# Approach To Lymphadenopathy

By

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# Introduction

- The lymphatic system is the part of the immune system comprising *lymphatic vessels* that carry a clear fluid called *lymph* (from Latin lympha "water") in a unidirectional pathway.
- The components of the lymphatic system are :-
  I. Lymph, the recovered fluid
  II. Lymphatic vessels, which transport the lymph
  III. Lymphatic tissue, composed of aggregates of lymphocytes and macrophages that populate many organs of the body; and
  IV. Lymphatic organs, in which these cells are especially concentrated and which are set off from surrounding organs by connective tissue capsules

# The lymph nodes

- Lymph nodes are bean-shaped organs found in clusters along the distribution of lymph channels of the body
- Every tissue supplied by blood vessels is supplied by lymphatic's except placenta and brain
- There are over 800 lymph nodes in the body and around 300 are located in the head and neck
- The superficial nodes are located in the subcutaneous connective tissue, and the deeper nodes lie beneath the fascia & muscles and within various body cavities

# Definition

**Lymphadenopathy:** refers to lymph nodes that are abnormal in:

- **Size**
- **Consistency**

Whether as a result of normal **reactive process** or **pathology**

**(Abnormalities may be localized or generalized)**

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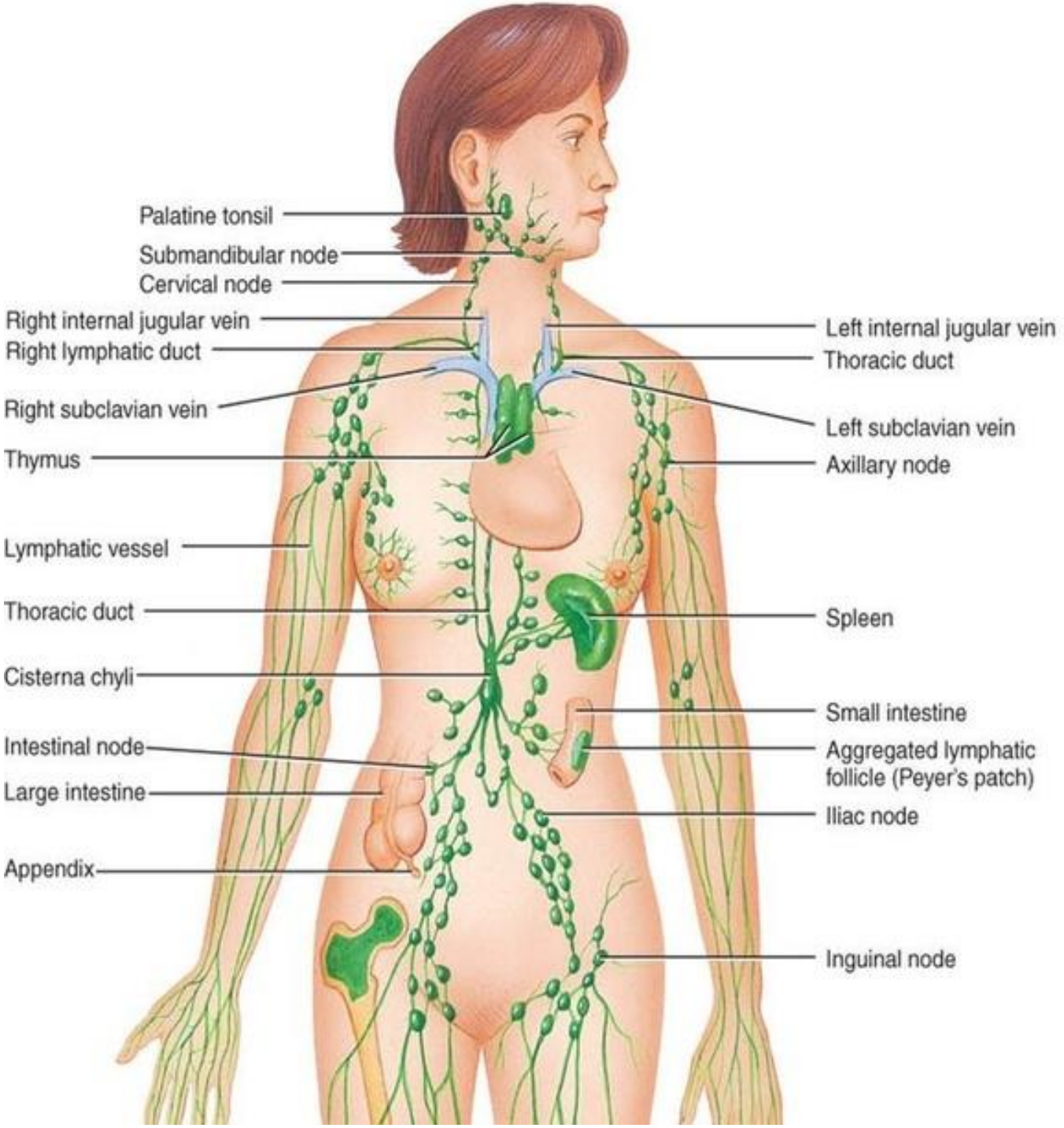
- **Generalized lymphadenopathy** is defined as: -

→Enlargement of **≥ 2 non-contiguous** lymph node groups

- **Regional (localized) lymphadenopathy If :**

  → Enlargement of a single node or multiple contiguous nodal regions


Palatine tonsil
Submandibular node
Cervical node
Right internal jugular vein
Right lymphatic duct
Right subclavian vein
Thymus
Lymphatic vessel
Thoracic duct
Cisterna chyli
Intestinal node
Large intestine
Appendix
Left internal jugular vein
Thoracic duct
Left subclavian vein
Axillary node
Spleen
Small intestine
Aggregated lymphatic follicle (Peyer's patch)
Iliac node
Inguinal node

# Common causes of generalized lymphadenopathy

**Infectious**

- EBV/CMV
- AIDS /AIDS related complications
- TB
- Toxoplasmosis

**Neoplasia**

- ALL / CLL
- Lymphoma

**Hyper-sensitivity**

- Serum Sickness
- Drugs (Phenytoin)
- SLE
- Rheumatoid Arthritis

**Metabolic**

- Hyperthyroidism
- Lipid storage disease

# Generalized Lymphadenopathy

# Common Causes of localized lymphadenopathy (Site Predilection)

**Pre-auricular**

- Viral Conjunctivitis
- Trachoma
- Cat-scratch disease
- Sarcoidosis

**Post-auricular/ Occipital**

- Rubella
- Scalp infection

**Cervical**

- Pharyngitis
- EBV
- TB
- Toxoplasmosis
- Sarcoidosis

**Submandibular**

- Pharyngitis/buccal cavity tumor
- Nasopharyngeal tumor
- Thyroid malignancy

# Common Causes of localized lymphadenopathy (Site Predilection)

- Pulmonary / Mediastinal / Esophageal Malignancy
- T.B.
- Sarcoidosis
- Toxoplasmosis

**Right supraclavicular**

- Intra-abdominal malignancy
- RCC
- Ovarian/Testicular /Prostate malignancy

**Left supraclavicular (Virchow's)**

- Sarcoidosis
- Infection(unilateral)
- Leprosy
- IMN
- CLL/Lymphoma

**Epitrochlear**

- Cancer Breast / Breast infection
- Melanoma
- Lymphoma
- Ipsilateral upper limb infection / Reaction to immunization

**Axillary**

# Common Causes of localized lymphadenopathy (Site Predilection)

- Lymphoma
- Bronchogenic Carcinoma
- T.B.
- Sarcoidosis
- Histiocytosis

**Hilar**

- Gut Adenocarcinoma
- Hodgkin's disease
- T.B.
- Lymphoma
- Bladder carcinoma

**Abdominal**

- Syphilis
- Genital herpes
- Lower extremity/local infection
- Lymphoma
- Metastatic carcinoma from: rectum, genitalia or lower limb(melanoma)

**Inguinal**

- Lymphomas
- Leukemias
- Cat-Scratch disease
- Metastasis
- Sarcoidosis
- Granulomas

**Any region**

# Localized lymphadenopathy

Submandibular

Cervical

# Localized lymphadenopathy

Right Supraclavicular

Left Supraclavicular

# Clinical Assessment

I. **History**: Detailed personal/present/past- history
II. **General Examination**: Review of ALL body systems
III. **Local (Physical) Examination**: Inspection and Palpation
IV. **Investigations**: Laboratory and Radiological

# History

- **Duration:**
  - **for < 2 weeks has a very low chance of representing a malignant condition**
  - **for > 1 year and has been stable in size over the year, less likely to be malignant (with exception of indolent NHL and low-grade Hodgkin lymphomas)**
- **The *Exposure history* as well as the *Travel history* may be important for diagnosis:**
  - **Exposure to Animals/Pets and biting insects**
  - **Cat-scratch disease (bartonella)**
  - **Exposure to infectious contacts**
  - **Consuming Undercooked meat for possible Toxoplasmosis**
  - **Environmental exposure such as tobacco, alcohol, and ultraviolet radiation may raise suspicion for metastatic carcinoma of the internal organs, cancers of the head and neck, and skin malignancies**
  - **Occupational exposure to silicon or beryllium**

# History

- ***Sexual*** **history is also important in determining potential sexually transmitted causes of inguinal and cervical lymphadenopathy; as: HIV, Syphilis, HBV, HSV, CMV**
- **IV- Drug Users: for possible HIV, HBV**
- **Drug history:**
  - Hydralazine
  - Phenytoin
  - Allopurinol
  - Atenolol
  - Carbamazepine
  - Cephalosporins
  - Quinidine
  - Sulfonamides
- **Blood Transfusion or recent transplant history: for possible infections as CMV and HIV**

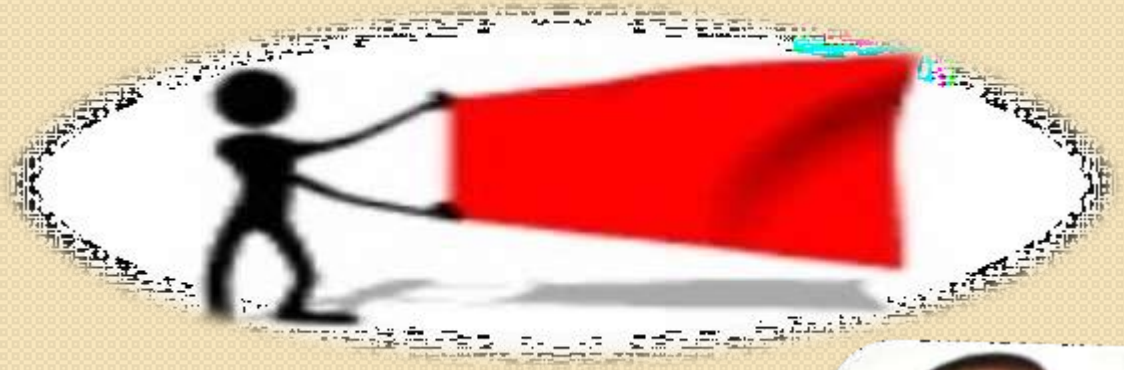
# History and Examination

- ***Constitutional symptoms*** **such as: fever *(nocturnal fever or Pel-Ebstein fever)*, malaise, fatigue, cachexia, unexplained loss of weight (>10% of body eight) and anorexia**
- **Presence of non-pitting edema with inguinal LNs may suggest filariasis**
- **Arthralgia, muscle weakness, unusual rashes may indicate possibility of autoimmune diseases**
- **compression symptoms as dyspnea & dysphagia due to pressure on trachea or esophagus by the enlarged lymph nodes**
- **Coexistence of splenomegaly implies a systemic disorders or a hematological disorder as:**

**(IMN, Lymphoma, acute or chronic leukemia, SLE, sarcoidosis, Toxoplasmosis, or cat-scratch disease)**

# RED FLAGS IN LYMPHADENOPATHY

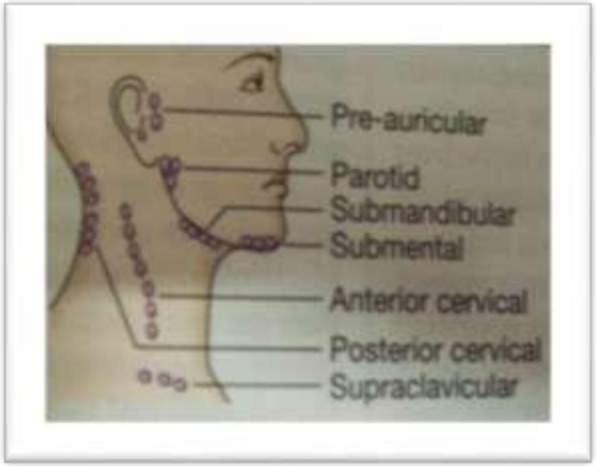
1. Fever, night sweats, and unexplained weight loss
2. A supraclavicular node
3. Hard and tender L.N. with a significant size or draining an area with a significant pathology
4. Matted or Fixed node(s)
5. Non-recessive node after 3 weeks period or after disappearance of fever

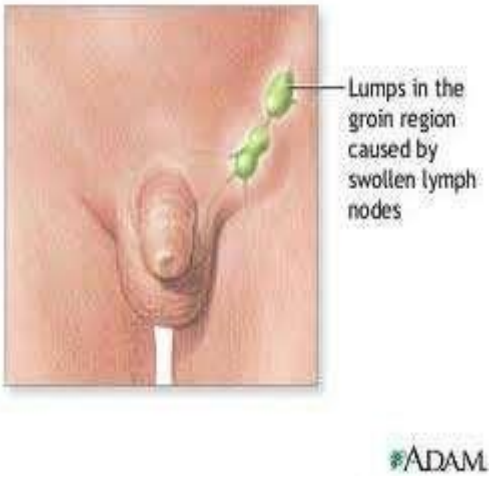


# Clinical Considerations

**The normally palpable L.Ns. Are:**

- **Submandibular**
- **Axillary**
- **Inguinal**




# Clinical Considerations

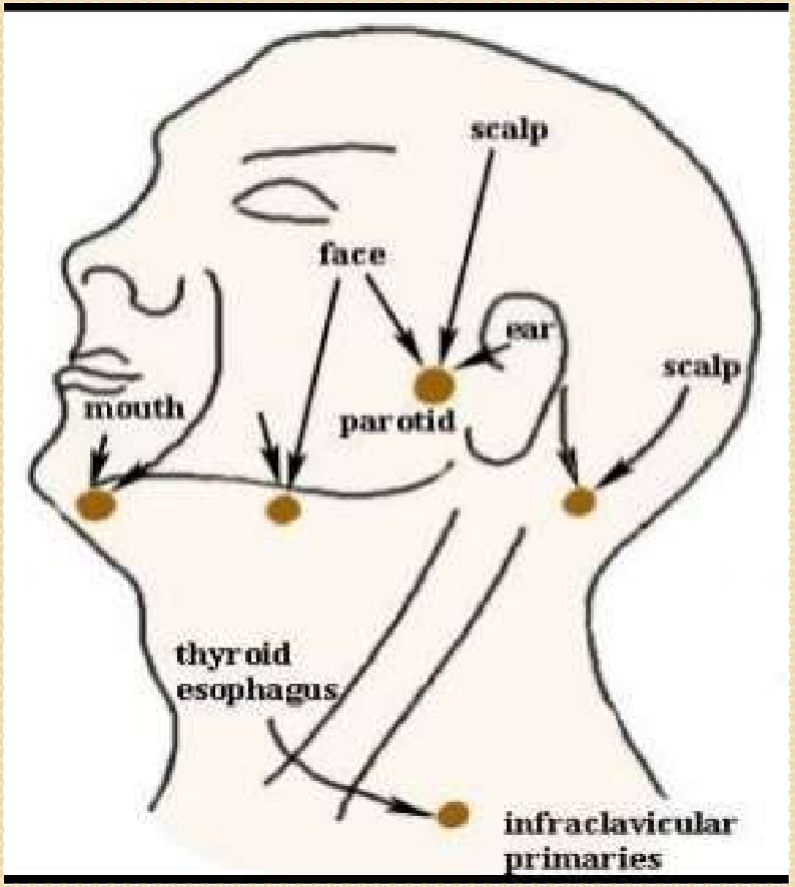
- Is the palpable mass a L.N. ?
- Epidemiological clues ?
- Site ? {Localized or Generalized}
- Number ?
- Size ?
- Character ? {surface and consistency}
- Discrete or Matted ?
- Tenderness ?
- Mobility ?
- Attachment ? And Relation to adjacent muscle ?
- Associated Systemic and/or Localizing symptoms or signs?

# Local Examination

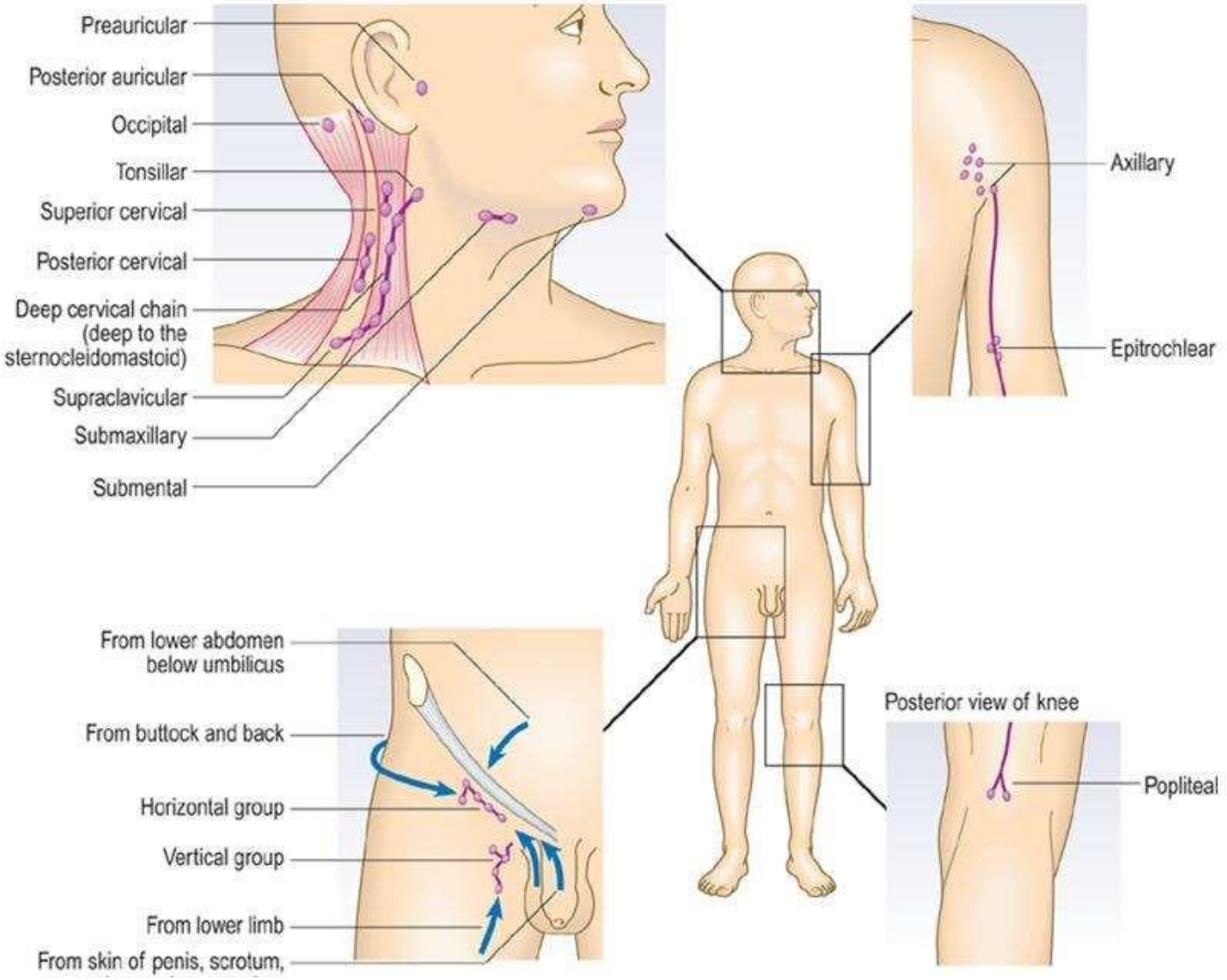
## Mapping

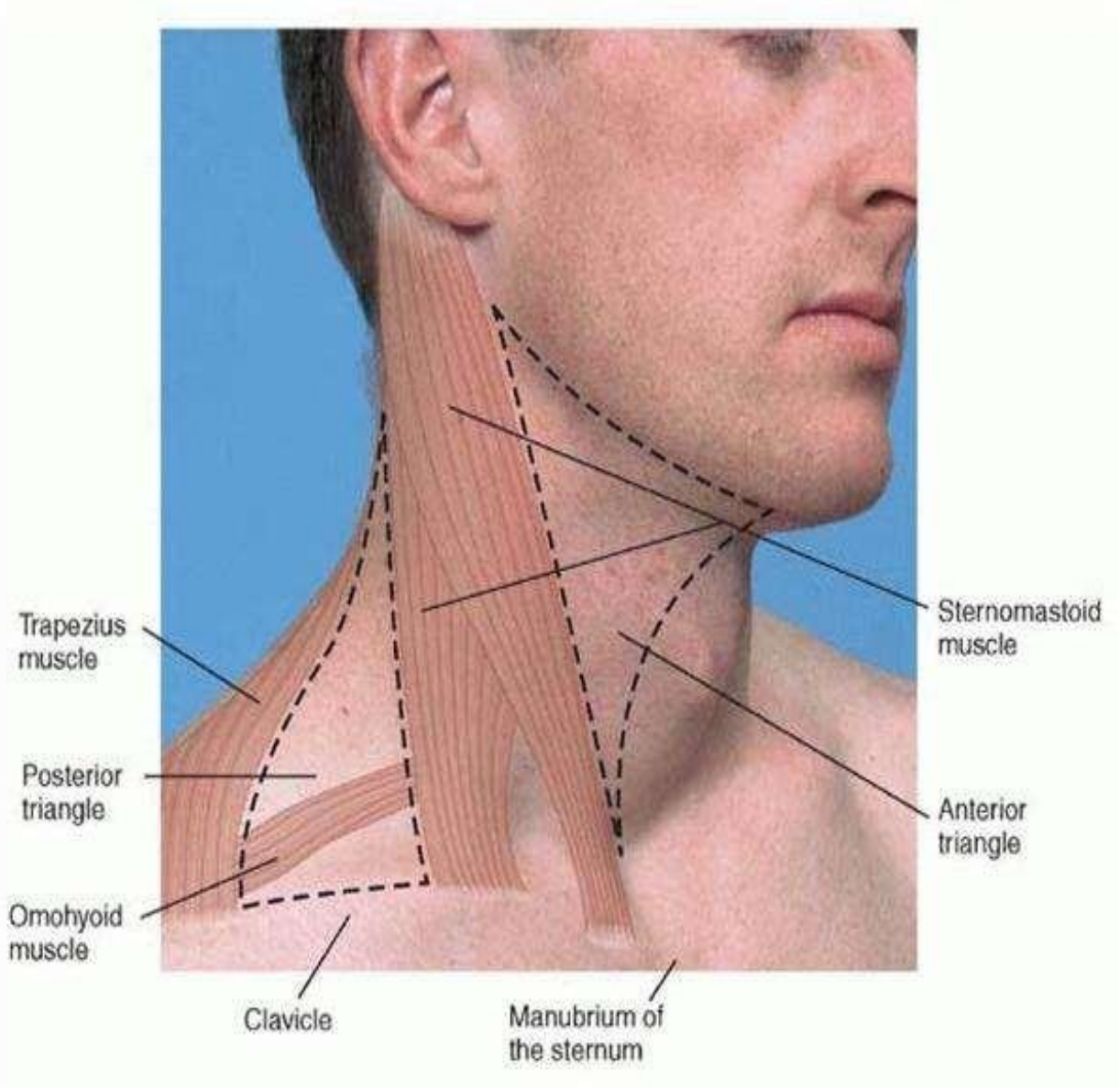
- The physical examination should be regionally directed by knowledge of the lymphatic drainage patterns
- All the normal anatomic sites should be inspected for any obvious enlargements.
- When lymphadenopathy is localized, the clinician should examine the region drained by the nodes for evidence of infection, lesions or tumors

## Examination



# Mapping of Different Nodes




Trapezius muscle
Posterior triangle
Omohyoid muscle
Clavicle
Manubrium of the sternum
Sternomastoid muscle
Anterior triangle

# Node Palpation

*** Confirm that the palpable mass is indeed a L.N..

{ NOT something else as: Thyroglossal cyst, Abscess, Branchial cyst, Enlarged parotid, salivary gland ..}

- **Exposure of the patient:**
  - Cervical: whole head and neck to clavicles
  - Axillary: uncover to the waist
  - Inguinal: umbilicus to knee
- Before performing palpation, ask the patient to identify painful areas so that you can examine those areas last
- During the procedure, pay attention to their facial expression to assess for sign of discomfort
- **Technique:** Use the pads of the index and middle finger to move the skin in circular motions over the underlying tissues in each area

# Axillary Node Palpation

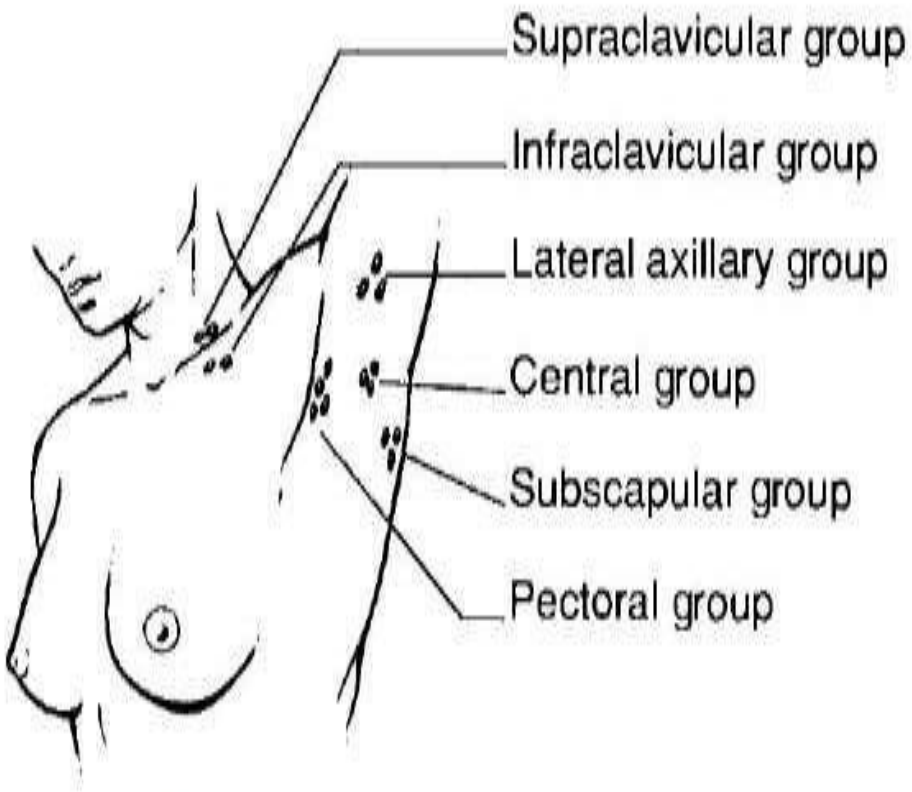



**Fig. 5–3** ***Axillary Lymph Node Groups.*** *Note that the lateral axillary group is on the inner aspect of the upper arm, near the axillary vein. The subscapular group lies deep to the anterior edge of the latissimus dorsi muscle. The pectoral group is behind the lateral edge of the pectoralis major muscle.*

# Epitrochlear node palpation:

Approximately 3 cm proximal to the medial humeral epicondyle, in the groove between the biceps and triceps brachii. Best approached in an anterior to posterior direction

Fig. 3.4 Epitrochlear lymph nodes.

# Inguinal node palpation

**horizontal group:→** along the inguinal ligament (both above and over)

**vertical group:→** beside great saphenous vein in the proximal thigh

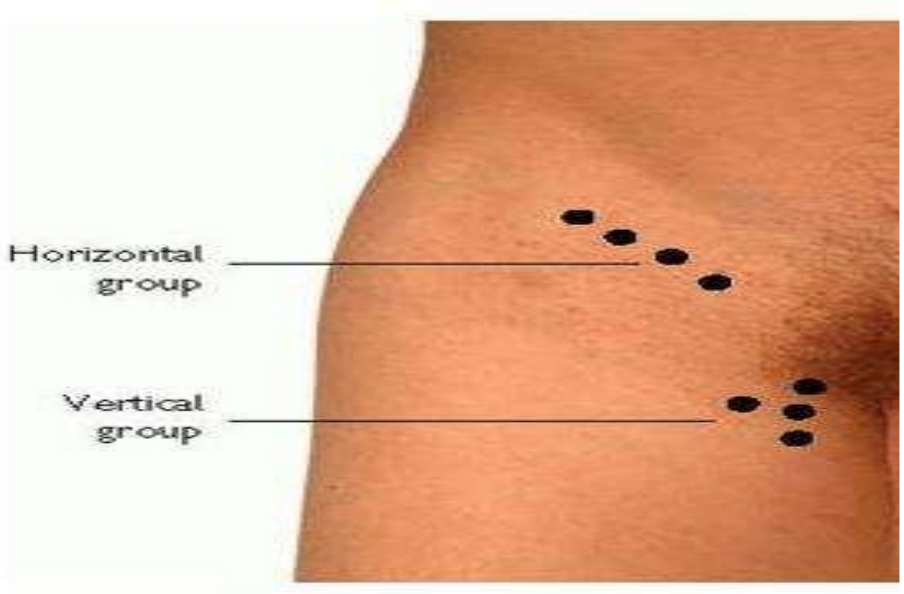



Fig. 3.3 Inguinal lymph nodes.

# Local examination

**You Have To Answer The Previous Questions of Clinical Considerations ..**

## ►►► Note for:

- **Number: (single or multiple), (localized or generalized)**
- **Site: Anatomic location can narrow the D.D.**
  - **T.B. and Hodgkin's ----- > cervical (earlier stages)**
  - **Cat-scratch disease ----- > cervical and axillary**
  - **IMN --- > cervical**
  - **Sexually-transmitted diseases ----- > Inguinal**
  - **Supraclavicular ----- > Highest risk of malignancy(90% in old patients)**
- **Size (up to 1 cm is considered normal).. Except epitrochlear :if >0.5cm**

***N.B.=The size is usually of little importance in adding information to establish diagnosis; however increase in size on serial examination may be of value..***

# Local examination

- **Surface and Consistency (Soft, hard, firm, rubbery, fluctuant, or variable)**
  - **Stony-hard nodes are typically a sign of cancer, usually metastatic**
  - **Firm, rubbery nodes suggest lymphoma**
  - **Softer nodes are the result of infections or inflammatory conditions**
  - **Suppurative nodes may be fluctuant**

- **Discrete or Matted *(T.B., Sarcoidosis)* or amalgamated *(metastatic carcinoma or lymphomas)***
- **Painless or Painful (when a lymph node increases in size its capsule stretches and causes pain, or when there is hemorrhage into the necrotic center of a malignant node)**

***N.B.=The presence or absence of tenderness does not necessarily differentiate benign from malignant nodes..***

# Local examination

- **Fixed or not to the underlying skin, deep fascia or muscles**

**→The patient is asked to contract the muscles against resistance:**

  - **If the swelling becomes MORE apparent it is SUPERFICIAL to muscles**
  - **If the swelling becomes LESS apparent it is DEEP to muscles**

- **The overlying skin has to be noted:**

  - **Skin redness, edema and brawny induration denote acute lymphadenitis**
  - **Skin over tuberculous lymphadenitis becomes red and glossy when they reach the point of bursting**
  - **Scar often indicates previous bursting of abscess or operation**
  - **Skin may appear tense and stretched with dilated subcutaneous veins when overlying a rapidly growing lymphoma**
  - **In secondary carcinoma, the skin may become fixed**

# Investigations

# Investigations

**It includes:**

I - Laboratory

II - Radiological

III. - Others (as: Bronchoscopy, Mediastinoscopy or Bone Marrow Biopsy)

IV. - Node Biopsy

# Investigations

## I - Laboratory:

- **CBC with differential count :→ provides useful data for the diagnosis of:**
  - **Acute or Chronic leukemia's**
  - **EBV or CMV mononucleosis(atypical lymphocytosis)**
  - **Pyogenic infections**
  - **Lymphoma with a leukemic component**
  - **Immune cytopenias (in illnesses such as SLE)**
- **ESR**
- **Serology:→ may demonstrate:**
  - **Antibodies specific to: components of EBV(viral Capsid Ag), CMV, HIV, Toxoplasma, Brucella, etc**
  - **PCR-for: CMV-DNA, T.B.**
  - **ANA/Anti-ds DNA antibody (SLE)**
- **Others:→ In cases of hilar LAD, do:**
  - **Serum ACE**
  - **Tuberculin T.**

# Investigations

## II - Radiological:

***They include:***

1. Chest X-Ray (CXR)
2. Node Ultrasonography (U/S) / Color Doppler U/S
3. Abdominal: U/S and CT
4. Magnetic Resonance Imaging scans(MRI)
5. Positron Emission Tomography scans(PET)

# Investigations

## CXR:

- To assess for mediastinal disease, Hilar nodes, or for Parenchymal lung disease (Pulmonary infiltrate)
- Mediastinal LAD would suggest:
  - **T.B.**
  - **Histoplasmosis,**
  - **Sarcoidosis**
  - **Lymphoma**
  - **Primary/metastatic lung cancer**

# Investigations

## III – Node Biopsy:

**Node Excision Biopsy:**

- **It is a valuable diagnostic tool**
- **It could be performed directly or via radiological interventional methods or via surgery.**
- **Its accuracy not only on the experience of the clinician, but also on the cytologist who reports it.**

# Self – Assessment Clinical Cases

## ONE

## Question

**A 66-y-old man presents with poor appetite and general malaise. Physical examination reveals palpable L.N.s.**

**The finding of L/N. in which of the following areas is most likely to be suggestive of malignancy?**

A. *Cervical*
B. *Supraclavicular*
C. *Epitrochlear*
D. *Axillary*
E. *Inguinal*

# ONE

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# TWO

## QUESTION

**A 66-y-old man is referred for further investigation of an enlarged supraclavicular L.N.**

**Which one of the following is the diagnostic technique of choice for evaluating LAD, if neoplasm is suspected?**

*A. CT scan*

*B. MRI*

*C. Open biopsy*

*D. FNA*

*E. Incisional wedge biopsy*

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## Three

## QUESTION

**A 69-y-old lifelong non-smoker is referred because of his abnormal blood tests: Hb=11.2, WBCs=86.400 (with 98% lymphocytes), PLTs=180.000.**

**O/E: his R.R. is 16 breaths/min, with widespread non-tender LAD and 5 cm-hepatomegaly and a palapable spleen. Pulmonary function tests show a FVC of 80% of predicted value and FEV 1 of 84%.**

**What is the most likely explanation for the abnormal pulmonary function tests?**

A. *CHF*
B. *Diffuse pulmonary lymphoma*
C. *Lung fibrosis*
D. *Pneumonia*
E. *Sarcoidosis*

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## Four

## QUESTION

A 25-y-old woman presents with widespread LAD. She is taking no regular medications and past medical history is irrelevant. Investigations show: Hb=8, WBCs=42 000, lymphoblasts=64%, PLTs=210 000.

Which of the following is the most likely underlying diagnosis?

A. AML
B. ALL
C. Glandular fever
D. Hodgkin's disease
E. Toxic shock syndrome

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## Five

## QUESTION

A 24-y-old man has noted for the last 2 Ms that his face is swollen in the morning. He has lost 10-Kg in weight over 6-Ms. He has no other complaints.

O/E: The ext. jugular veins are dilated. CXR: shows a mediastinal mass.

Which one of the following is the most likely diagnosis of his SVC obstruction?

A. Adenocarcinoma of the lung
B. Hodgkin's disease
C. Sarcoidosis
D. Seminoma
E. Tuberculosis

## Five

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THANK YOU