LYMPHOMAS

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DEFINITION

- Lymphomas can be defined as a group of cancers that begin in the lymphocytes of the immune system.
- Present as solid tumors of lymphoid cells.
- Are treatable with chemotherapy,and in some cases, radiotherapy, and/or bone marrow transplantation.
- Can be curable,depending on the histology,type,and stage.

CAUSES

- Exact causes are unknown.
- Several factors have been linked to an increased risk of developing lymphoma:

  1-Age

  2-Infections: Viruses,Bacteria,

  3-Medical conditions that comprise the immune system.

  4-Exposure to toxic chemicals: benzene, pesticides,insecticides,herbicides.

  5-Genetics: Family history of lymphoma.

CLASSIFICATION

- Lymphomas are morphologically subdivided into two major categories:
  1-Non-Hoddgkin's lymphoma (NHL).
  2-Hodgkin's disease(HD)/Hodgkin's lymphoma(HL).

CLASSIFICATION SYSTEMS

- Multiple classification schemes:
  1-Rapport.
  2-Kiel.
  3-Lukes Collins.
  4-REAL: (Revised European-American Classification of Lymphoid Neoplasms) :attempted to apply immunophenotypic and genetic features.
  5-WHO classification.

CLINICAL BEHAVIOR-1

- Indolent lymphomas: survival is measured in years,if left untreated.
- Aggressive lymphomas: survival is measured in months if left untreated.
- Highly aggressive lymphomas: survival is measured in weeks, if left untreated.

CLINICAL BAHAVIOR-2

- Indolent lymphomas are not curable.
- Aggressive lymphomas are curable.
- Highly aggressive lymphomas are curable.

STAGING-1

- TNM system: for solid tumors but is not applicable to lymphomas.Is based upon the concept of a primary tumor and metastasis.
- Staging systems for lymphomas are anatomical classifications,which are based upon the concept of contaguos disease.

STAGING-2

- Ann Arbor Staging System: is a four stage system.

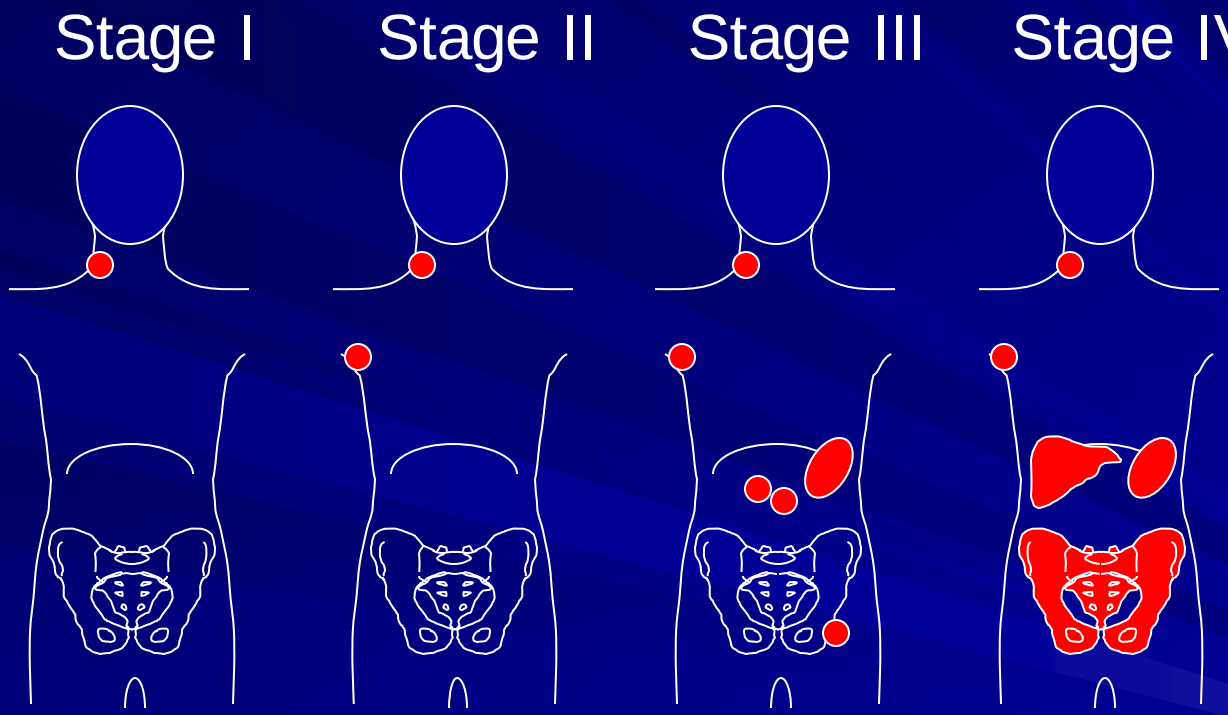
1-Stage I:Involvement of single lymph node region(I) or of single extra lymphatic organ or site(Ie).

2-Stage II: involvement of 2 or more LN regions on the same side of the diaphragm.

3-Stage III: As stage II but on both sides of the diaphragm.

4-Stage IV:Diffuse or disseminated foci of involvement of one or more extralymphatic organ or site,with or without associated lymphatic involvement.

Staging of lymphoma



A: absence of B symptoms

B: fever, night sweats, weight loss

STAGING-3

- Chest radiographs.
- Neck, chest, abdomen and pelvis CT.
- Bone marrow aspirate and trephine biopsy.
- Other imaging techniques: PET Scan, MRI

STAGING NOTATION

- The following notations are used to describe the stage of the disease:

1-The presence of systemic symptoms is noted as “B” and their absence as “A”.

2-Bulky disease is noted as “X”.

3-Extranodal disease is noted as “E”.

B SYMPTOMS

1-Fever: temperature> 38 °C.

2-Weight loss: unexplained loss of >10% of body weight over the past 6 months.

3-Sweats:the presence of drenching night sweats.

Pruritus, fatigue, and ,malaise?.In fewer than 10%of patients.

INITIAL EVALUATION

- The initial evaluation of the patient with suspected NHL must establish the precise
  1-Histologic subtype.
  2-Extent and site of the disease (localized or advanced,nodal or extranodal).
  3-Performance status of the patient.

Treatment approach and prognosis are strongly dependent upon this information.

HISTORY AND PHYSICAL EXAMINATION

- As with other diseases history and physical examination are very important in the evaluation of a patient with suspected lymphoma.

HISTORY

- The following portions of the history are of particular importance:

1- Lymphadenopathy-More than two-thirds of patient with NHL presents with peripheral lymphadenopathy.

2- Systemic complaints-About 40% of pts. with NHL present with systemic complaints of fever, weight loss, or night sweats.

3- Risk factors-A personal or / and family history of prior malignancy, treatment with radiation therapy, chemotherapy, immunotherapy and/or organ transplantation.

PHYSICAL EXAMINATION

- Physical examination needs to be directed to all potentially involved LNs sites:

1-Cervical,supraclavicular,axillary,inguinal, femoral.

2-Liver and spleen.

3-Abdominal nodal sites (mesenteric,retro-peritoneal).

4-Less commonly involved nodal sites(occipital, preauriculas,epitrochlear).

INVOLVEMENT OF OTHER SITES

- Involvement of head and neck.
- Involvement of chest and lungs.
- Abdominal and pelvis involvement.

EXTRANODAL SITES

- 10-35% of pts.with NHL will have primary extranodal lymphoma at initial diagnosis,and about 50% will have extranodal disease during the course of the disease.
- Every organ can be involved by the disease.

OTHER CLINICAL PRESENTATIONS

- Abnormal laboratory results-Less common presentations include unexplained anemia, thrombocytopenia, or leukopenia.
- Potential oncologic emergencies:
  1-Spinal cord compression.
  2-Pericardial tamponade.
  3-Superior or inferior V.cava obstruction.
- Paraneoplastic syndromes.

LYMPH NODE AND TISSUE BIOPSY

- The decision to biopsy a LN?
- A LN should be considered for biopsy if one or more of the following is present:
  1-The LN is significantly enlarged.
  2-The LN persists for longer than 4-6 weeks.
  3-The LN is progressively increasing in size

INITIAL LABORATORY STUDIES

- After the biopsy,the following baseline blood tests should be obtained:

  1-Complete blood count(CBC),WBC differential,and blood film.

  2-Biochemical tests.

  3-Surrogate tumor markers:-beta-2 microglobulin,LDH.

  4-Immunologic and molecular studies.

PROGNOSIS AND TREATMENT

- Prognosis depends upon the histologic subtype,the extent and site of disease ,and the performance status of the patient.
- International prognostic index (IPI):Stage, age,LDH,number of extranodal sites, and ECOG performance status.

International Prognostic Index (IPI)

The following factors were found to correlate with shorter overall or relapse-free survival :

1-Age >60 years

2-LDH greater than normal.

3-ECOG performance status > 2

4-Stage III or IV.

5-Number of extranodal dis.sites >1.

Eastern cooperative oncology group (ECOG, Zubrod) performance scale

Performance status	Definition
0	Fully active; no performance restrictions
1	Strenuous physical activity restricted; fully ambulatory and able to carry out light work
2	Capable of all selfcare but unable to carry out any work activities. Up and about >50 percent of waking hours
3	Capable of only limited selfcare; confined to bed or chair >50 percent of waking hours
4	Completely disabled; cannot carry out any selfcare; totally confined to bed or chair

Excerpted from Oken, MM, et al. Am J Clin Oncol 1982; 5:649.

Karnofsky performance status scale

Value	Level of Functional Capacity
100	Normal, no complaints, no evidence of disease
90	Able to carry on normal activity, minor signs or symptoms of disease
80	Normal activity with effort, some signs or symptoms of disease
70	Cares for self, unable to carry on normal activity or to do active work
60	Requires occasional assistance, but is able to care for most needs
50	Requires considerable assistance and frequent medical care
40	Disabled, requires special care and assistance
30	Severely disabled, hospitalization is indicated although death is not imminent
20	Hospitalization is necessary, very sick, active supportive treatment necessary
10	Moribund, fatal processes progressing rapidly
0	Dead

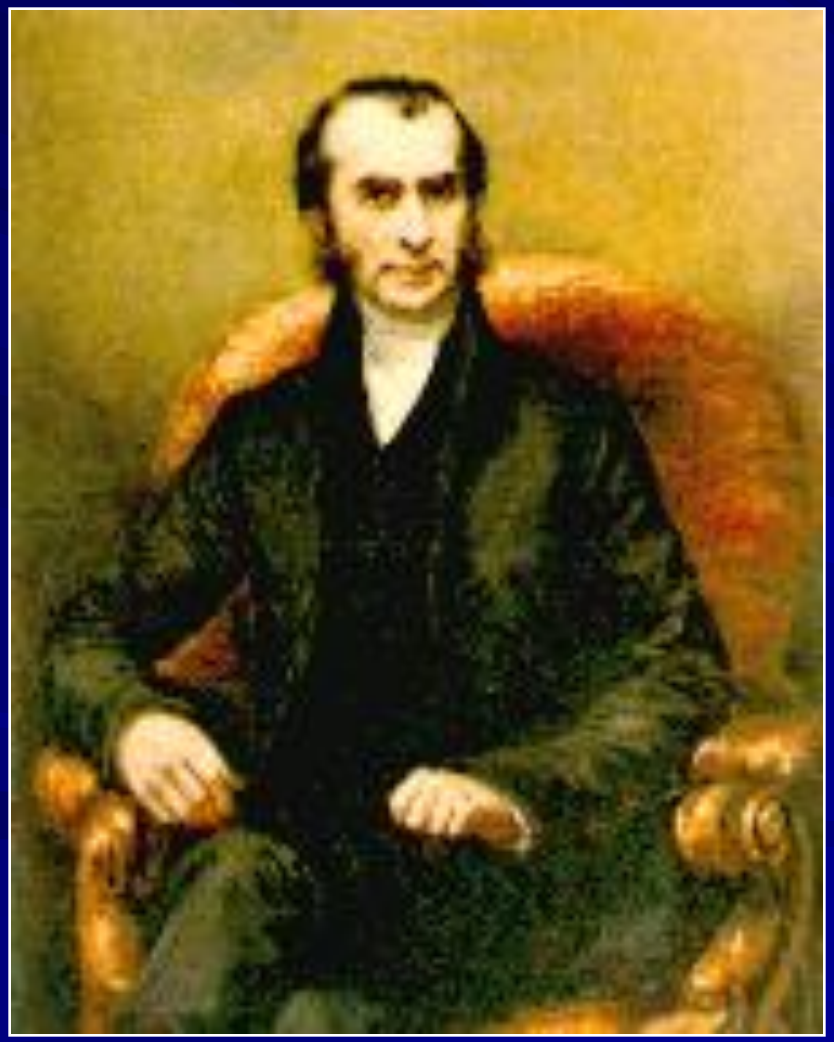
TREATMENT

- No treatment : Watchful waiting.
- Chemotherapy.
- Radiotherapy.
- Immunotherapy : Chemoimmunotherapy.
- Bone marrow transplantation.

HODGKIN'S LYMPHOMA (DISEASE)

(HL)

Hodgkin lymphoma



Thomas Hodgkin
(1798-1866)

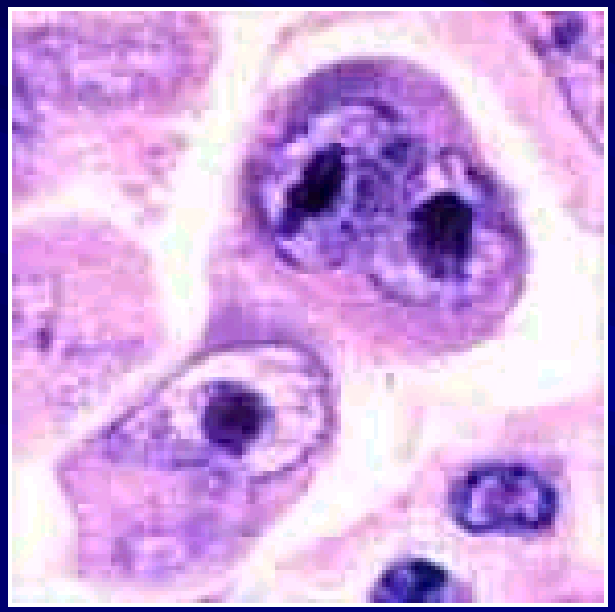
HISTORY

- HL was first named after Thomas Hodgkin, who first described abnormalities in lymph system in 1832.
- In 1865 (33 years later) Wilks reported on a series of patients with the same disease that Hodgkin had previously described and for the first time he called the disease “Hodgkin’s Disease” on honor of his predecessor

HODGKIN'S LYMPHOMA

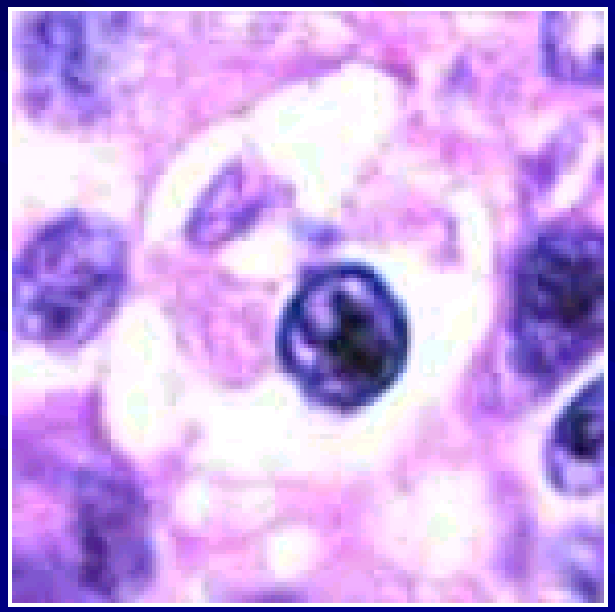
- Reed-Sternberg cells (RS cells) are the characteristic histopathologic finding in HL.
- Occurrence shows two peaks:
  1-Young adults (age 15-35).
  2-Over 55 years.
- Survival rate is high ≈ 90%,making it one of the more curable forms of cancer.

RS cell and variants



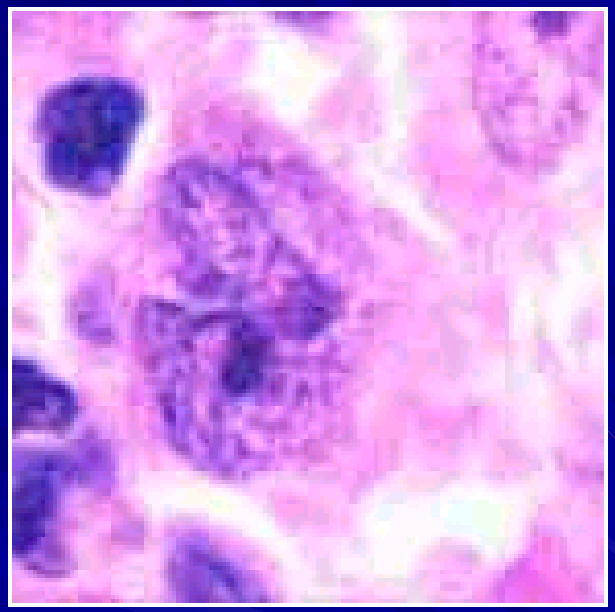
classic RS cell

(mixed cellularity)



lacunar cell

(nodular sclerosis)



popcorn cell

(lymphocyte predominance)

CLASSIFICATION OF HLs

- Unlike NHLs, HLs are not categorized into indolent, aggressive, and highly aggressive categories.

Classical Hodgkin lymphomas:

1-Nodular sclerosis HL.

2-Mixed cellularity HL.

3-Lymphocyte depleted HL.

4-Lymphocyte-rich classical HL.

Nodular lymphocyte-predominant HL.

EPIDEMIOLOGY

- Unlike other lymphomas, whose incidence increases with age , HL has a bimodal incidence curve.
- It occurs most frequently in two separate age groups:
  1-Young adulthood (age 15-35 yrs)
  2-Over 55 years.
- It is more common in males, but in Jordan is more in females.

ADVERSE PROGNOSTIC FACTORS

- Adverse prognostic factors:
  - 1- Age > 45 years.
  - 2- Stage IV disease.
  - 3- Hb < 10,5 g/dL.
  - 4- Lymphocyte count > 600/dL.
  - 5- Male gender.
  - 6- Albumin < 40 g/L.
  - 7- WBC count > 15,000 /uL.

OTHER ADVERSE FACTORS

- Other studies reported other prognostic factors such as:

1- Mixed-cellularity or lymphocyte-depleted histologies.

2-Large numbers of involved nodal sites.

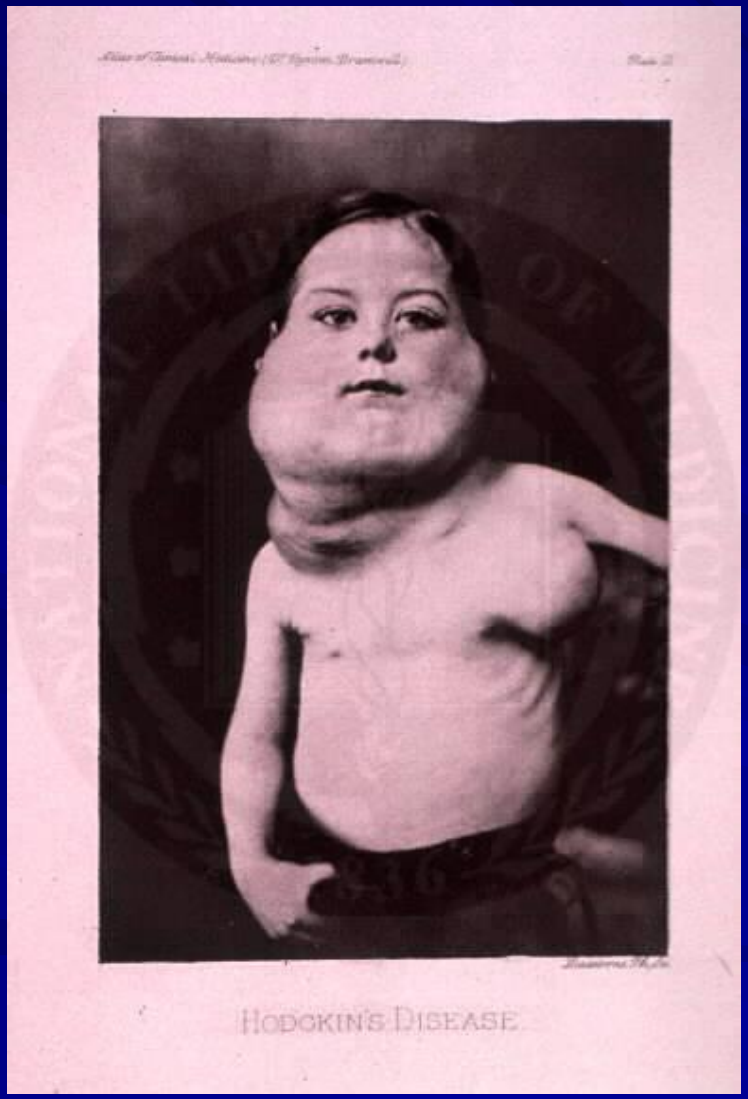
3- Advanced stage.

4-The presence of B symptoms.

5-High ESR.

6- Bulky disease.

Classical Hodgkin Lymphoma

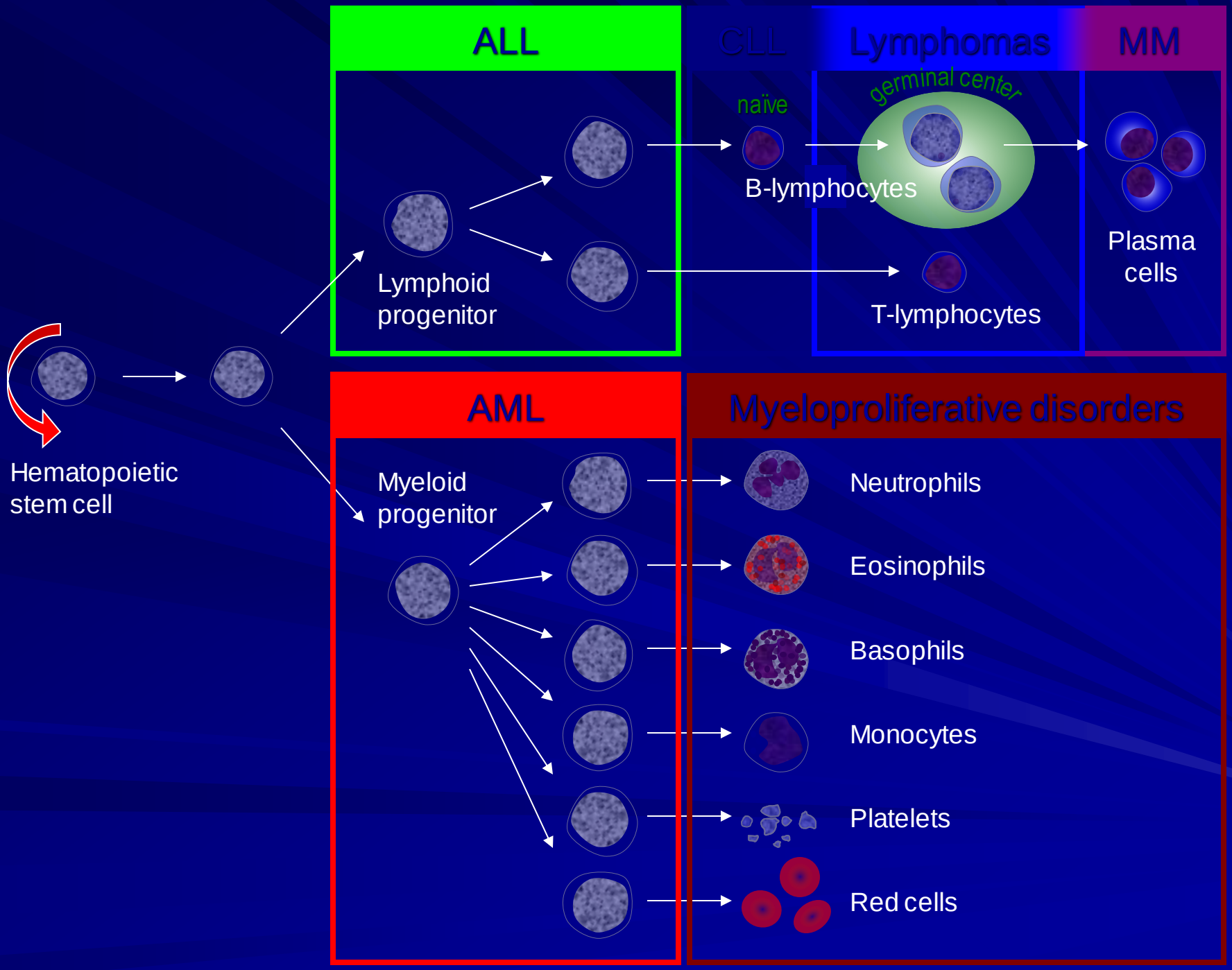


TREATMENT

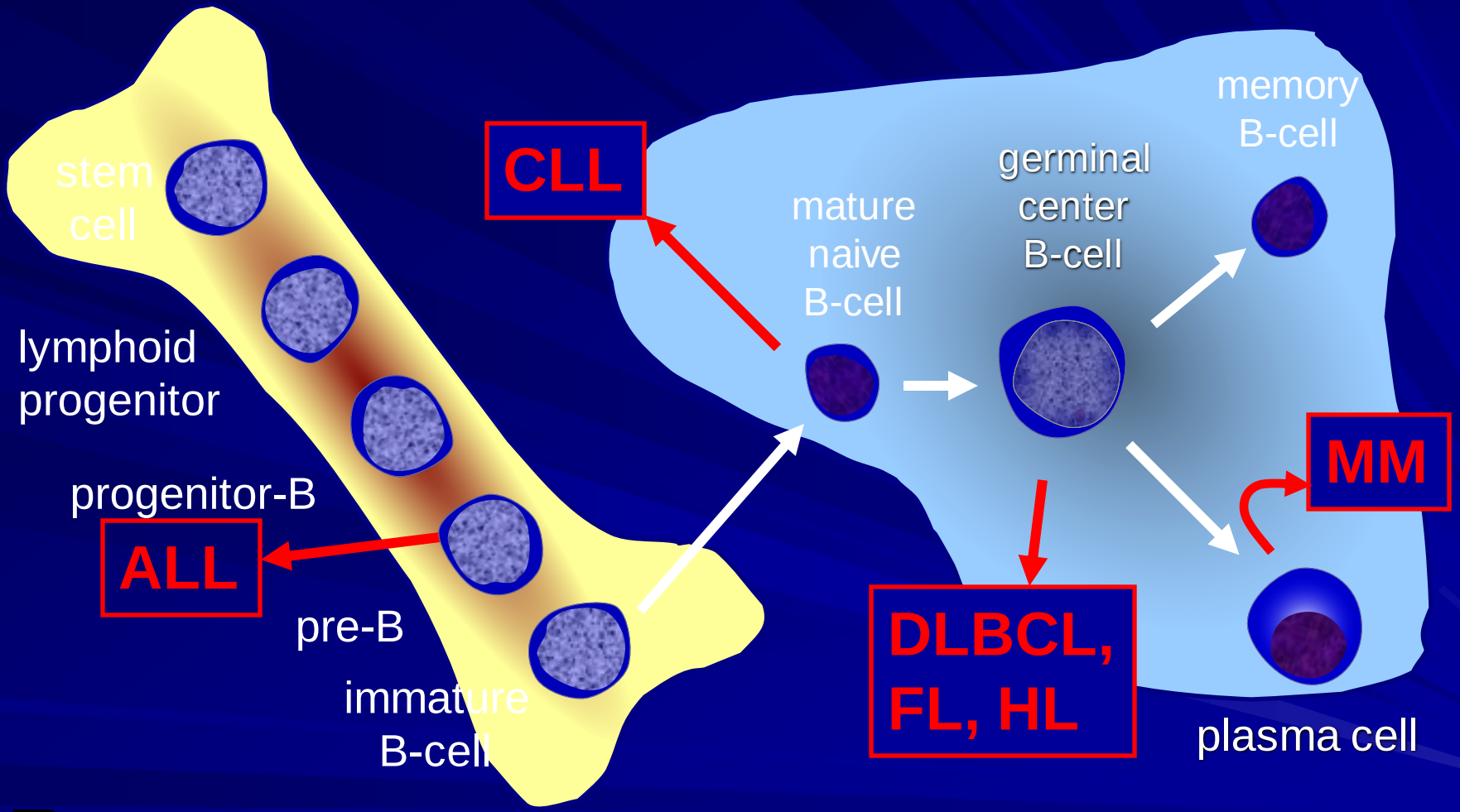
- Chemotherapy : ABVD, Stanford V,
  BEACOPP.
- Radiotherapy.
- Bone marrow transplantation (HSCT).

Treatment and Prognosis

Stage	Treatment	Failure-free survival	Overall 5 year survival
I,II	ABVD x 4 & radiation	70-80%	80-90%
III,IV	ABVD x 6	60-70%	70-80%


ALL
CLL
Lymphomas
MM
naïve
germinal center
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
AML
Myeloproliferative disorders
Myeloid progenitor
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells

B-cell development



THANK YOU