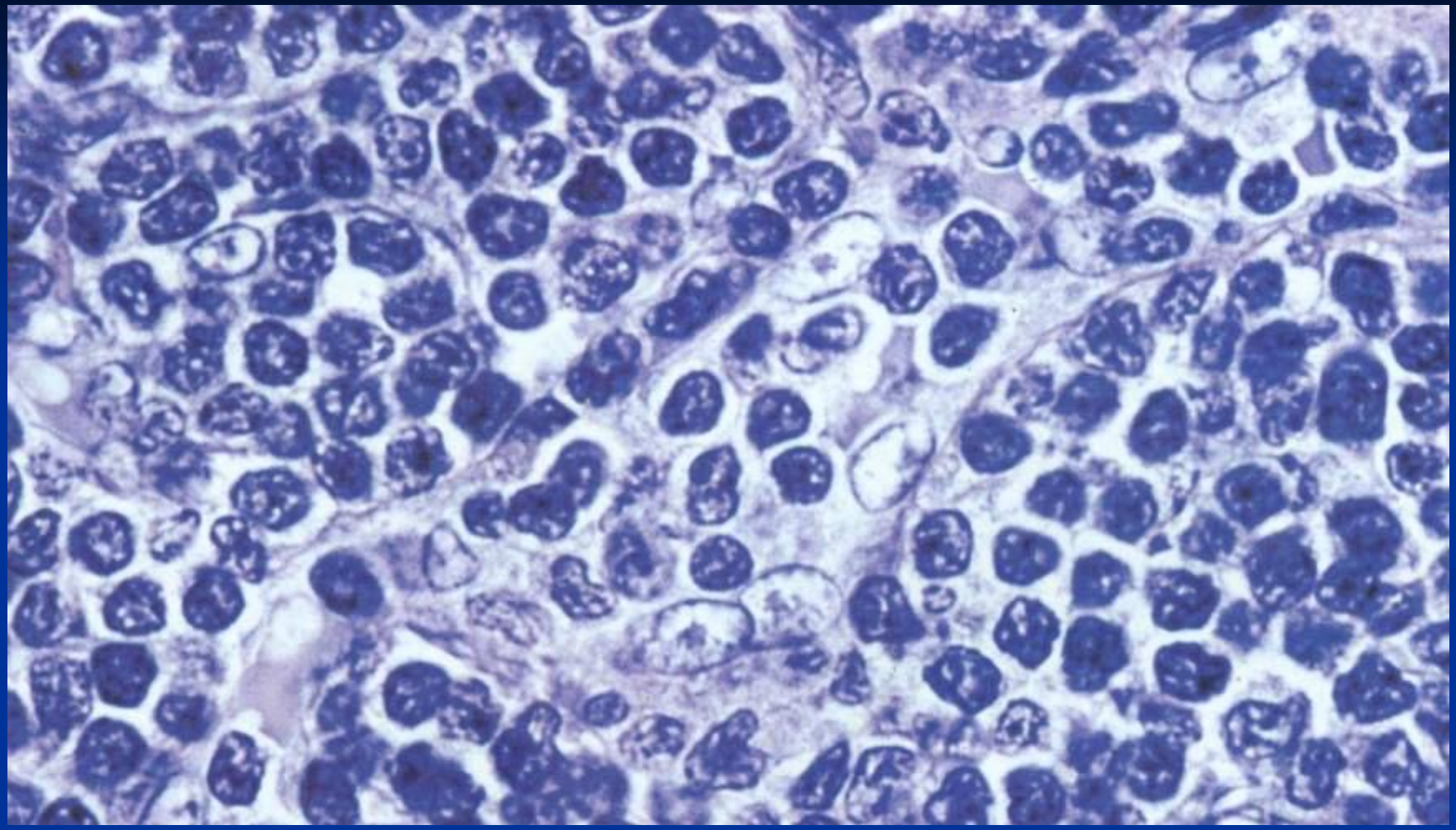
- Skin involvement (20%)
- Dense dermal infiltrates
- (No epidermotropism)

T-Cell PLL

- Spleen - dense red and white pulp infiltrates
- Lymph nodes - diffuse, but tends to be prominent in paracortical areas, sometimes with sparing of follicles
- High endothelial venules prominent and infiltrated



LN: diffuse infiltration with a spared B-cell follicle



T-PLL cells in the lumen of high endothelial venule and the adjacent cortex

T-Cell PLL

Immunophenotype

CD2+, CD3+, CD7+

TdT-, CD1a-

CD4+ and CD8- in 60%

CD4+ and CD8+ in 25% (almost unique to T-PLL)

CD4- and CD8+ in 15%

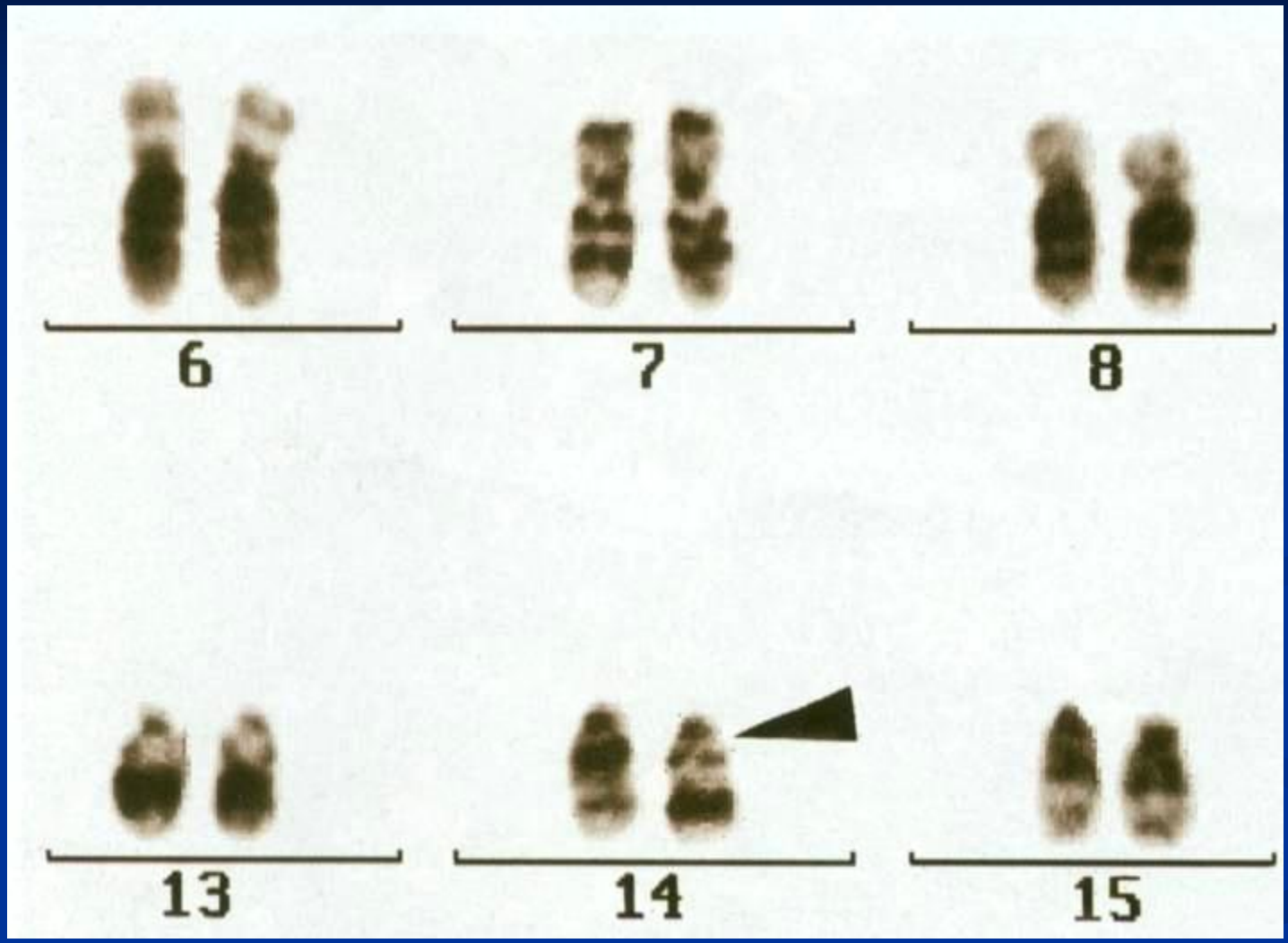
T-Cell PLL

- TCR gamma and beta chains clonally rearranged

T-Cell PLL

Cytogenetics

- inv 14 most frequent abnormality
- Breakpoints q11 and q32 (80%)
- t(14;14)(q11;q32) in 10%
- Juxtaposition and activation of TCR αβ locus with oncogenes TCL1 and TCL1b at 14q32.1
- Abnormalities of chromosome 8 seen in 70-80%
- Other less common abnormalities



Inv 14q (q11 ;q32)

T-Cell PLL

- Postulated cell of origin - mature post thymic cell
- subset with co-expression of CD4 and CD8 suggests that some may arise from a T-cell at an intermediate stage between cortical thymocytes and peripheral blood T-lymphocytes

T-Cell PLL

Prognosis

- Poor
- Survival less than one year
- Treatment with CAMPATH-1H somewhat encouraging; also pentostatin and CHOP regimen
- Bone marrow transplantation being explored