Lymphoma

Lymphoma

- Main types:

1) Hodgkin lymphoma

2) Non Hodgkin lymphoma

   # B-cell lymphoma

   # T-cell lymphoma

Hodgkin lymphoma

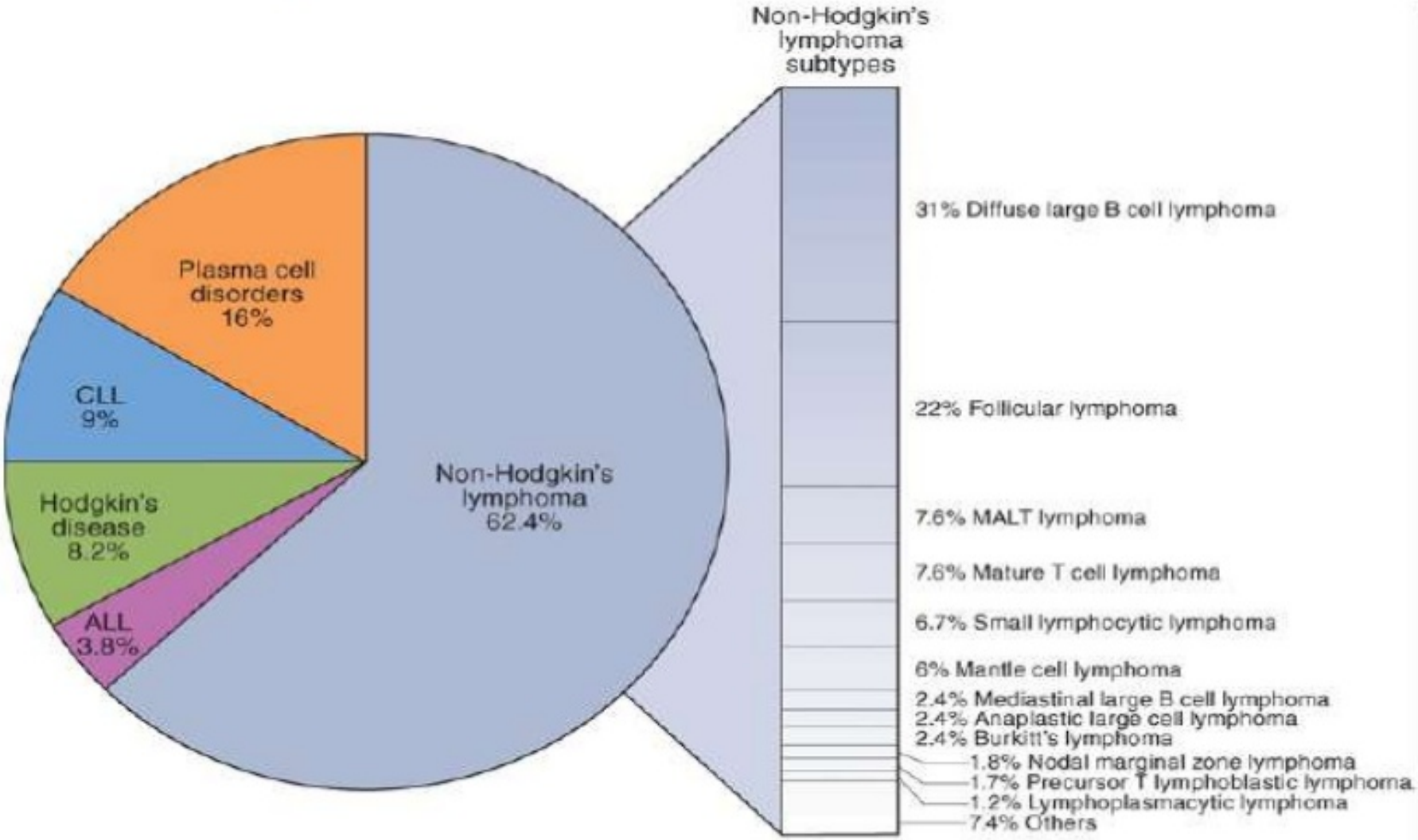
1) Nodular lymphocyte predominance Hodgkin's lymphoma

2) Classical Hodgkin's lymphoma

- Nodular sclerosis Hodgkin's lymphoma
- Lymphocyte-rich classical Hodgkin's lymphoma
- Mixed cellularity Hodgkin's lymphoma
- Lymphocyte depletion Hodgkin's lymphoma

Epidemiology

Chapter 110. Malignancies of Lymphoid Cells



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

Relative frequency of lymphoid malignancies. ALL, acute lymphoid leukemia; CLL, chronic lymphoid leukemia; MALT, mucosa-associated lymphoid tissue.

Hodgkin lymphoma

- **Definition:**

A neoplastic transformation of lymphocytes particularly in lymph nodes.

Characterized by:

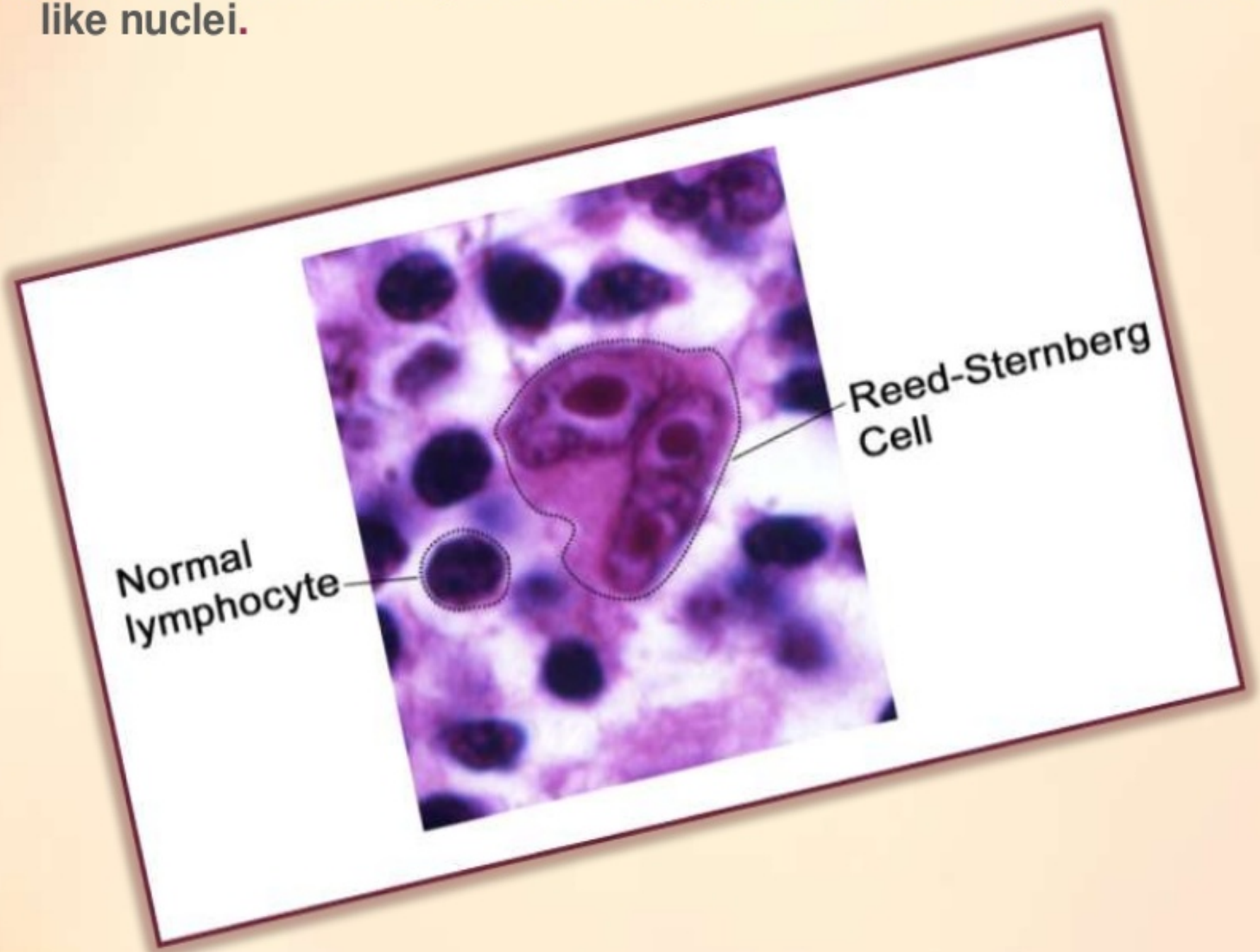
1) **the presence of Reed-Sternberg cells on histology**

2) **spreading in an orderly fashion to contagious lymph nodes**

(For example, Hodgkin lymphoma that starts in the cervical lymph nodes may spread first to the supraclavicular nodes then to the axillary nodes)

Red-Sternberg cells

Cells with *mirror image* nuclei and prominent, eosinophilic, inclusion-like nuclei.



Etiology

- **Hodgkin disease has bimodal age distribution--one peak in the 20s and 60s.**
- Doctors **seldom know why** one person develops Hodgkin lymphoma and another does not. But research shows that **certain *risk factors*** increase the chance that a person will develop this disease.
- Having one or more risk factors does not mean that a person will develop Hodgkin lymphoma. Most people who have risk factors never develop cancer.

Risk factors

1) Certain *viruses*:

- *Epstein-Barr virus* (EBV)
- *Human immunodeficiency virus* (HIV)

2) Weakened immune system:

- *inherited* condition
- certain drugs used after an organ transplant

3) Age:

- Hodgkin lymphoma is most common among teens and adults aged 15 to 35 years and adults aged 55 years and older.

4) Family history:

- Family members, especially brothers and sisters, of a person with Hodgkin lymphoma or other lymphomas may have an increased chance of

Clinical presentation

- **Enlarged, painless, rubbery, non- erythematous, nontender lymph nodes are the hallmark of the disease.**
- May become painful after drinking alcohol
- **Patients may develop "B" symptoms which are:**
  - **# Drenching night sweats.**
  - **# 10% weight loss**
  - **# Fever**
- 25% have "B" symptoms
- **Although pruritus is common in the disease it is not one of the "B" symptoms.**
- **Cervical, supraclavicular and axillary lymphadenopathy are the most common initial signs of the disease.**

Clinical presentation

- Extralymphatic sites may be involved such as:

  # Spleen

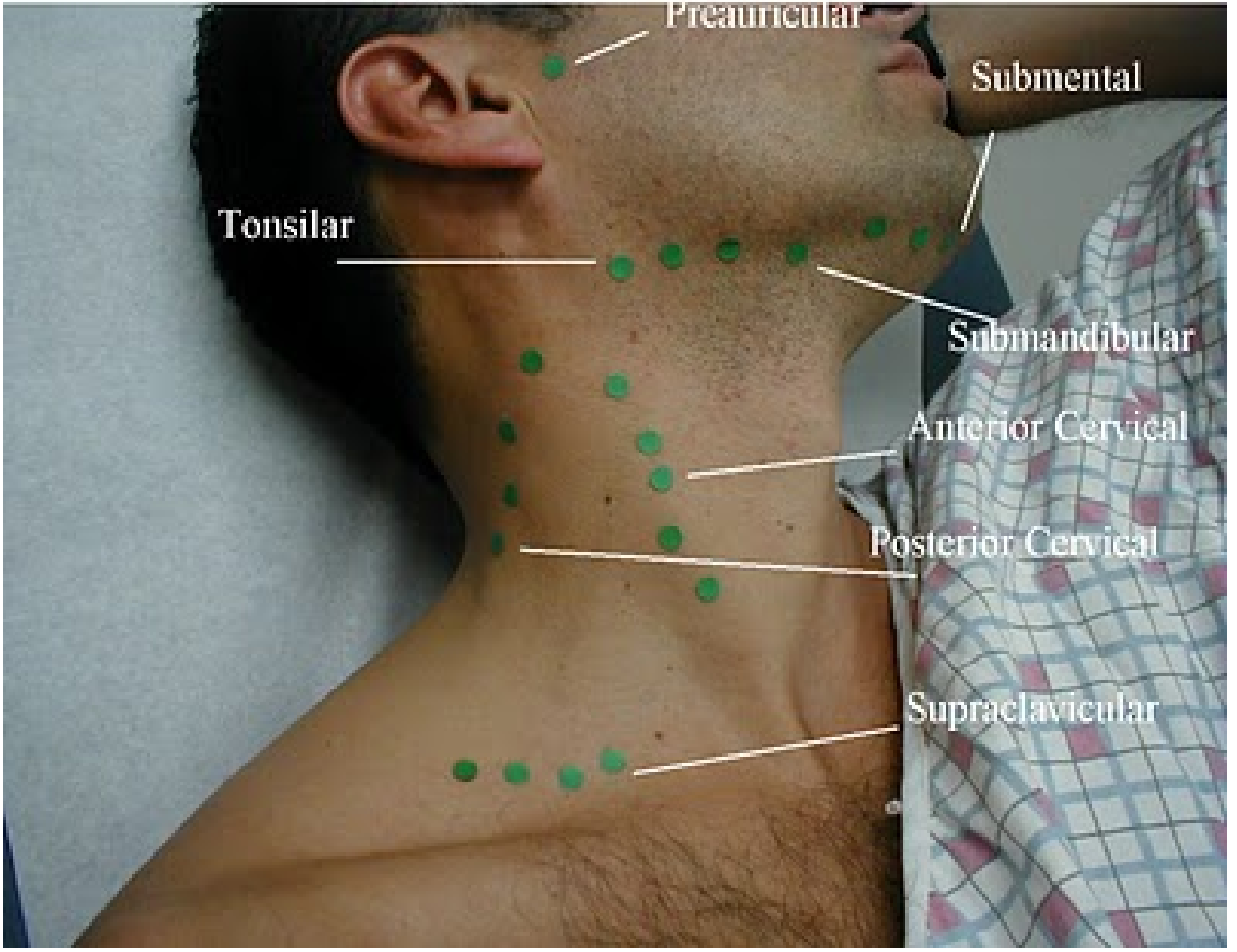
  # Liver

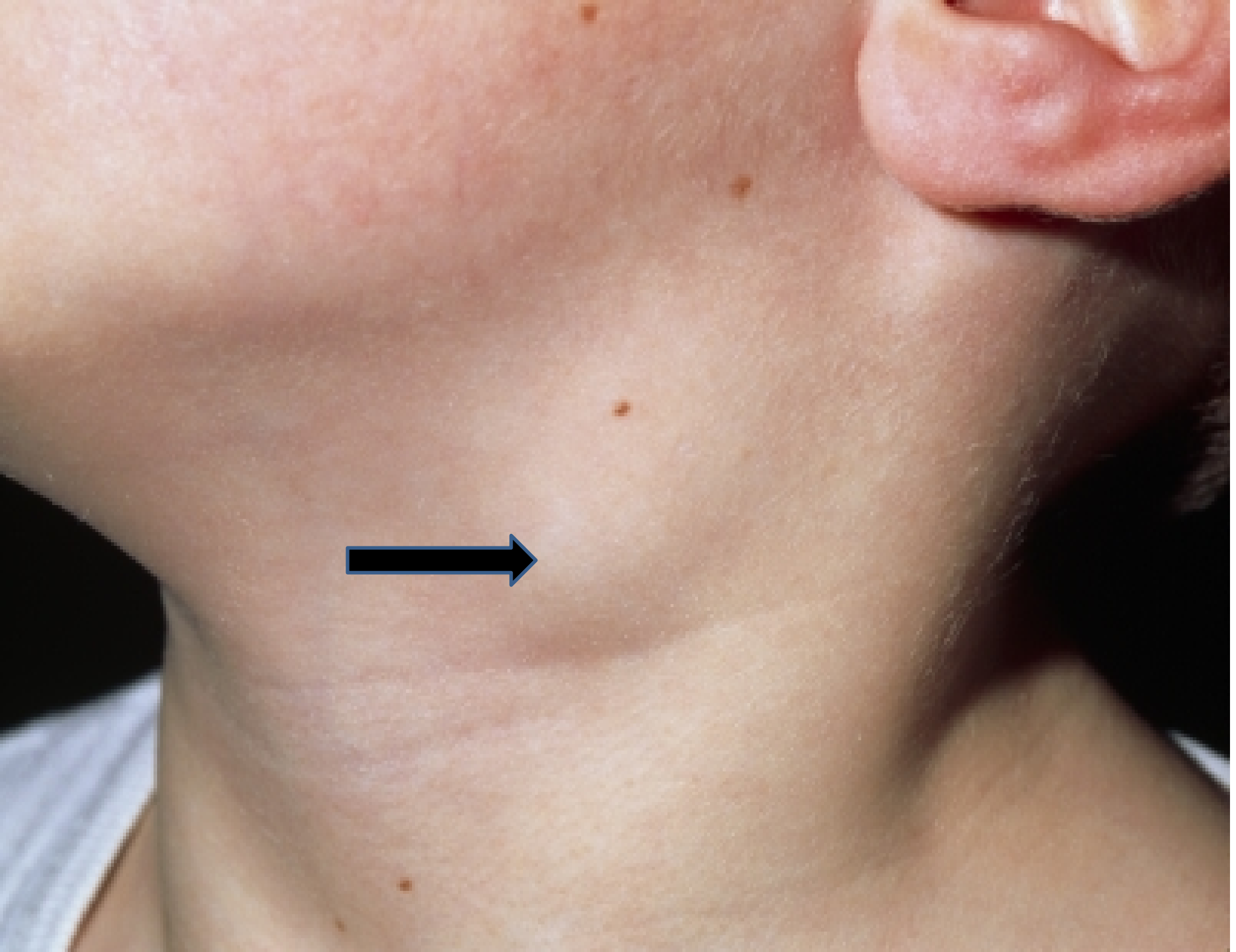
  # Bone marrow

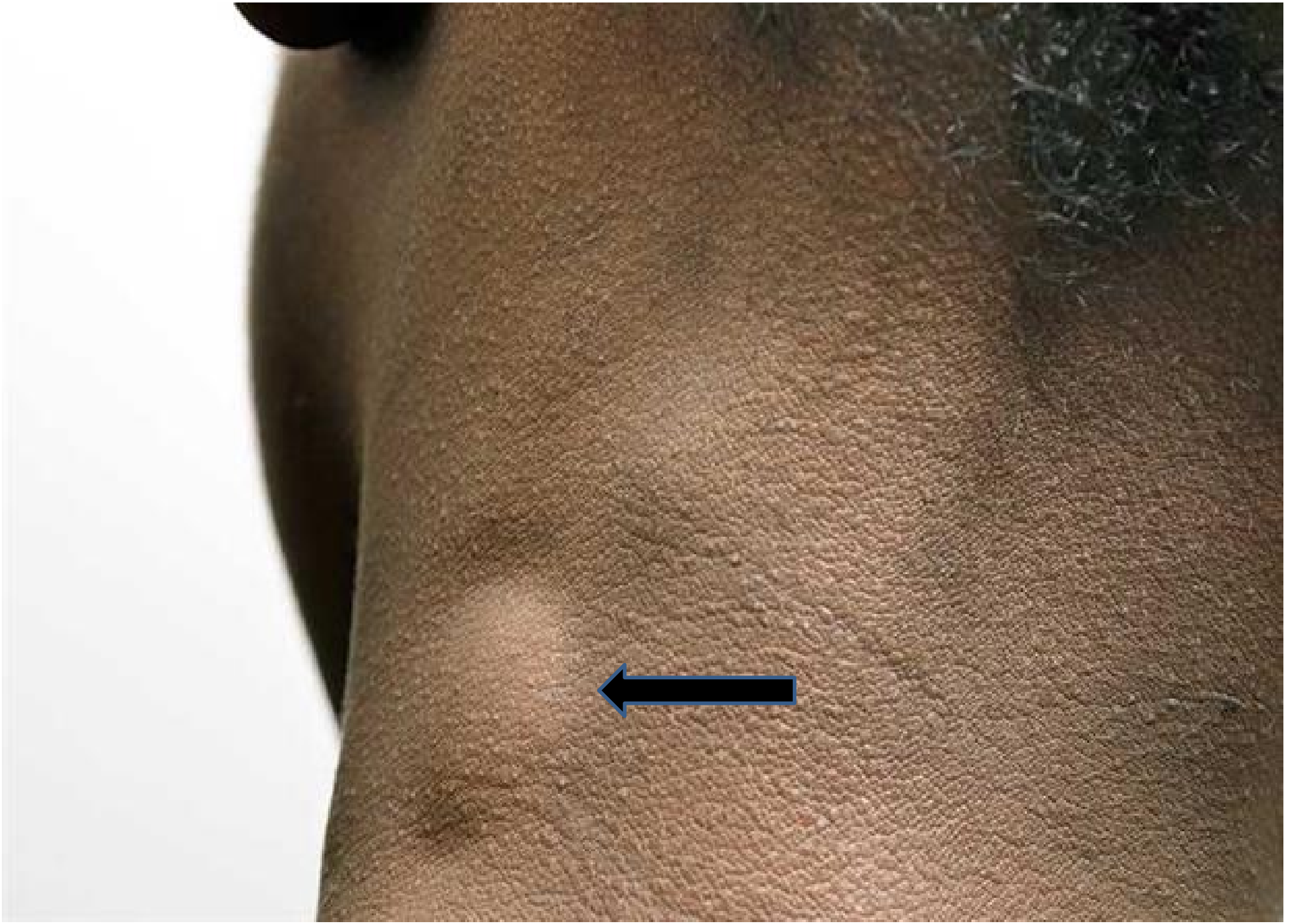
  # Lung

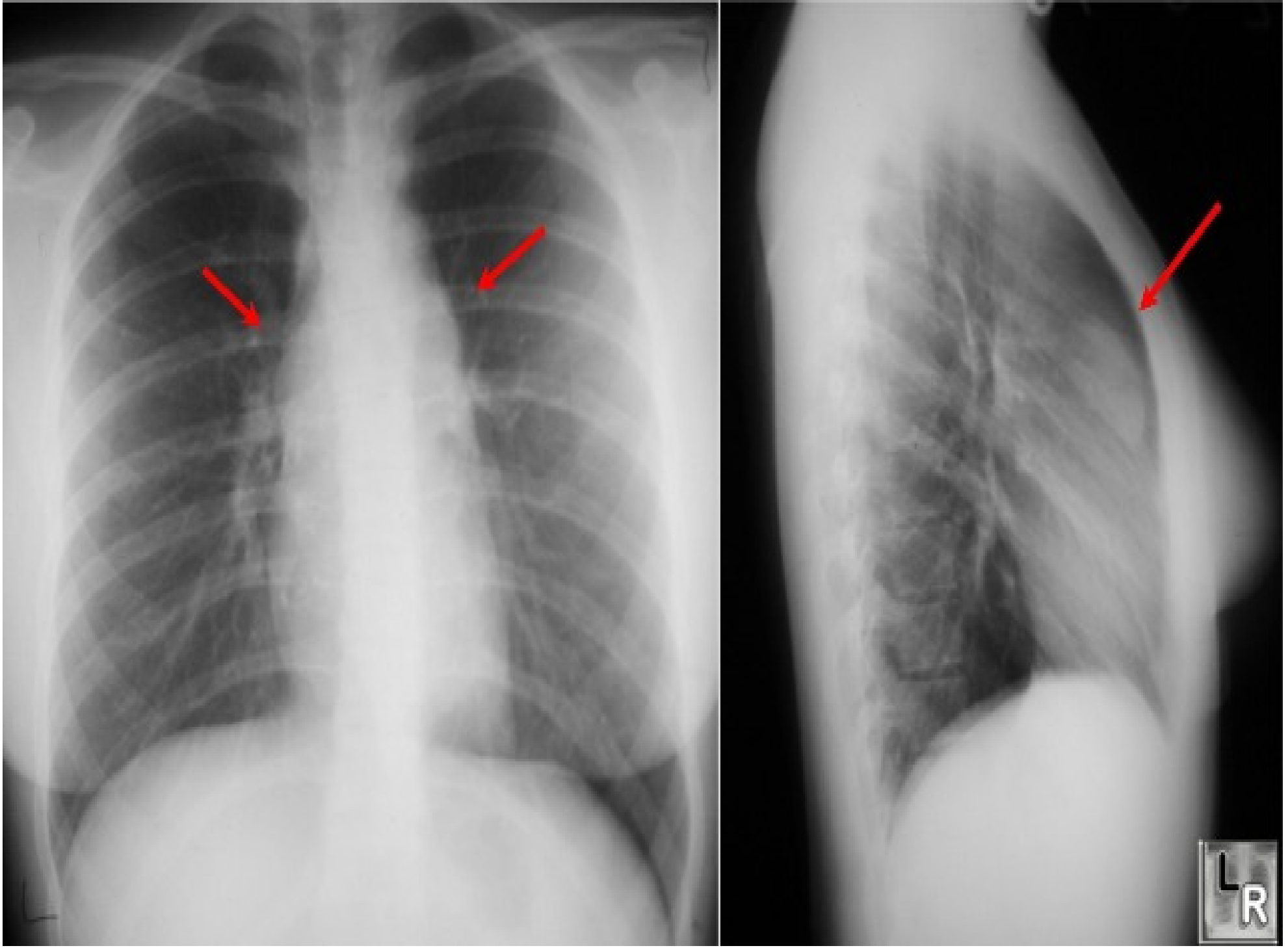
  # CNS

- Extralymphatic involvement is more common with non-hodgkin lymphoma.


Preauricular
Submental
Tonsilar
Submandibular
Anterior Cervical
Posterior Cervical
Supraclavicular



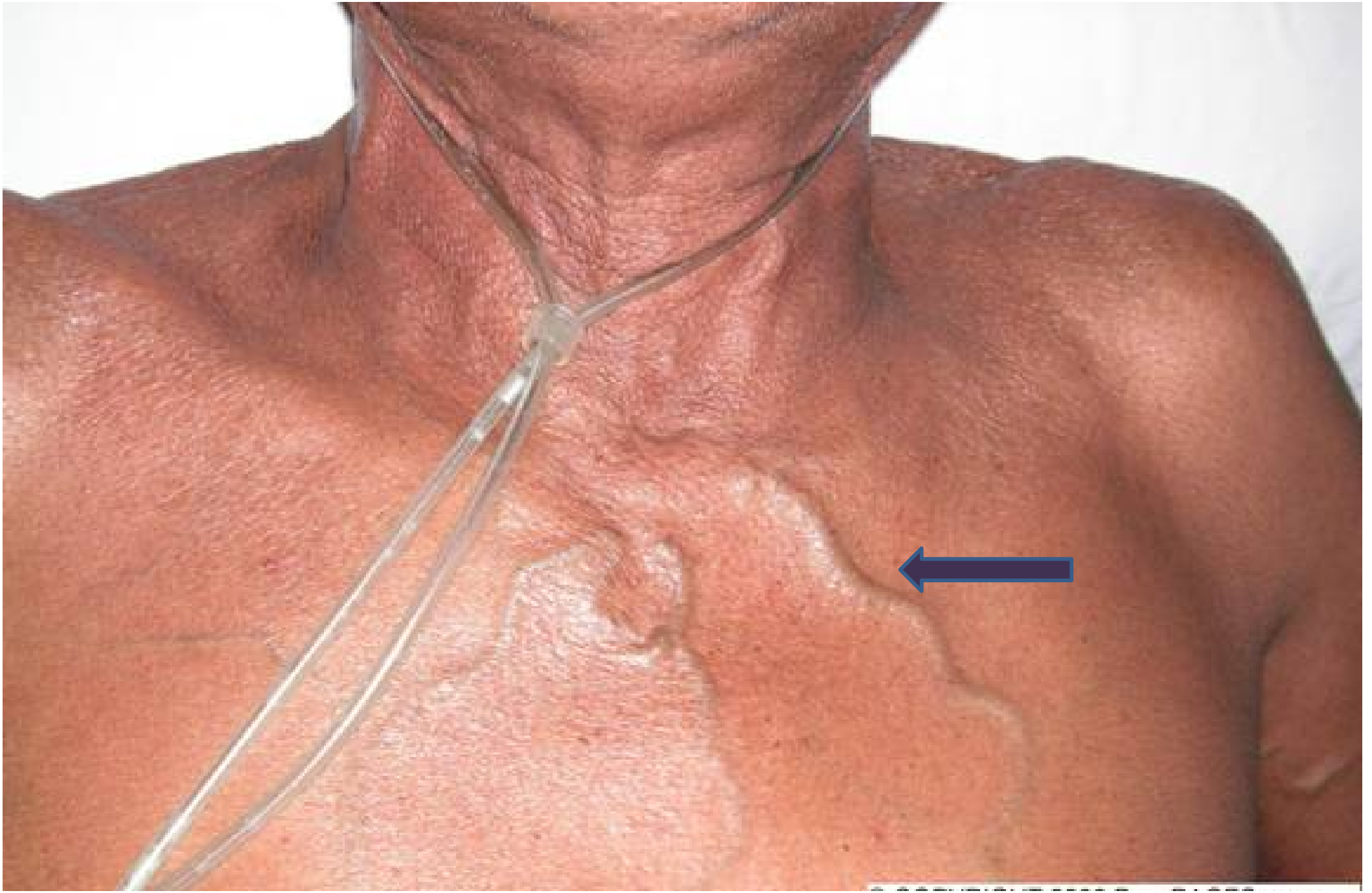




Clinical presentation

Emergency presentation:

- Infections
- SVC obstruction (facial edema, increased JVP and Dyspnea)



Staging

The doctor considers the following to determine the stage of Hodgkin lymphoma:

- The number of lymph nodes affected.
- Whether these lymph nodes are on one or both sides of the diaphragm.
- Whether the disease has spread to the bone marrow, spleen, liver, or lung.
- Each stage is divided into A or B symptoms according to the presence of systemic symptoms.

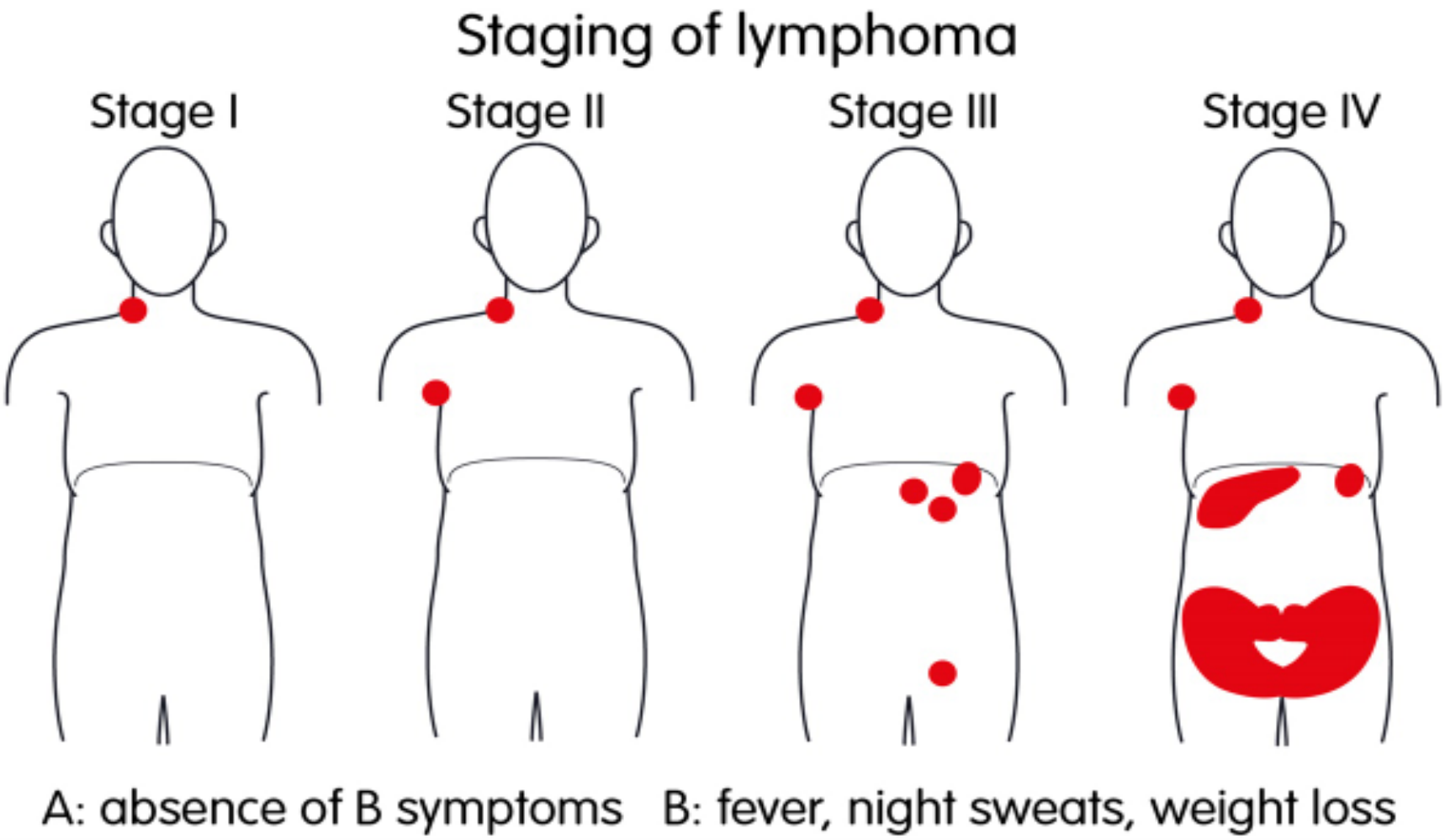

Staging of lymphoma
Stage I
Stage II
Stage III
Stage IV
A: absence of B symptoms
B: fever, night sweats, weight loss

Table I-6-1. Ann Arbor Staging of Hodgkin and Non-Hodgkin Lymphomas

Stage I	Involvement of a single lymph node region or of a single extralymphatic organ or site
Stage II	Involvement of ≥ two lymph node regions or lymphatic structures on the same side of the diaphragm or with involvement of limited, contiguous extralymphatic organ or tissue
Stage III	Involvement of lymph node regions on both sides of the diaphragm which may include the spleen or limited, contiguous extralymphatic organ or site or both
Stage IV	Diffuse or disseminated foci of involvement of ≥ one extralymphatic organ or tissue, with or without associated lymphatic involvement

Extranodal site of NHL	Number (*n* = 96)
Intestine (small and large)	23
Tonsil	21
Stomach	09
Parotid	06
Testis	05
Nasopharynx	04
Orbital mass	03
Brain tumor	03
Retroperitoneum	03
Bone	03
Others	16
Total	96

NHL – Non hodgkin lymphoma

Diagnosis

- **An excisional lymph node biopsy is the essential first step in diagnosis.**

- A biopsy is the only sure way to diagnose Hodgkin lymphoma. The biopsy can be:

  1) Excisional biopsy

  2) Incisional biopsy

  3) Fine needle aspiration usually cannot remove a large enough sample for the *pathologist* to diagnose Hodgkin lymphoma.

- **After that the most important step is to determine the extent of the disease because the stage will determine the nature of the therapy, that is, radiation vs. chemotherapy**

Investigations used for staging

- **Chest x-ray :** X-ray pictures may show swollen lymph nodes or other signs of disease in the chest .
- **CT:** Chest, abdomen and *pelvis* **(CT is sensitive enough to detect any abnormal nodes)**
- ***MRI***
- ***PET scan***
- **LP for CSF cytology if any CNS signs**
- **Lymphangiography and laparotomy are no longer used for staging.**
- **A bone marrow biopsy is used when :**

  1) B symptoms

  2) Stage3 or 4

Abnormal lab tests (don't alter the stage of the disease)

- CBC: anemia and high WBC (Eosinophilia is common)
- LDH: high (poor prognostic factor)
- ESR: high (poor prognostic factor)
- LFTs: help determine the need for liver biopsy

Histology

- Hodgkin has several histological subtypes.

- Lymphocyte-predominant has the **Best prognosis**.

- Lymphocyte-depleted has the **Worst prognosis.**

Rye classification	Histological features	Prognosis
Lymphocyte predominant	Lymphocytes and RSCs	Best
Nodular sclerosis	Nodules of lymphoreticular cells and lacunar RSCs	Good
Mixed cellularity	Mixture of lymphocytes, eosinophils, plasma cells, and RSCs	Fair
Lymphocyte depleted	Lymphocytes and RSCs	Poor

RSCs: Reed-Sternberg cells

Treatment

- Therapy is entirely based on the stage.
- Localized disease **(stage IA and IIA)** is managed predominantly with **radiation**.
- All patients with evidence of **"B" symptoms** as well as **stage III and IV** are managed with **chemotherapy**.
- The most effective combination chemotherapeutic regimen for Hodgkin lymphoma is **ABVD** (adriamycin, bleomycin, vinblastin and dacarbazine).

Treatment

- **ABVD** is superior to **MOP** (meclorethamine, vincristin(oncovin) , prednisolone and procarbazine) because ABVD has fewer side effects such as:

1) Permanent sterility

2) Secondary cancer formation

3) Aplastic anemia

4) Peripheral neuropathy

International Prognostic Index

- The International Prognostic Index (IPI) was first developed to help doctors determine the prognosis for people with fast-growing lymphomas. The index depends on 5 factors:

1) The patient's age

2) The stage of the lymphoma

3) Whether or not the lymphoma is in organs outside the lymph system

4) Performance status (PS) – how well a person can complete normal daily activities

5) The blood (serum) level of (LDH)

Good prognostic factors	Poor prognostic factors
Age 60 or below	Age above 60
Stage I or II	Stage III or IV
No lymphoma outside of lymph nodes, or lymphoma in only 1 area outside of lymph nodes	Lymphoma is in more than 1 organ of the body outside of lymph nodes
PS: Able to function normally	PS: Needs a lot of help with daily activities
Serum LDH is normal	Serum LDH is high

Non-Hodgkin lymphoma (NHL)

- **Definition**:

  The neoplastic transformation of either B or T cell lineages of lymphatic cells.

- NHL causes the accumulation of neoplastic cells in both the lymph nodes as well as more often diffusely in extralymphatic organs and the bloodstream.

- Absent reed-Sternberg cells.

Risk factors

INFECTIONS:

- *Human immunodeficiency virus* (HIV)
- *Epstein-Barr virus* (EBV): linked to ***Burkitt lymphoma***.
- *Helicobacter pylori:* Extranodal tissues generating lymphoma include **MALT** (Mucosa associated lymphoid tissue)
- *Human T-cell leukemia/lymphoma virus*(**HTLV-1**)
- *Hepatitis C virus*

Age:

- Most people with non-Hodgkin lymphoma are older than 60.

Clinical Presentation

- Clinical presentation is the same as for Hodgkin lymphoma.
- **The difference is that Hodgkin is localized to cervical and supraclavicular nodes 80%-90% of the time. Whereas NHL is localized 10-20% of the time.**
- CNS involvement is more common with NHL.
- HIV positive patients often have CNS involvement.

Staging and diagnosis

- Staging and Diagnosis are the same as for Hodgkin lymphoma.
- **Differences:**
- Bone marrow biopsy is more central in the initial staging of NHL
- Because the presence of bone marrow involvement means the patient has stage IV disaese and therefore needs combination chemotherapy, further invasive testing such as laparotomy is not required.

Grades

- NHL divided into **Low** or **high grade**
- A high grade lymphoma has cells which look quite different from normal cells.

  They tend to grow fast (aggressive).usually look follicular. Incurable. Wider dissemination at presentation.
- Low grade lymphomas have cells which look much like normal cells and multiply slowly(indolent).usually look diffuse. Long term treatment maybe achievable.

Low-grade lymphomas

- Many low-grade lymphomas remain indolent for many years.
- Treatment of the non-symptomatic patient is often **Avoided**.
- In this case **watchful waiting** is often the initial course of action. This is carried out because the harms and risks of treatment outweigh the benefits.
- If a low-grade lymphoma is becoming **symptomatic**, radiotherapy or chemotherapy are the treatments of choice.
- They don't cure the lymphoma, they can alleviate the symptoms.
- Patients with these types of lymphoma can live near-normal lifespans, but the disease is **Incurable**.

High-grade lymphomas

- Treatment of the aggressive, forms of lymphoma can result in a cure in the majority of cases.
- However, the prognosis for patients with a poor response to therapy is worse.
- Treatment for these types of lymphoma typically consists of aggressive chemotherapy, including the **CHOP** or **R-CHOP** regimen.

Treatment

- Same principles of treating Hodgkin Lymphoma.
- The initial chemotherapeutic regimen is **CHOP**
- (cyclophosmamide, hydroxy-adriamycine, oncovin and prednisolone).
- CNS lymphoma is often treated with radiation in addition to CHOP.
- Relapses can be controlled with BM transplantation.
- Some pts express **CD-20** antigen in greater amount. In this case, monoclonal antibody **Rituximab** should be used.
- Rituximab is an anti-CD20 antibody that has limited toxicity and add survival benefit to the use of CHOP.