

Malignant Lymphoma

BY

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Definitions

Lymphoma
Is a neoplasm of
The Immune System cells
(lymphocytes)

**Why are lymphomas unique
and important?**

Epidemiologically

- It is the **most common** occurring Hemopoetic system malignancy
- Approximately **1,000** people worldwide are diagnosed with lymphoma
EVERY DAY.

- All over the world
- Both gender : males & females
- Age : pediatric , adults , elderly

Clinically

- lymphomas have a **wide range** of clinical presentation.
- Lymphomas are considered in **most of the differential diagnosis** in medicine

Lymph nodes
Skin Jaw
Brain
Kidney
Liver
lung

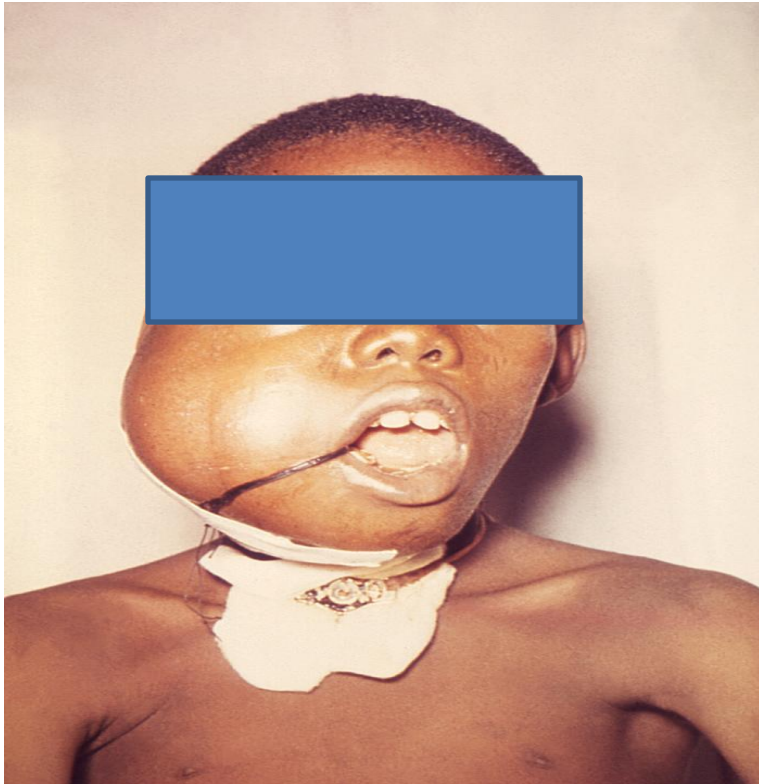
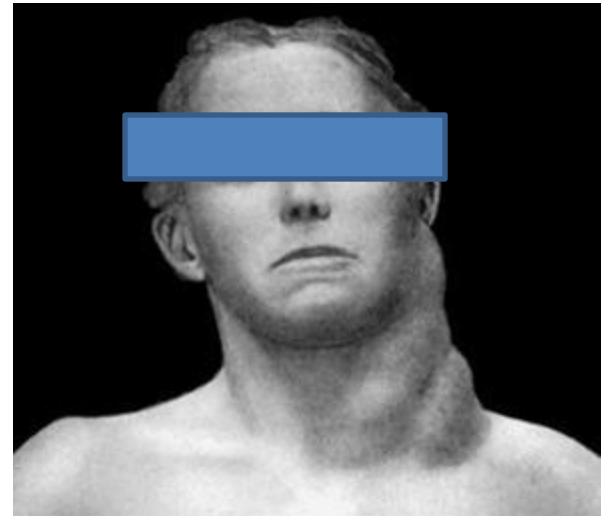
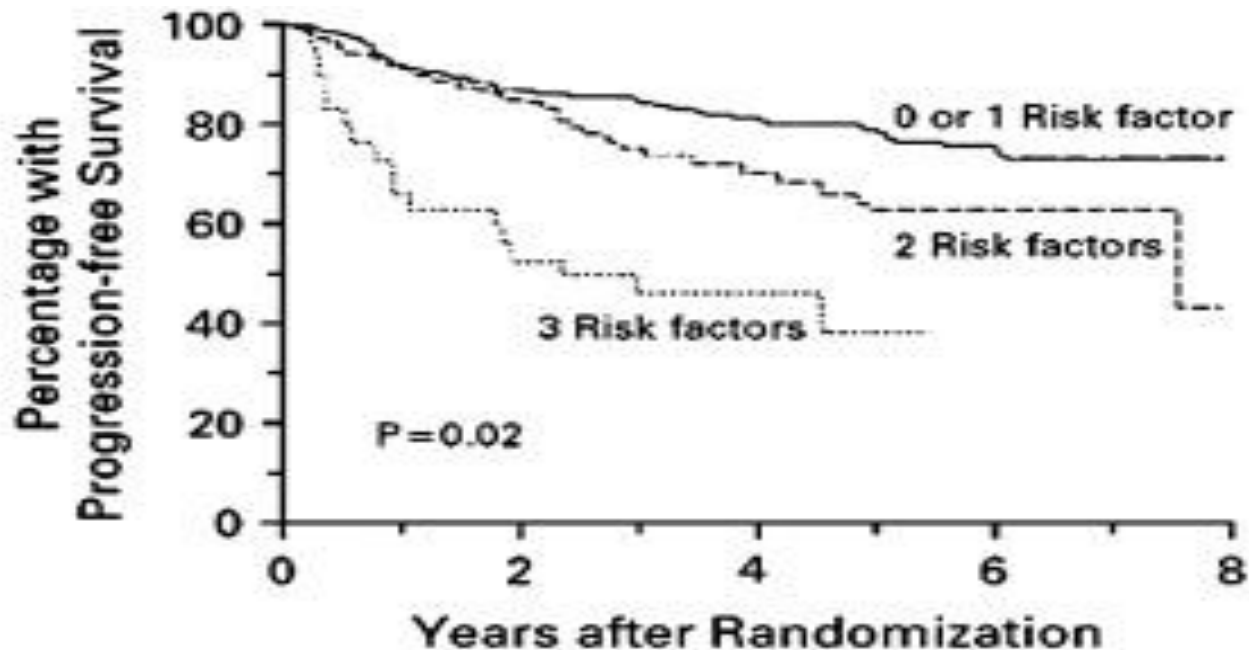


FIGURE 3: Primary cutaneous follicular center B-cell lymphoma.
Papules and nodules in the dorsal region



lymphomas are potentially curable malignancy.



NO. AT RISK

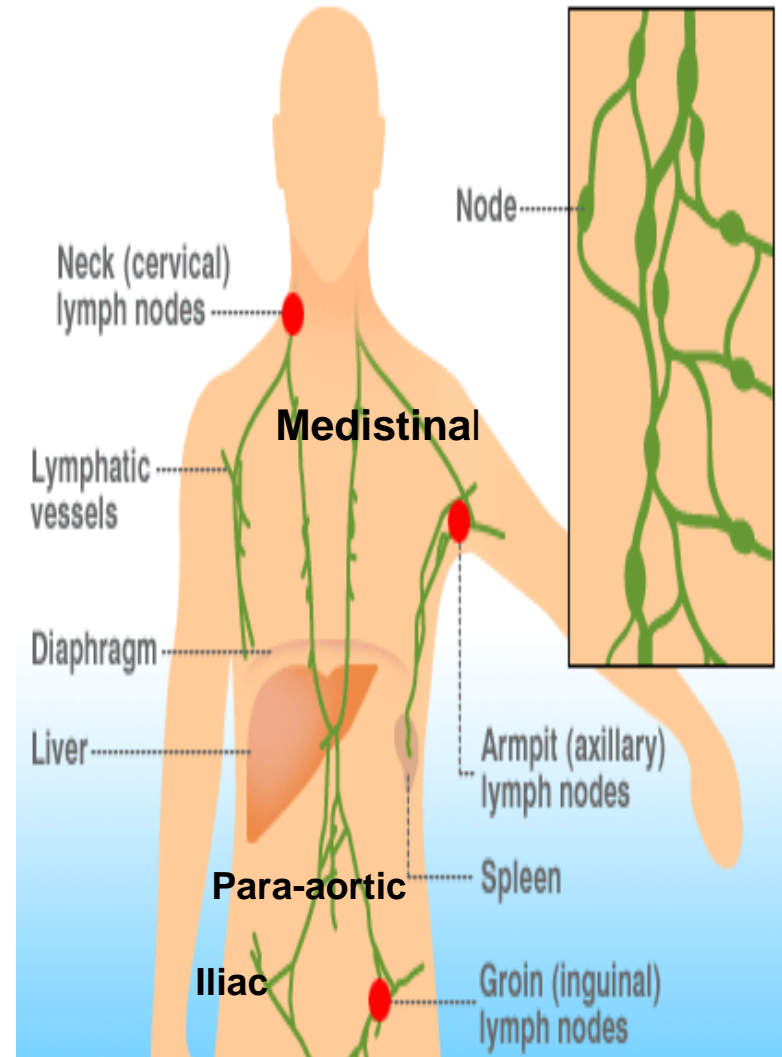
0 or 1 Risk factor	289	257	172	94	7
2 Risk factors	82	74	47	26	10
3 Risk factors	28	18	10	4	0

Why are lymphomas unique and important? = 3Cs

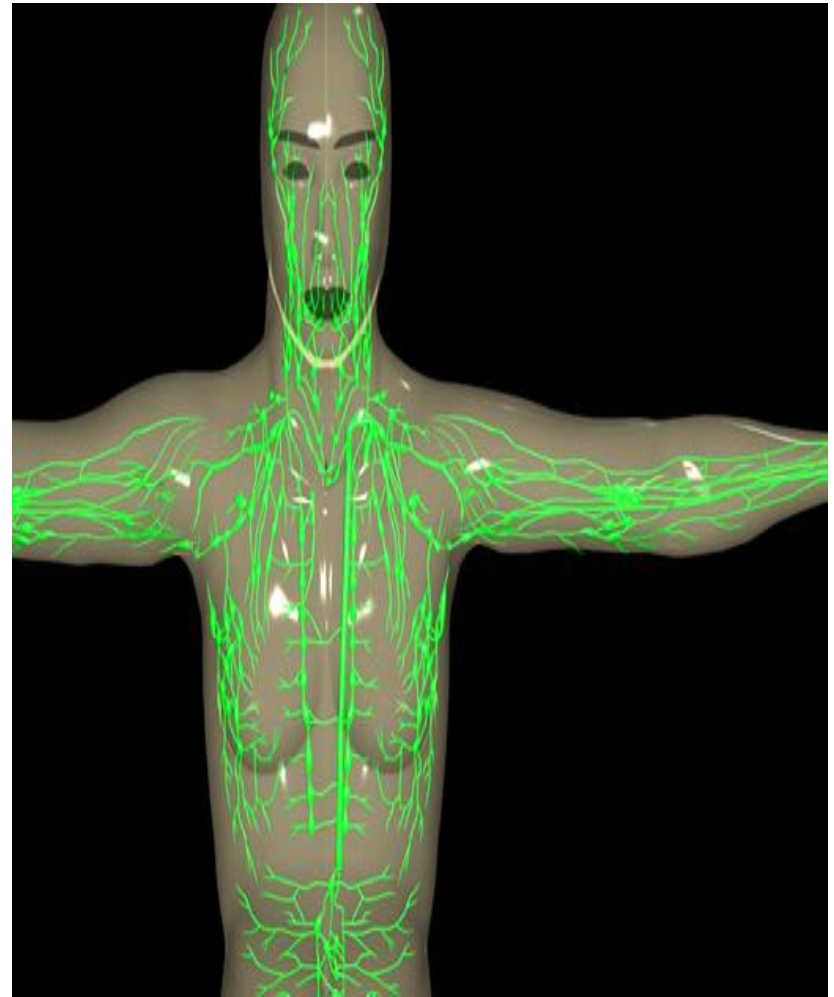
- Common
- Clinical wide range of presentation
- Curable

The Lymphatic system

- The lymphatic system:
 - 1- A network of tubes (vessels)
 - 2- grapelike clusters called lymph nodes.
- The vessels transport colorless fluid called lymph and cells of the immune system (**lymphocytes**) throughout the body.



- **The lymphatic system:**
1- vessels
2- lymph nodes.



- The lymphatic system serves many purposes including:
- It is responsible for absorbing and filtering the fluid which surrounds the cells and tissues of the body.

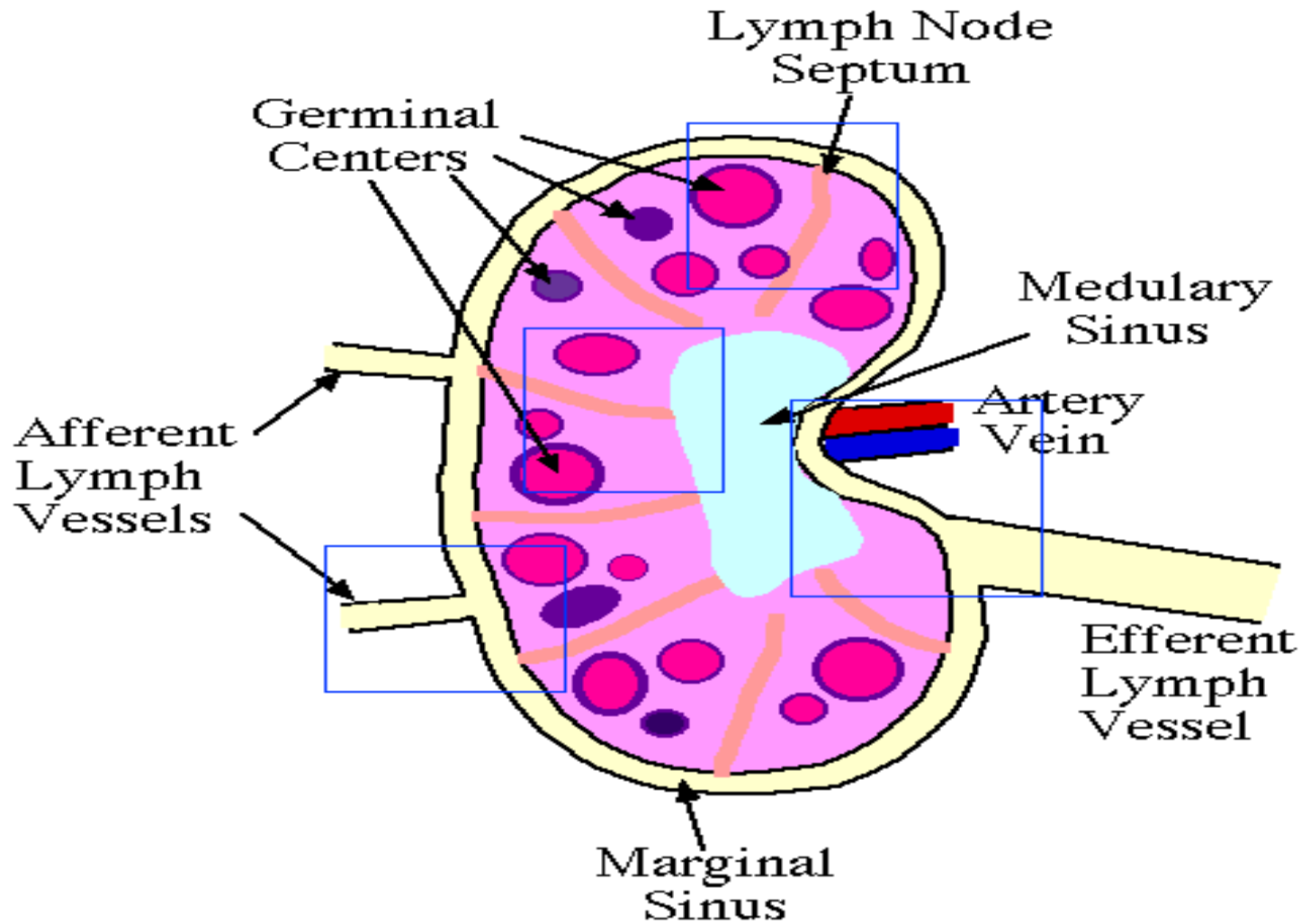
1- Absorbing

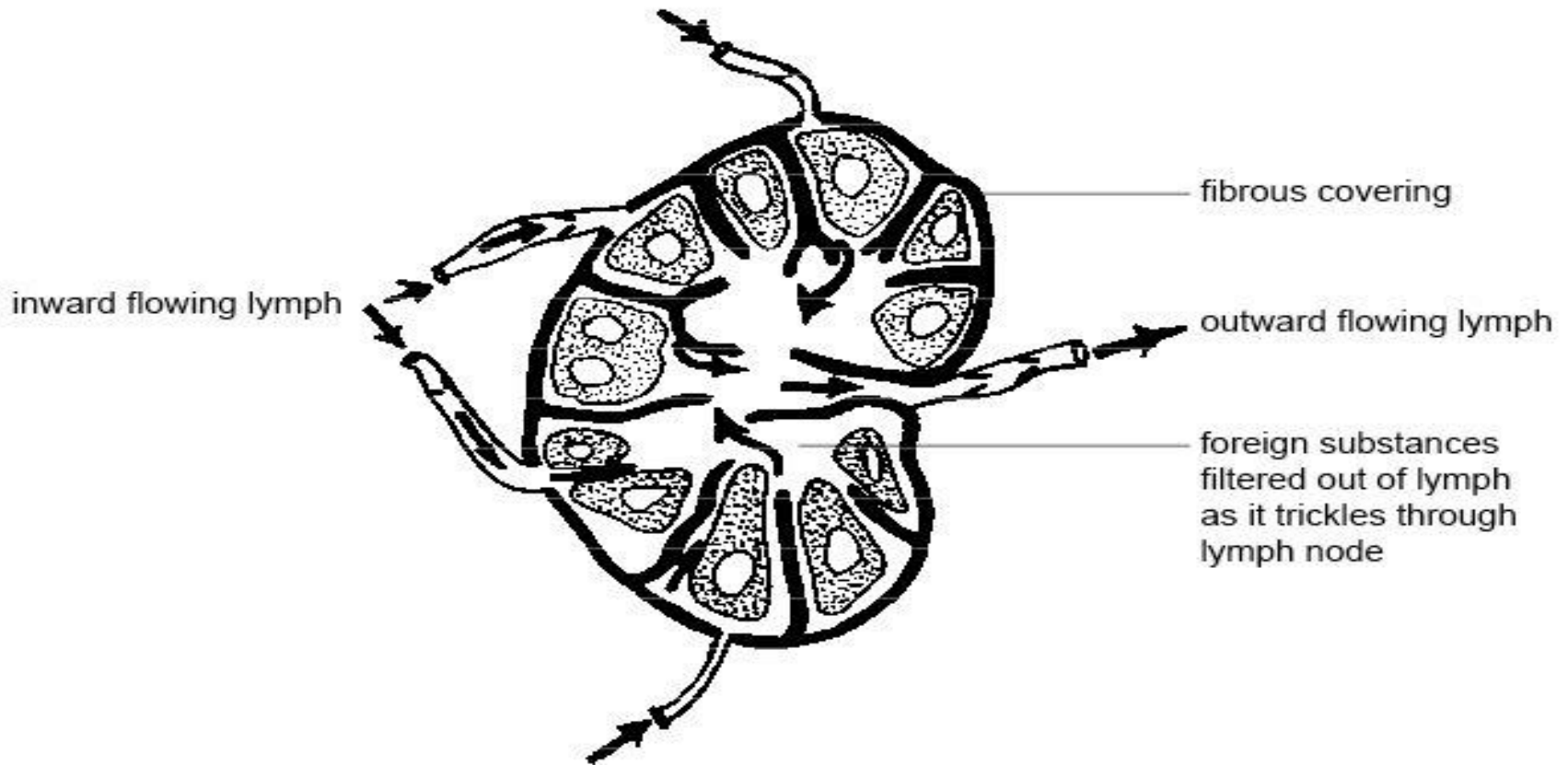
2- Transport of fluid

3- Filtration

4- Initiation of immune responses.

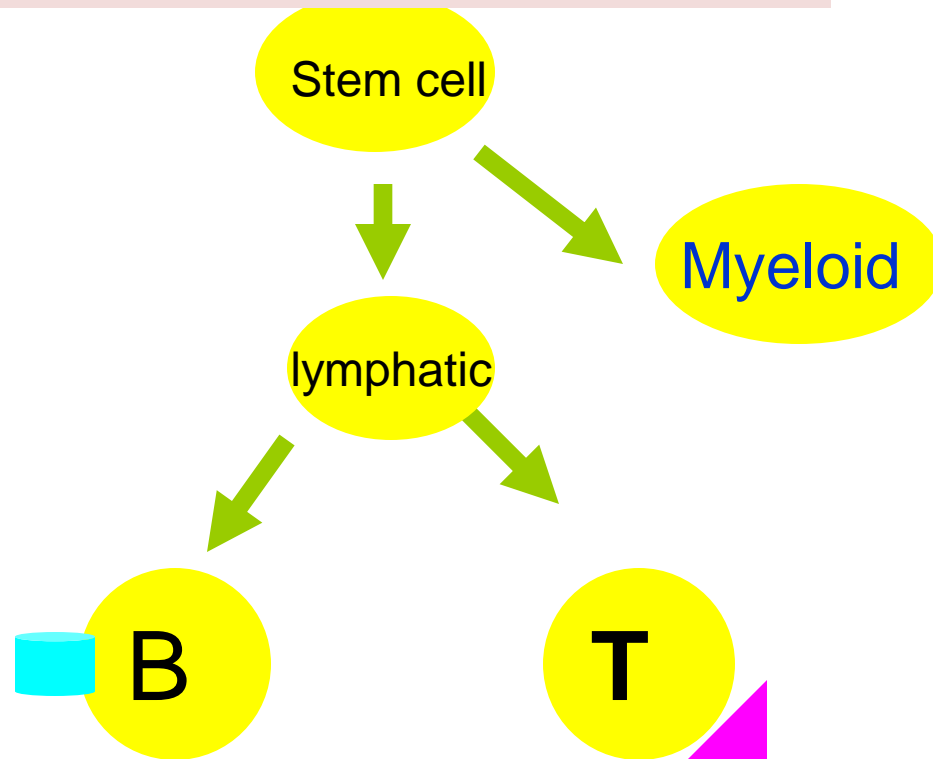
Lymph Node





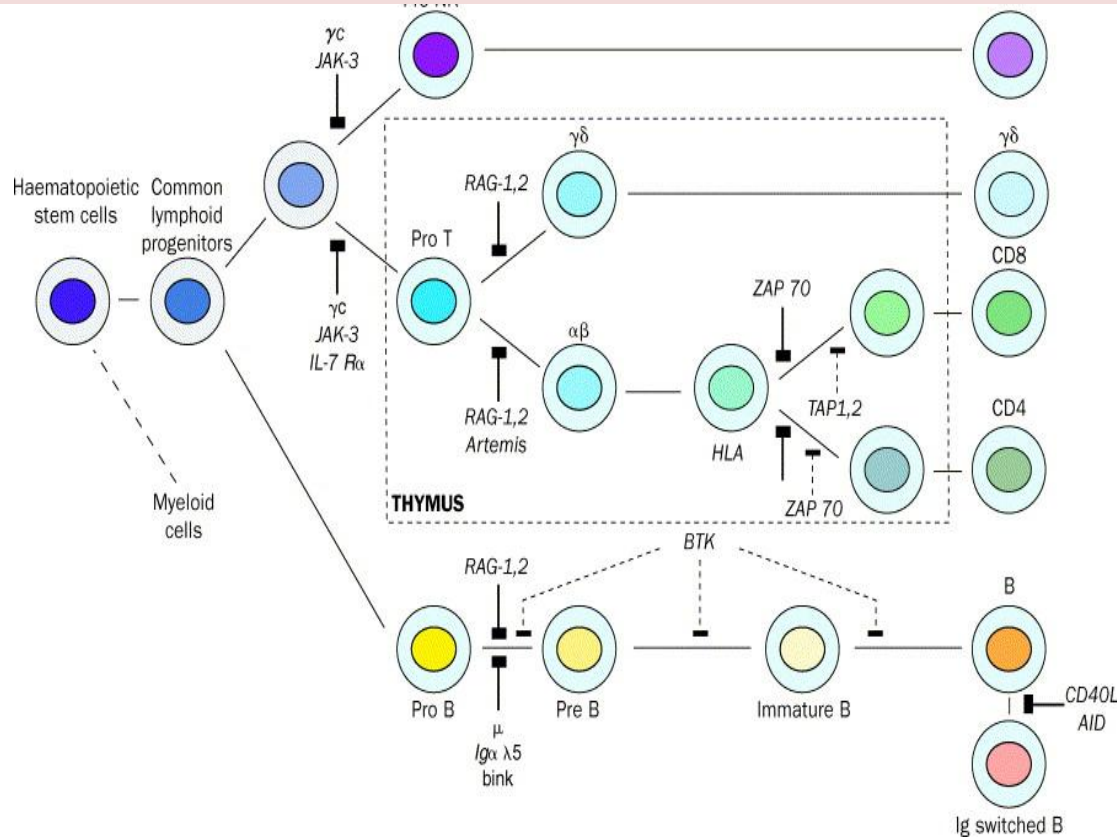
- Lymph nodes are small sac-like structures located along the lymph vessels. They are the home of lymphocytes.
- Inside the lymph nodes lymphocytes come into contact with foreign materials (antigens) in a manner that stimulates their activity.

Lymphocyte development

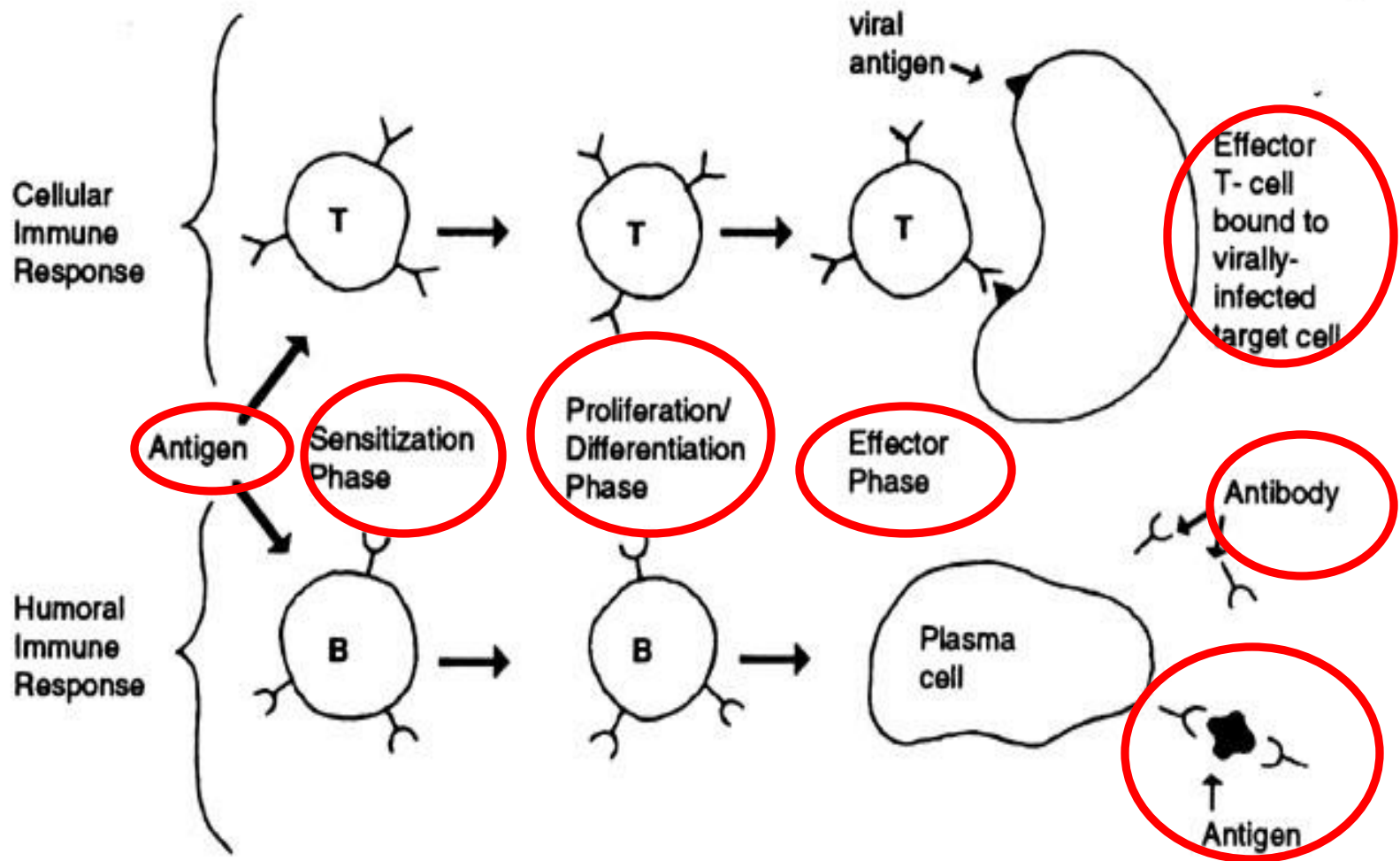


***PROLIFERATION AND
MATURATION***

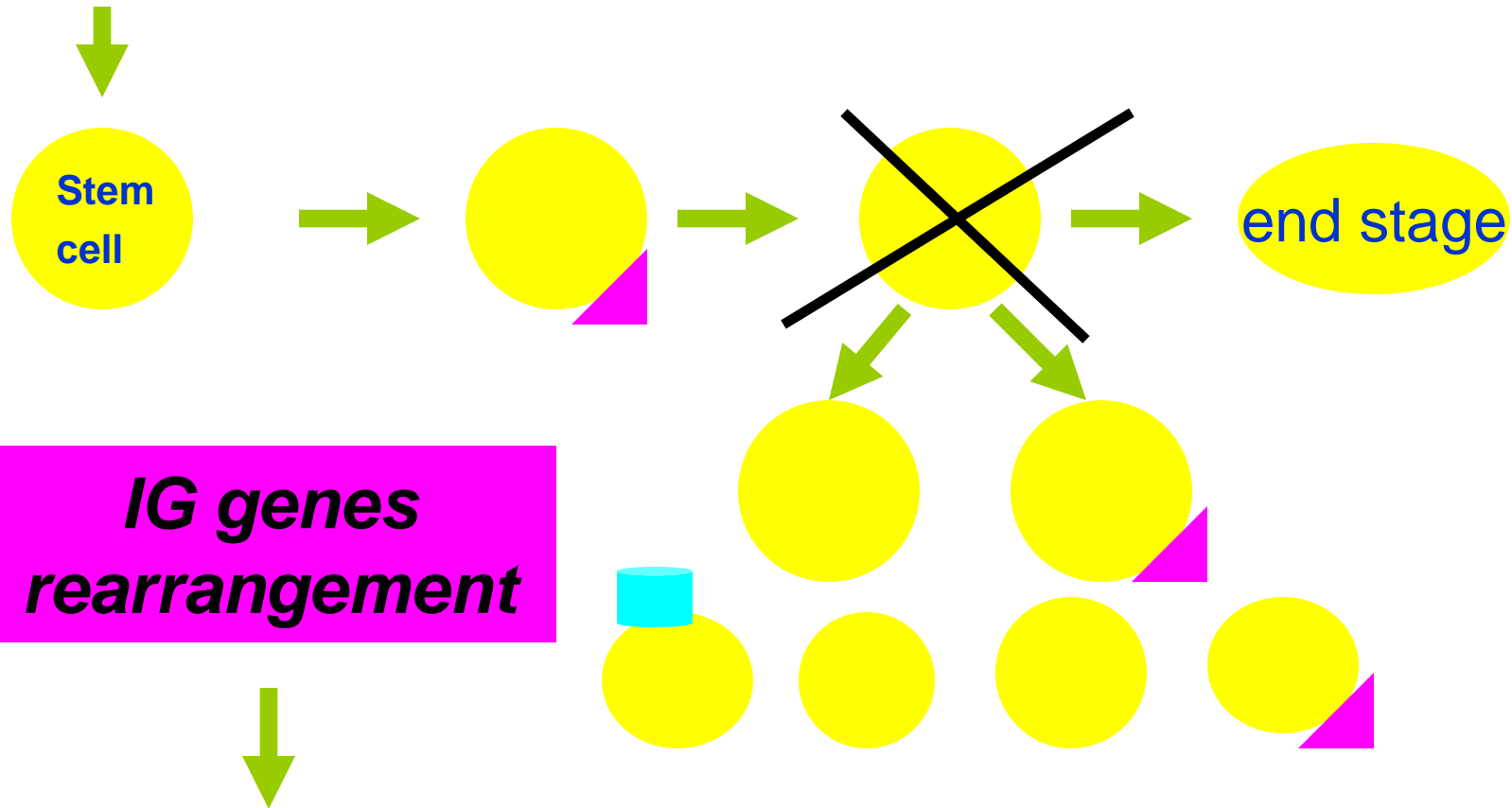
All lymphocytes originate from stem cells in the bone marrow



The two main categories of lymphocytes are B cells and T cells.



Lympho-proliferative disorders



***IG genes
rearrangement***

Genetic mutation

***Cell Arrest & clonal
expansion***

- **Lymphoma: Types**

There are two types of Lymphoma:

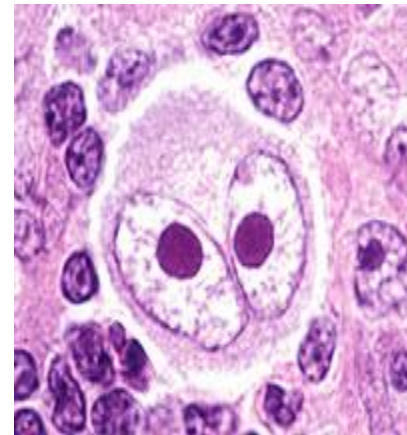
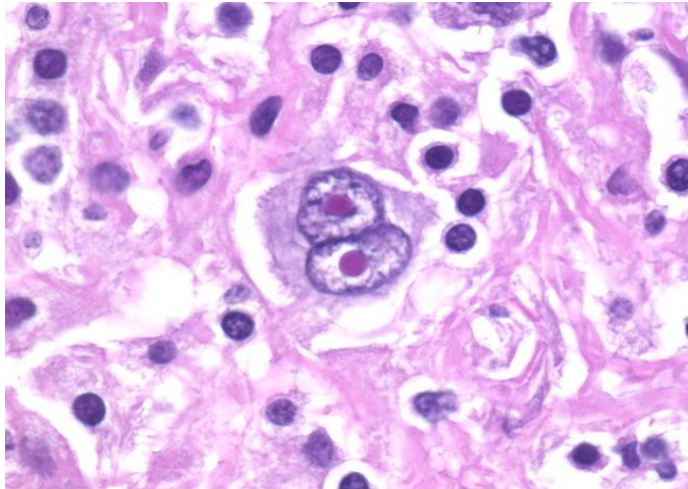
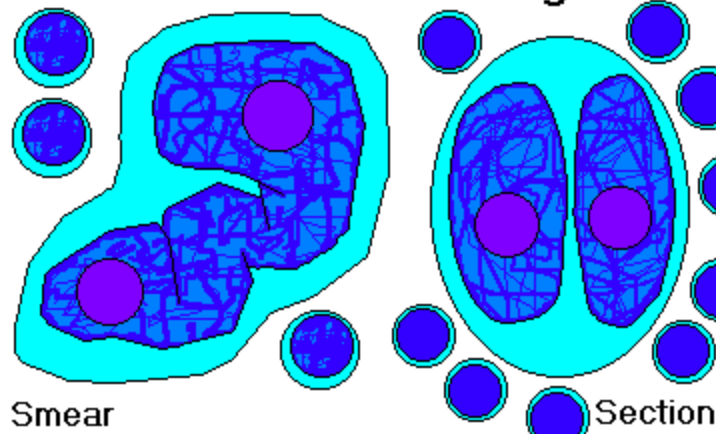
1. Hodgkin's Lymphoma (Hodgkin's Disease) = **B lymphocytes**
2. Non-Hodgkin Lymphoma
B & T lymphocytes

Hodgkin's Disease

- Background
 - First described in 1832 by Dr. Thomas Hodgkin
 - characterized by the presence of Reed-Sternberg cells
 - described by Sternberg in 1898 and **Reed** in 1902
 - It was classified as an infectious disease until 1950's

- **Hodgkin's Lymphoma**

Classic Reed-Sternberg Cells



Hodgkin's Disease

- Epidemiology
 - > males
 - whites > blacks > Asians
 - no clear risk factors, several implicated
 - EBV
 - HIV
 - Rare familial aggregations

NHL: Epidemiology

- **Risk factors**
 - **immunodeficiency states**
 - AIDS, post-transplant, genetic
 - **autoimmune diseases**
 - Sjogrens
 - SLE
 - **infections**
 - H. pylori = MALT lymphoma
 - EBV = Burkitt's lymphoma

Non-Hodgkin Lymphoma

- B cell (85%)

or

- T cell (15%) more aggressive

Approach to the Patient

- **History :**

Gender , Age

Onset , course , duration

Distribution of the swellings

Chest symptoms

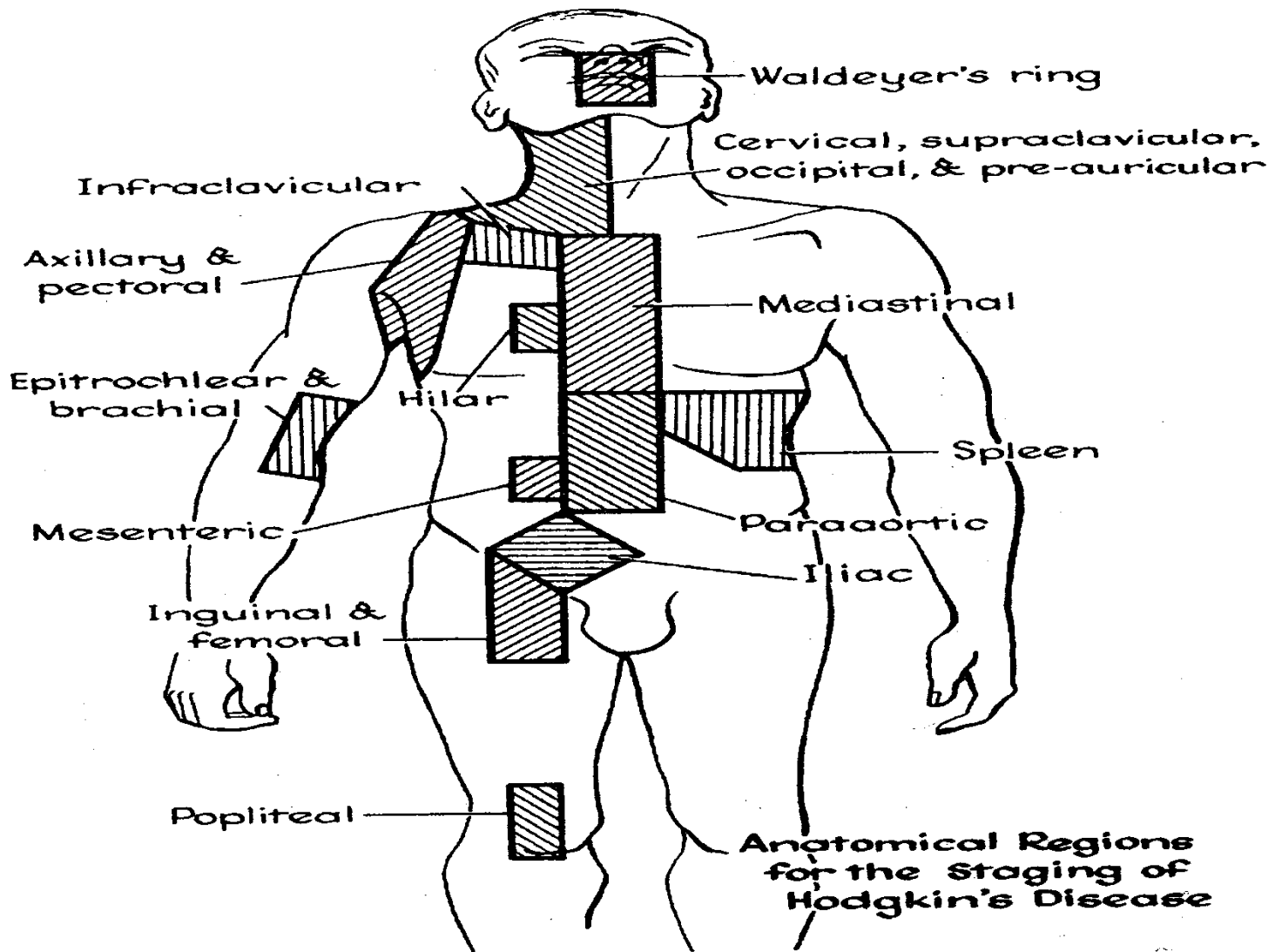
Abdominal symptoms

Approach to the Patient

- **History :**

B symptoms = **SWEATING , FEVER , WEIGHT LOSS**

- recurrent drenching **night sweats** during previous month
- unexplained, persistent, or recurrent **fever** with temps above 38 C during the previous month
- unexplained **weight loss** of more than 10% of the body weight during the previous 6 months



– Evaluation of the lymph nodes, spleen and liver

Comparison between HD & NHL

Hodgkin Lymphoma	Non Hodgkin' Lymphoma
Less common	More common
Usually limited disease	Usually disseminated
Lymph nodes in continuous stations	Skip lesions
Less extra-nodal and visceral Lesions	More extra-nodal and visceral lesions
Less bone marrow involvement	More bone marrow involvement
Usually indolent and good prognosis	Can be indolent or aggressive

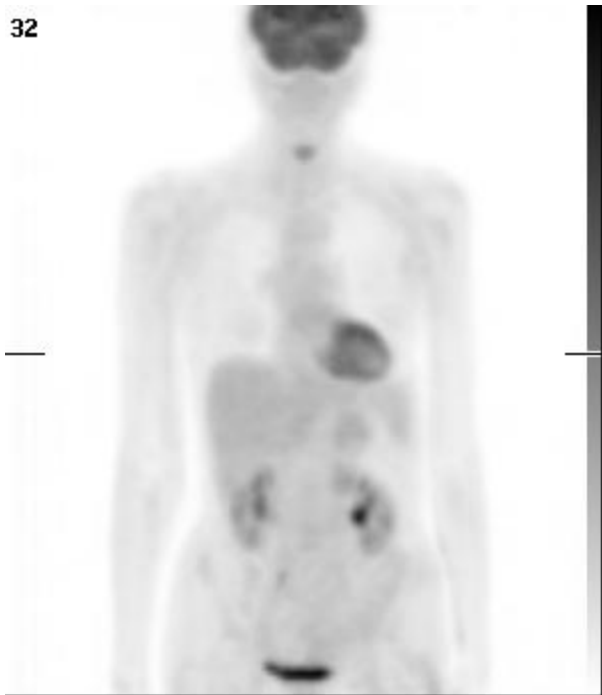
Lymphoma patients evaluation

- **Approach to the Patient**

- staging evaluation

- CBC, diff, plt's = should be done before LN biopsy ???? To rule out leukemia
 - ESR, LDH, albumin, LFT's, Renal Functions
 - CT scans chest/abd/pelvis
 - bone marrow evaluation
 - **PET or gallium scan**

PET scan in Lymphoma



Normal PET scan

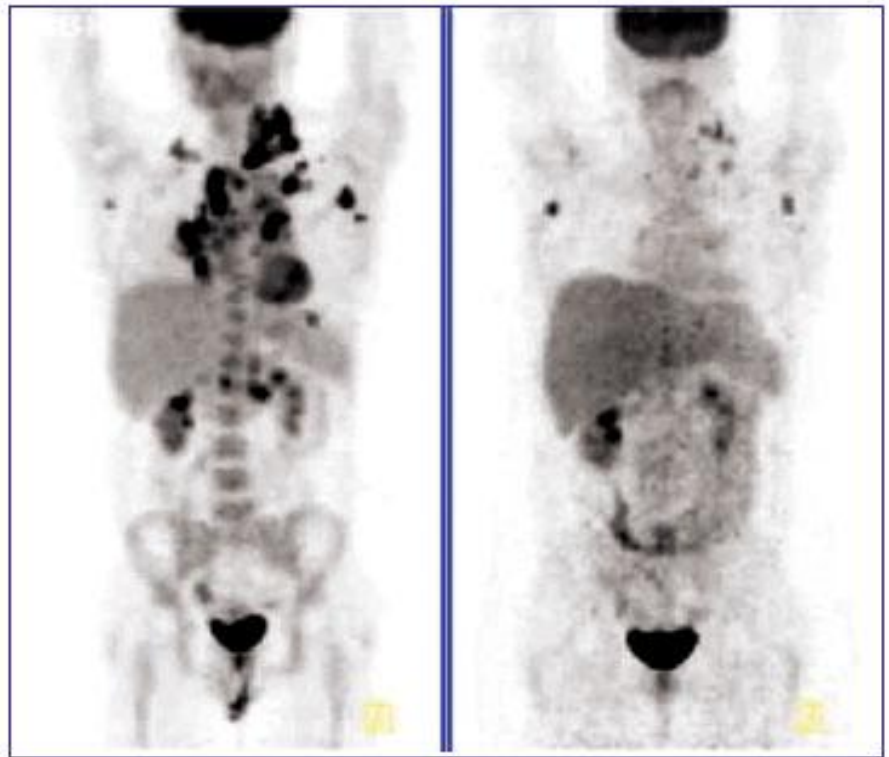


Figure 8 – Therapy control of a patient with non-Hodgkin lymphoma. A partial response is observed after therapy however, persistent activity is seen in the axillary and left cervical regions

Before TTT

After TTT

Differential diagnosis

Causes of generalized lymphadenopathy

- Infection :
 - Viral : Infectious mononucleosis, Infective hepatitis, AIDS
 - Bacterial : Tuberculosis, Brucellosis, 2ry syphilis
 - Protozoal : Toxoplasmosis
 - Fungal : Histoplasmosis
- Malignant :
 - **Leukemia = do CBC before LN biopsy**
 - Lymphoma
 - Metastatic carcinoma

Causes of generalized lymphadenopathy

- Immunological :
 - [Systemic lupus erythematosus](#)
 - [Felty's syndrome](#)
 - [Still's disease](#)
 - Drug hypersensitivity as [Hydantoin](#), [Hydralazine](#), [Allopurinol](#)
- Misc. :
 - [Sarcoidosis](#)
 - [Amyloidosis](#)
 - [Lipid storage disease](#)
 - [Hyperthyroidism](#)

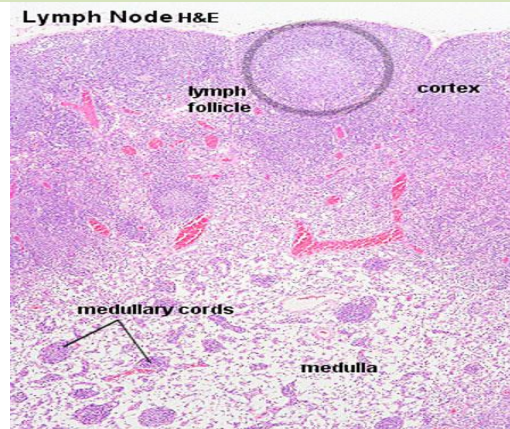
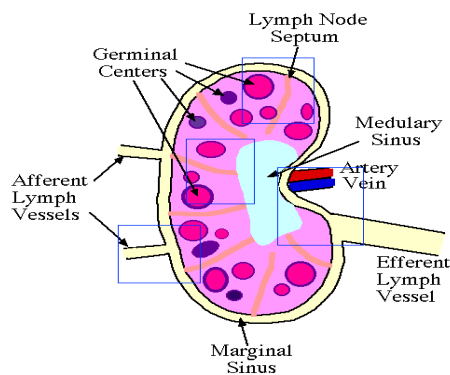
Lymphoma patients evaluation

- **Approach to the Patient**

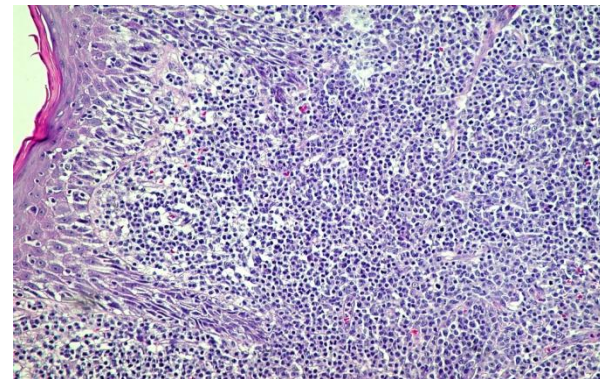
- **Diagnosis :**

- By lymph node biopsy :**

- Whole lymph node need to be excised**



Normal



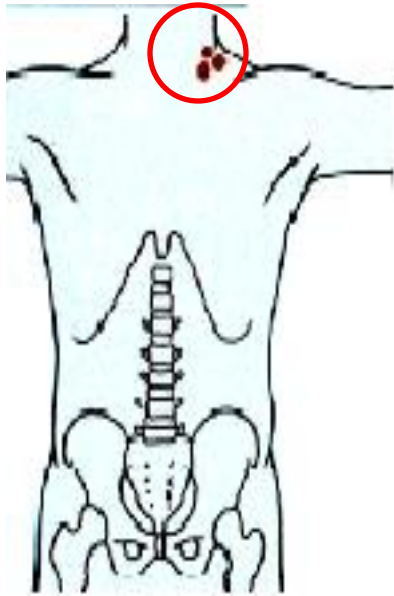
lymphoma

Staging

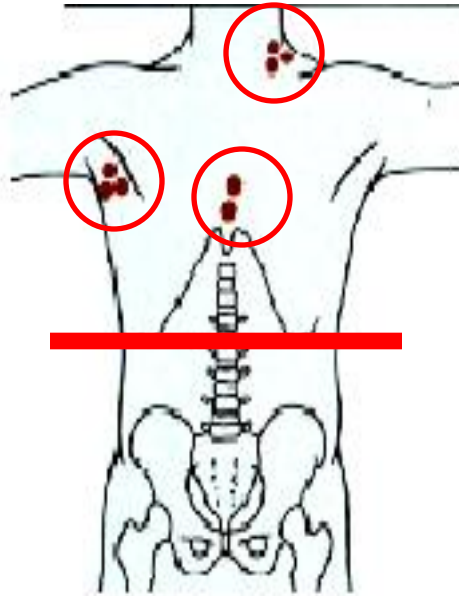
Ann Arbor Staging System

- **Stage I:** single lymph node region (I) or single extralymphatic organ or site (I_E)
- **Stage II:** ≥ 2 lymph node regions on same side of diaphragm (II) or with limited, contiguous extra lymphatic tissue involvement (II_E)
- **Stage III:** both sides of diaphragm involved, may include spleen (III_S) or local tissue involvement (III_E)
- **Stage IV:** multiple/disseminated foci involved with ≥ 1 extralymphatic organs (i.e. bone marrow)
- (A) or (B) designates absence/presence of “B” symptoms

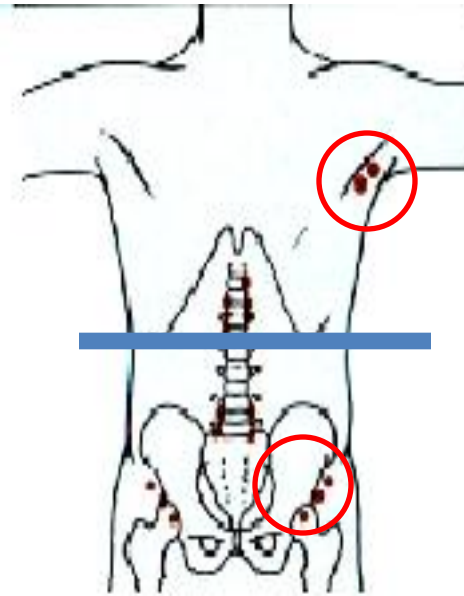
Ann Arbor Staging System for Hodgkin's Disease and Non-Hodgkin's Lymphoma



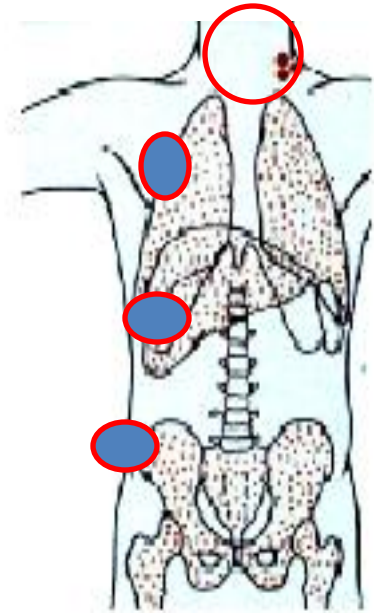
Stage I



Stage II



Stage III

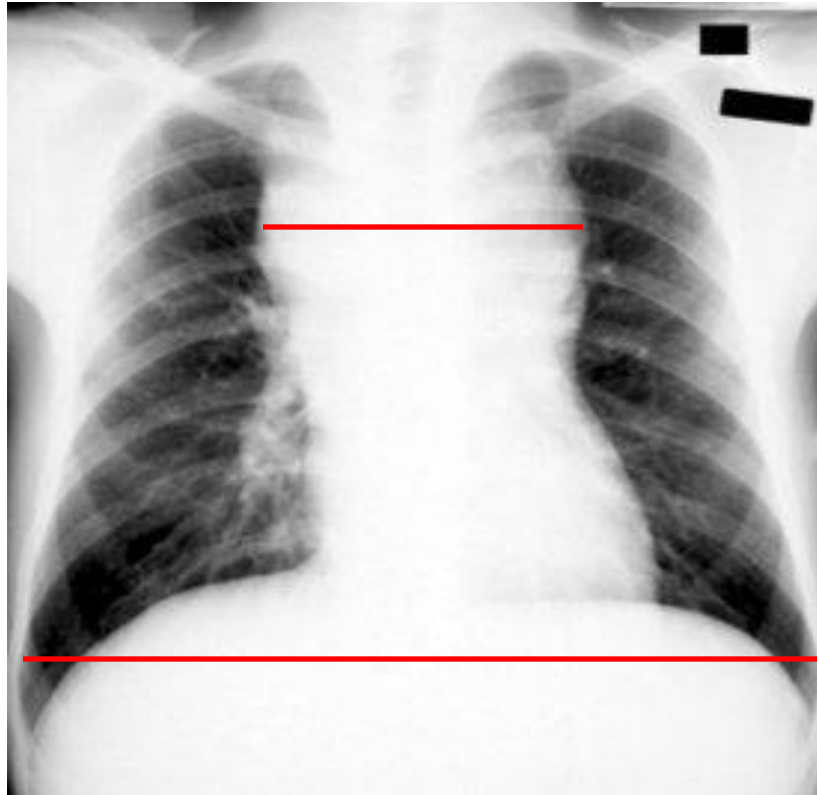


Stage IV

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Modified Ann Arbor Staging

- “E” designation for extranodal disease
- B symptoms
 - Sweating
 - Fever
 - Weight loss
- Criteria for bulk
 - 10 cm nodal mass
 - mediastinal mass $> 1/3$ thorax diameter



$> \frac{1}{2}$ chest diameter

Prognostic Factors

Hodgkin Lymphoma

- Adverse prognostic features for stage I & II

- more than 3 nodal sites
- bulky LNs
- ESR > 50
- B symptoms
- invasion into critical organs
- male
- age > 40
- MC or LD subtype

- adverse prognostic for advanced stage (III-IV)

- male sex
- age ≥ 45
- albumin < 4 gm/dl
- HgB < 10.5 mg/dl
- stage IV disease
- WBC count > 15,000/mm³
- lymphocyte count < 600/mm³

Hodgkin's Disease

- Results of Treatment

<u>• stage</u>	<u>5 year overall survival</u>
—I & II	90%
—III	80%
—IV	65%

NHL: Classification

- Terminology (refers to **natural history**)
 - low grade = **Indolent**
 - intermediate grade & high grade = **Aggressive**
- Principle
 - Indolent: **slow growing, incurable**
(difficult to be eradicated from the body)
 - Aggressive: **rapidly growing, curable**

Lymphoma Biology

- **Aggressive NHL**
 - **short** natural history (patients die within months if untreated)
 - disease of rapid cellular proliferation
- **Indolent NHL**
 - **long** natural history (patients can live for many years untreated)
 - disease of slow cellular accumulation

NHL: Approach to the Patient

- **Indolent NHL:** typical scenario
 - patient presents with painless adenopathy
 - otherwise asymptomatic
 - follicular small cell histology
 - average age 59
 - usually stage III-IV at diagnosis

NHL: Approach to the Patient

- Indolent NHL: typical scenario
 - watchful waiting: 2-4 years
 - first remission length: 3-4 years
 - second remission: 2-3 years
 - third remission: 1-2 years
 - each subsequent remission shorter than prior
 - median survival 8-12 years

NHL: Approach to the management

- **Indolent NHL:**

Treatment options

- Watchful waiting
- Radiation to involved fields
- Single agent chemotherapy
 - Chlorambucil \pm prednisone
- Combination chemotherapy
- Monoclonal antibodies (Rituximab)

NHL: Approach to the Patient

- **Aggressive NHL:** typical scenario
 - patients notes B symptoms of several weeks duration
 - work-up reveals pathologic adenopathy
 - histology: diffuse large cell lymphoma
 - about 50% patients stage I-II, 50% stage III-IV
 - average age 64y

NHL: Approach to the Patient

- **Aggressive NHL:** treatment approach
 - Stage I-II: combined modality therapy
 - chemotherapy + radiotherapy
 - cure rate around 70%
 - Stage III-IV (also bulky stage II)
 - chemotherapy x 6-8 cycles
 - cure rate around 40%

Aggressive NHL: prognosis

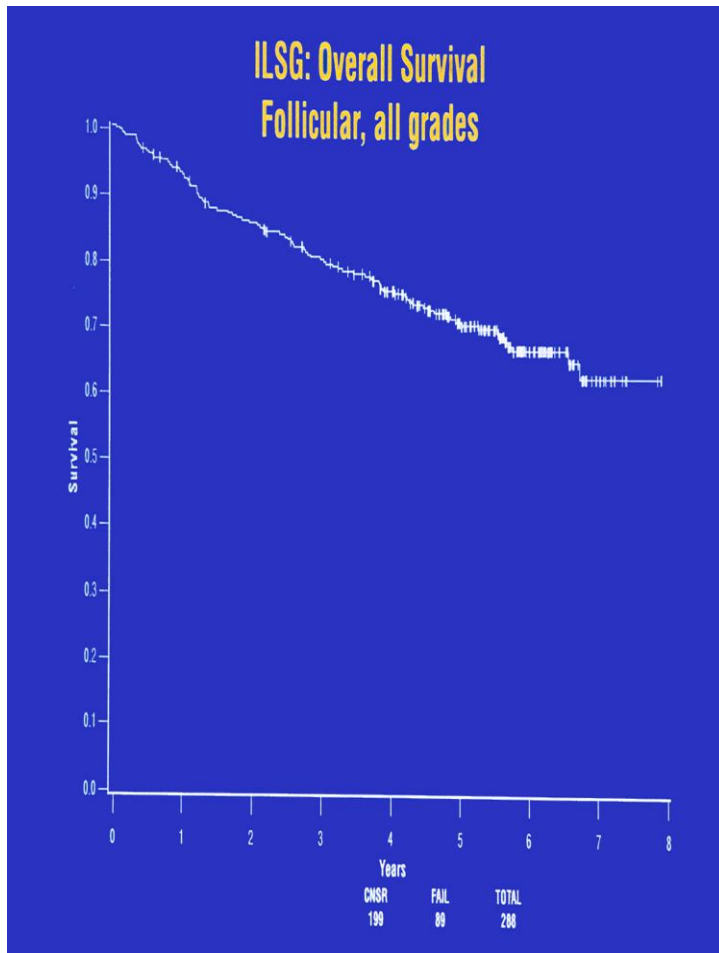
- International Prognostic Index
 - Risk Factors (0-5)
 - **age > 60**
 - **extranodal sites**
 - **performance status ≥ 2**
 - **elevated LDH**
 - **stage III-IV**

CR and OS stratified by IPI

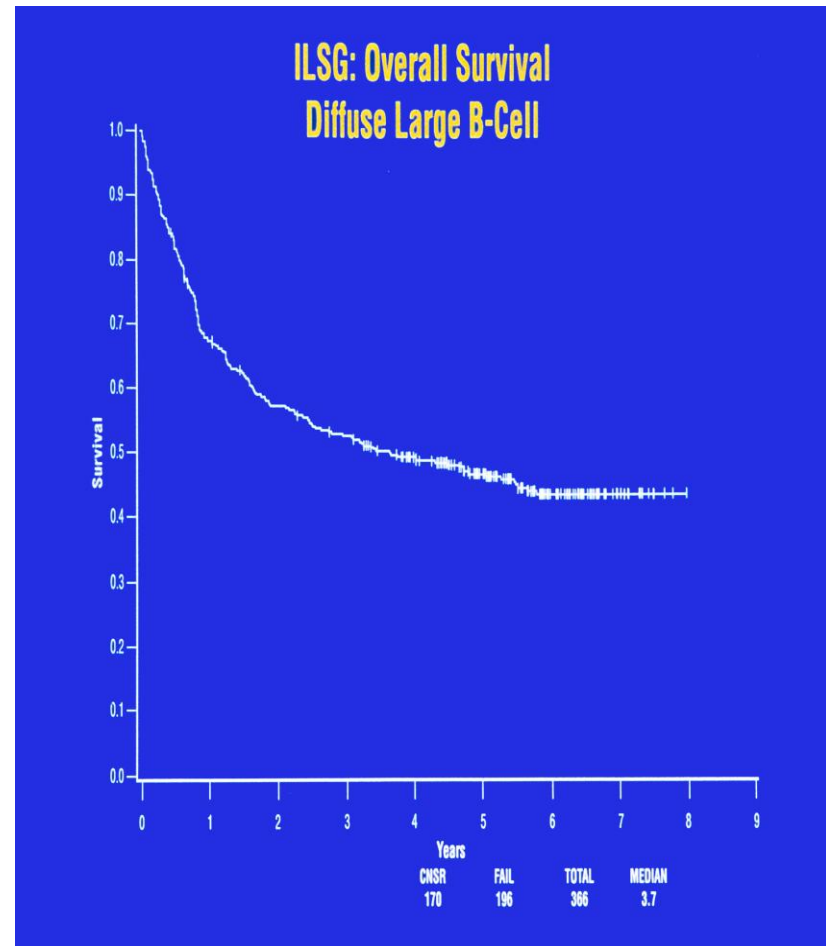
<u># RF's</u>	<u>CR</u>	<u>5 yr OS</u>
0,1	87%	73%
2	67%	51%
3	55%	43%
4,5	44%	26%

Survival

Indolent



Agressive



Summary

Lymphoma
Is a neoplasm of
The Immune System cells
(lymphocytes)

Why are lymphomas unique and important? = 3Cs

- Common
- Clinical wide range of presentation
- Curable

- **Lymphoma: Types**

There are two types of Lymphoma:

1. Hodgkin's Lymphoma (Hodgkin's Disease) = **B lymphocytes**
2. Non-Hodgkin Lymphoma
B & T lymphocytes

Approach to the Patient

- **History :**

B symptoms = **SWEATING , FEVER , WEIGHT LOSS**

NHL incidence increasing, Hodgkin's decreasing

- **History** :B symptoms = **SWEATING , FEVER , WIEGT LOSS**

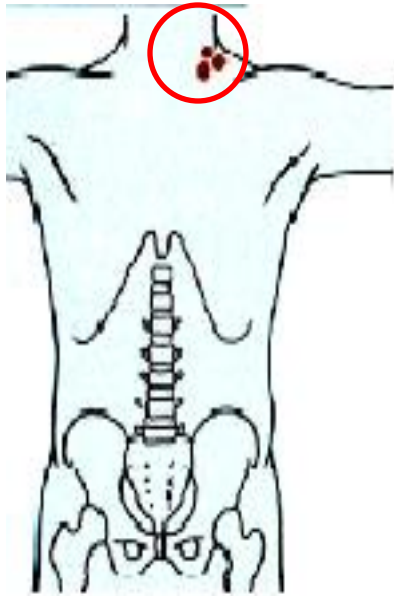
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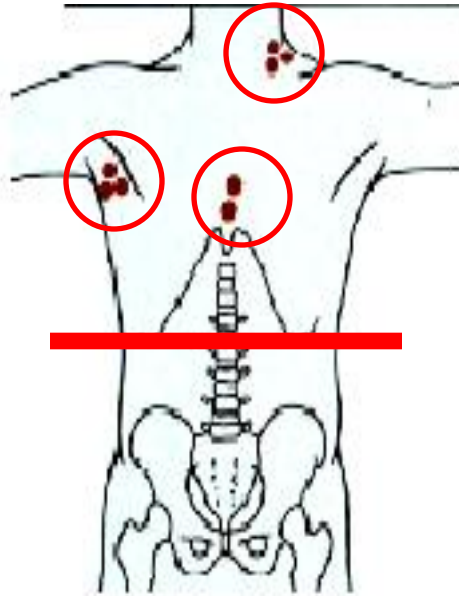
Diagnosis :By lymph node biopsy :

Whole lymph node need to be excised

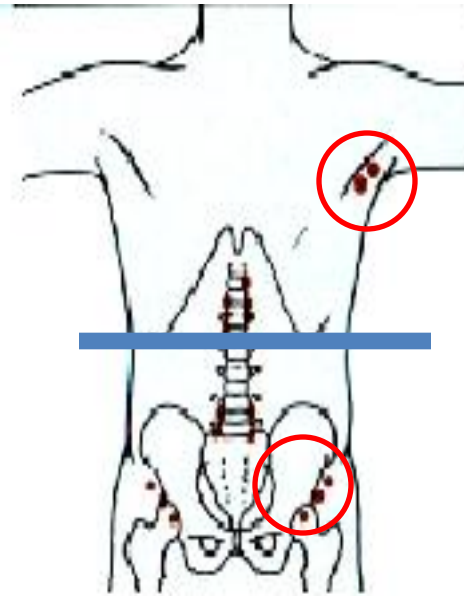
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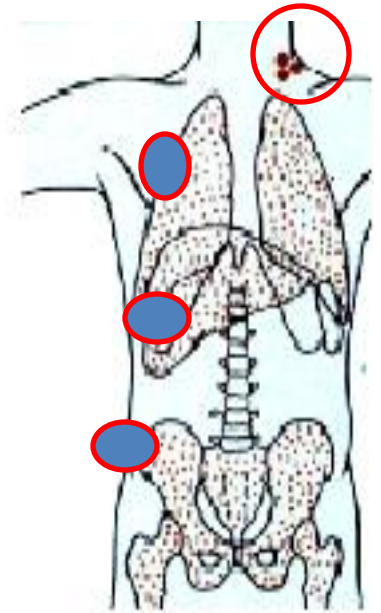
Stage I



Stage II



Stage III



Stage IV

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Prognosis

- Hodgkin's **cure rate quite high**
 - Depending on disease stage
- NHL depends on:
 - histologic subtype
 - indolent vs. aggressive
 - indolent: watchful waiting perfectly acceptable for asymptomatic patients
 - aggressive: require aggressive treatment ASAP to achieve cure