


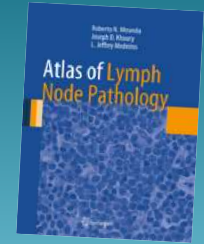
# Approach to Child with Lymphadenopathy



# Outline

- \* Introduction
- \* Anatomy
- \* Pathophysiology
- \* Generalized lymphadenopathy
- \* Regional lymphadenopathy
- \* Investigation
- \* Management

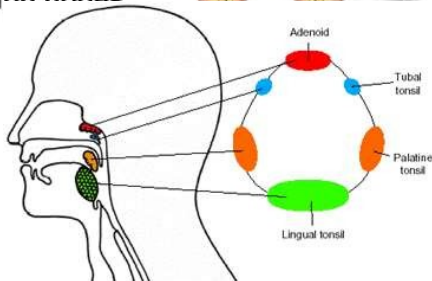
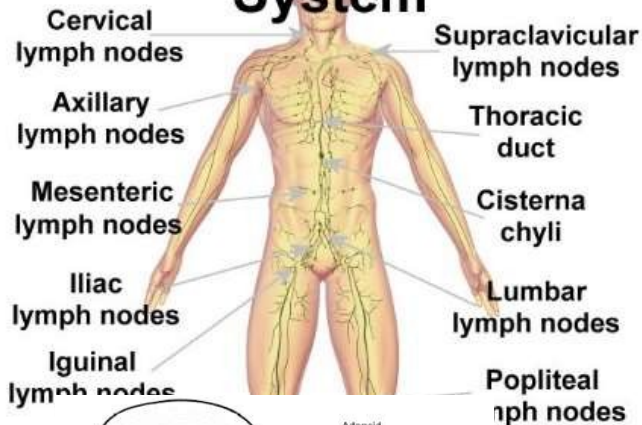
# Introduction



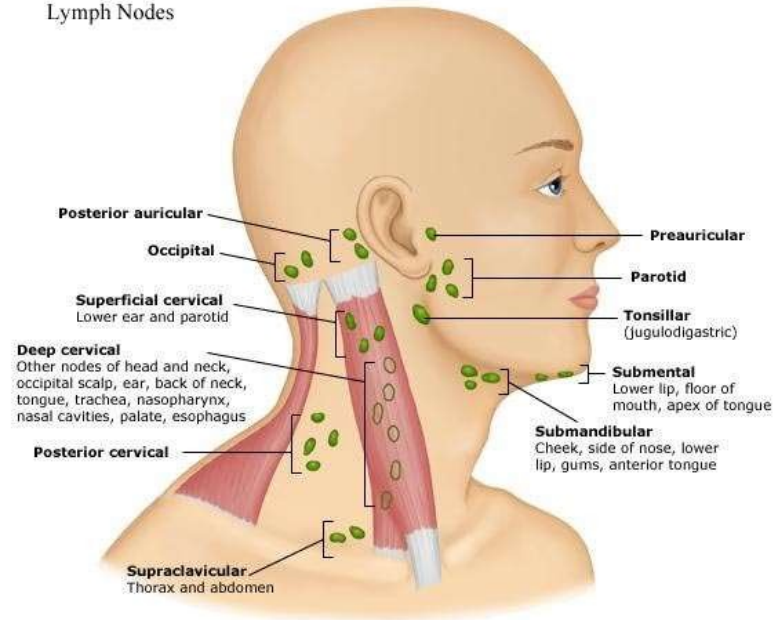
- \* **Lymphatic system**
  - \* Network of organs, lymph nodes, lymph ducts and lymph vessel that make and drain lymph from tissues to the bloodstream.
  - \* This lymphoid tissue concerned with immune function in defending body against antigen.
- \* **Primary lymphoid organ (thymus & bone marrow)**
- \* **Secondary lymphoid organ (lymph nodes, tonsil & others)** Our concern is with secondary
- \* Lymphoid tissue enlarges until puberty & progressively atrophy throughout life
  
- \* **Functions**
  - \* Removal of interstitial fluid from tissues, collection of lymph plasma
  - \* Absorption & transport of fatty acids and fats
  - \* Formation of a defense mechanism for the body

# Groups of Lymph Nodes

## The Lymphatic System



## Lymph Nodes

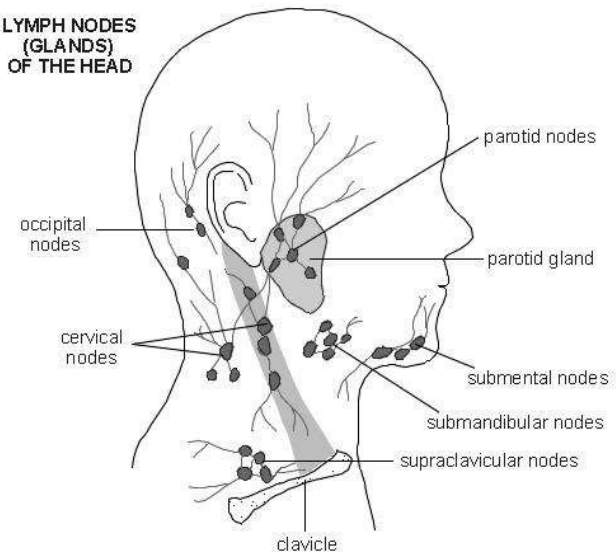


# Lymphadenopath



- \* Enlargement of lymph node
- \* **Normal** lymph nodes are **discrete, non tender**, and **mobile** without fixation to underlying tissues.
- \* Significant enlarged:
  - \* >1 cm in cervical and axillary,
  - \* >1.5cm in inguinal nodes

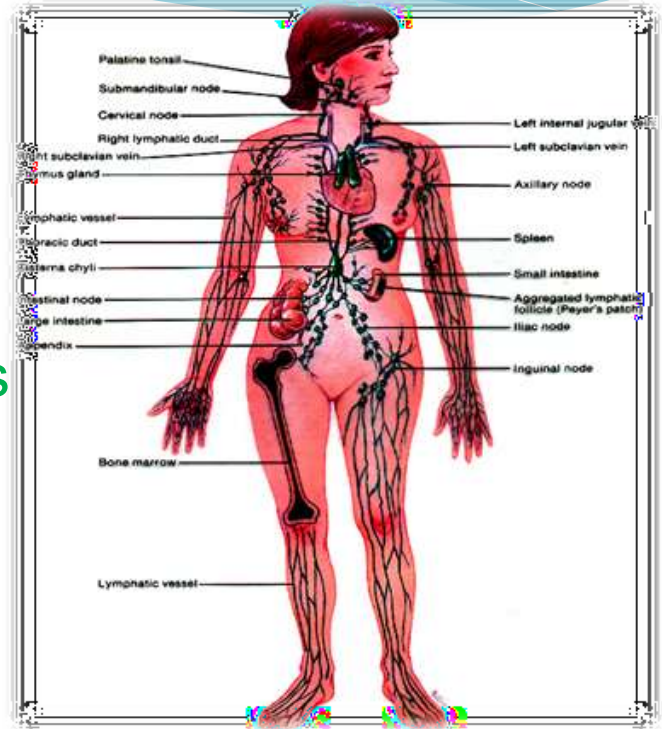
LYMPH NODES  
(GLANDS)  
OF THE HEAD



# Pathophysiology



- \* Localized response from lymphocyte and macrophage – **viral/ bacterial infection**
- \* Localized infiltration by inflammatory cells in response to infection of nodes- **lymphadenitis**
- \* Proliferation of neoplastic lymphocyte or macrophages- **neoplasm**

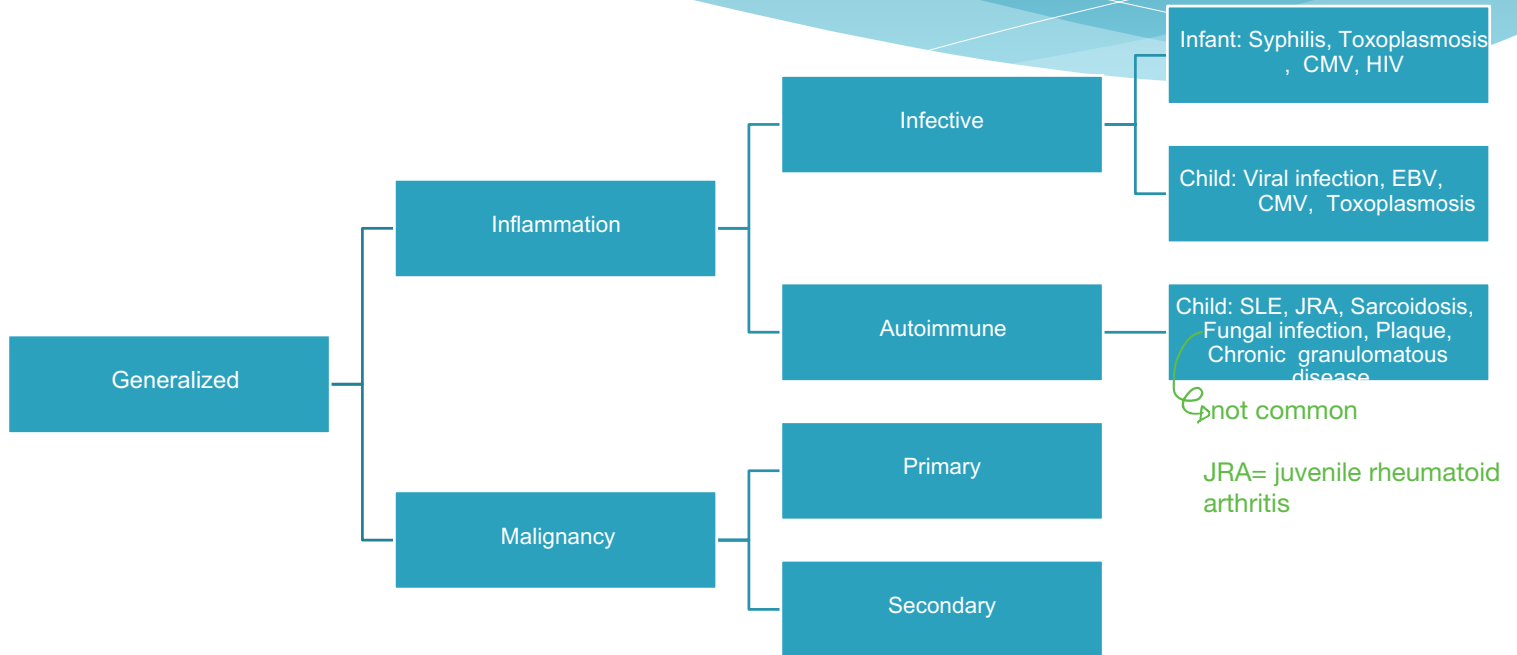


# Lymphadenopath

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- \* Generalized lymphadenopathy (enlargement of >2 noncontiguous node regions) is caused by **systemic disease**
- \* <sup>Localized</sup> Regional lymphadenopathy is most frequently the result of **infection in the involved node** and/or its **drainage area** Can involve one or more lymph nodes but they are in the same area

# Generalized adenopathy





# Generalized

enlargement of more than 2 noncontiguous lymph node groups

## Infectious

Specifically hepatitis B

- Viral (most common): URTI, measles, varicella, rubella, hepatitis, HIV, EBV, CMV, adenovirus
- Bacterial: syphilis, brucellosis, tuberculosis, typhoid fever, septicemia
- Fungal: histoplasmosis, coccidioidomycosis
- Protozoal: toxoplasmosis

## Non-infectious inflammatory diseases

- Rheumatologic diseases: Sarcoidosis, rheumatoid arthritis, SLE
- Storage diseases: Neimenn-Pick disease, Gaucher disease
- Serum sickness
- Rosai-Dorfman disease

Also carbamazepine, but phenytoin and allopurinol are the most important drugs for you to remember

Drug reaction: phenytoin, allopurinol

Hyperthyroidism

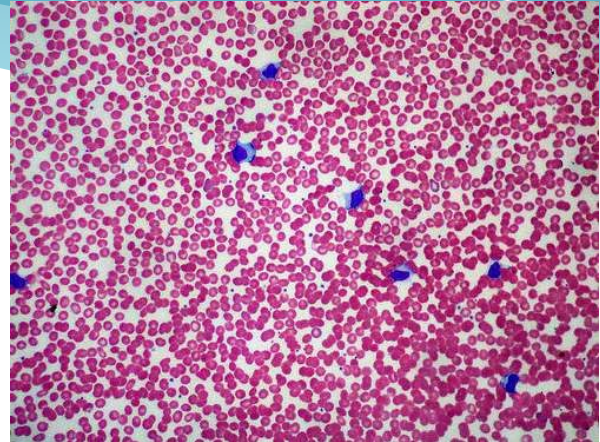
# Infectious Mononucleosis (Glandular Fever)

- Caused by Epstein Barr Virus
  - Signs/Symptoms
    - \* Prolong fever
    - \* Exudative pharyngitis
    - \* Painless generalized lymphadenopathy
    - \* Splenomegaly Hepatosplenomegaly
  - Diagnosis
    - 50% lymphocytosis with **>10% Atypical lymphocytes** on peripheral blood smear
    - \* Positive monospot test (Paul Bunnell test) In more than 4 yrs old
    - \* Serum heterophile Antibody definitive (positive at 2-6weeks) ELISA in less than 4 yrs old
  - Complication: splenic rupture, respiratory obstruction, encephalitis, lymphoma Respiratory obstruction is the most common in all ages
  - Treatment
    - Mainly supportive
    - \* Tonsillar hypertrophy → produce airway obstruction: need to place nasopharyngeal tube and start high dose steroids
    - \* Do not give amoxicillin → develop an iatrogenic rash in 80% of patients. There is no specific treatment, but don't use amoxicillin as confirmation (some doctors give amoxicillin as a way to confirm the diagnosis, because it will cause rash in 80% of these patients.
- If Paul Bunnell test is done in less than 4 years old, it will be negative (useless). So, in less than 4yrs order serology (ELISA), IgG and IgM.

# Infectious Mononucleosis Findings



exudative tonsillitis



Atypical lymphocytes



# Cytomegalovirus

## S

- \* From Herpesviridae family
- \* Infectious mononucleosis like syndrome
- \* CF: fatigue, malaise, myalgia, headache, fever, hepatosplenomegaly, elevated liver enzymes
- \* Ix: atypical lymphocytosis in peripheral blood smear, CMV DNA PCR
- \* Tx: not indicated for immunocompetent persons

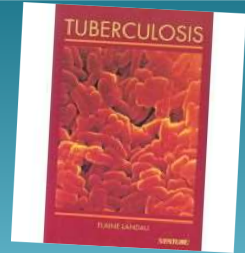
More than 4 yrs > paul bunnell  
Less than 4 > serology or PCR

CF: Also Puffiness around eye, and most importantly  
Generalized lymphadenopathy

If immunocompromised give acyclovir

# TB

## Lymphadenitis



- Most commonest form of extrapulmonary manifestation of TB in children
- Tonsillar, anterior cervical, submandibular, and supraclavicular nodes secondary to extension of the primary lesion of TB (lung/abdomen)
- Inguinal, epitrochlear, or axillary regions result from regional lymphadenitis associated with tuberculosis of the skin or skeletal system.
- Characteristic: firm, discrete and nontender – often feel fixed to overlying tissue → disease progress, multiple node infected (matted)
- Unilateral
- Reactive tuberculin test
- Dx: fine – needle aspiration of node (through histologic and bacterial conformation)
- Response well to anti – TB therapy rifampin, isoniazid, pyrazinamide, and ethambutol

For diagnosis you need to have positive tuberculin test and/or quantiferon skin test. For definitive dx go for biopsy either fine needle or excisional

# Syphili

## S

- \* *Treponema pallidum*
- \* Vertical transmission, sexual contact with infectious lesion, blood product Usually vertical
- \* 4 stages: **primary, secondary, latent and tertiary**
- \* Primary:
  - \* glands of penis, vulva or cervix
  - \* Other: anus, fingers, oropharynx, tongue
  - \* Regional lymphadenopathy Usually in inguinal area
- \* 2nd: localized or diffuse mucocutaneous rash, patch alopecia condylomata with generalized non tender lymphadenopathy
- Latent\* 3rd: CNS involvement or CVS
- \* Ix: VDRL As screening test
- \* Tx: IM Benzathine Penicillin

# Toxoplasmosi

## S

- \* *Toxoplasma gondii*
- \* Mechanism
  - \* Consumption of undercooked meat
  - \* Ingestion of oocytes from cat feces
- \* Symptoms
  - \* Malaise, fever, sore throat, myalgias
  - \* 90% have cervical lymphadenitis
- \* Diagnosis by serologic testing
  - \* Complications
    - \* myocarditis
    - \* pneumonitis
- \* Risk of TORCH infection to fetus
- \* Treatment with pyrimethamine or sulfonamides Treatment of choice is sulfonamides

# Toxoplasmosis Notes

Usually a neonate get it as a congenital infection. Generalized lymphadenopathy, CNS involvement (scattered calcification), and hepatosplenomegaly

If the child gets the infection later in life, usually it will be asymptomatic. But if he is immunocompromised he will have malaise, fever, sore throat, and lymphadenopathy specially cervical.

Risk factors:

- consumption of undercooked or raw meat
- Ingestion of oocyte from cat feces

Complications

- If congenital > CNS and intellectual problem
- If later in life and he is immunocompromised > myocarditis or pneumonitis

Diagnosis

- In congenital > By TORCH screen
- If later in life (acquired) > serology or PCR



# Storage diseases

Storage diseases that cause generalized lymphadenopathy are Gaucher disease and Niemann-Pick disease

## Gaucher disease

- multisystemic lipidosis characterized by hematologic problems, hepatosplenomegaly, and skeletal involvement
- results from the deficient activity of the lysosomal hydrolase, acid  $\beta$ -glucosidase
- CFx:
  - \* easily bruising owing to thrombocytopenia Easily bruising is characteristic for them
  - \* chronic fatigue secondary to anemia
  - \* hepatomegaly with or without elevated liver function test results
  - \* splenomegaly And organomegaly in general as result of infiltrates
  - \* bone pain
    - Lymphadenopathy

Treatment of Gaucher disease

- Usually by bone marrow transplantation
- Research about replacing lysosomal hydrolase

## Niemann-Pick disease

It is three types but we will talk about it in general

Extra

- 3 types:
  - \* Type A & B deficient activity of acid sphingomyelinase
  - \* Type C is defective cholesterol transport But with time they will develop
- Characterized by a normal appearance at birth. ↑ Hepatosplenomegaly, moderate lymphadenopathy, and psychomotor retardation are evident by 6 mo of age, followed by neurodevelopmental regression.
- With advancing age, the loss of motor function and the deterioration of intellectual capabilities are progressively debilitating; and in later stages, spasticity and rigidity are evident.
- Affected infants lose contact with their environment - DEATH

# Localized

enlargement of a single node or multiple contiguous nodal regions

Cervical (most common adenopathy in children, often INFECTIOUS cause):

## • Infectious

- Viral upper respiratory infection
- Infectious mononucleosis (EBV, CMV)
- Group A Streptococcal pharyngitis
- Acute bacterial lymphadenitis (eg: Staphylococcus aureus)
- Kawasaki disease (unilateral cervical lymph node > 1.5 cm)
- Rubella Rubella usually cause generalize but can cause localize
- Cat scratch disease Usually it is cold abscess
- Toxoplasmosis Toxoplasmosis usually cause generalize but can cause localize
- Tuberculosis, atypical mycobacteria

We have two presentations either acute or chronic .

For acute usually it is secondary to bacterial infection (s. aureus or group A strept) present as fever, swelling, pain, and tenderness



## • Neoplastic (malignant childhood tumours develop in the head and neck in 1/4 of cases) non-Hodgkins starts as localized then generalized

- Neuroblastoma, Leukemia, non-Hodgkins, and Rhabdomyosarcoma are most common in those < 6 years old.
- In older children, Hodgkin's and non-Hodgkin's lymphoma are more common.
  - Acute leukemia, Neuroblastoma, Rhabdomyosarcoma

# Suppurative Bacterial Lymphadenitis

- \* Staphylococcus aureus and Group A Streptococcus
- \* Common history reveals recent
  - ✓ URI
  - ✓ Earache
  - ✓ Sore Throat/Toothache
  - ✓ Skin Lesions: erythema and tender of overlying skin
- \* Tx: Oral or IV antibiotics depending on severity of infection
- \* If not resolving or getting worse Ultrasound or CT scan to evaluate for phlegmon/abscess
- \* Surgical I&D vs Surgical Excision if abscess

Fever, tenderness and redness over lymph node



# Cat Scratch Disease

- \* Bartonella Henselae
  - Commonest cause of chronic lymphadenitis
  - \* 90% have had exposure to cat bite or scratch
    - CF: Red papules over scratch area + lymphadenopathy in the draining limb
    - Nodes involved: tender, overlying erythema, enlarged, (10-40%) suppurative
    - Axillary nodes are most frequently affected, followed by cervical, submandibular, and preauricular nodes.
- \* Diagnosis with serology for antibodies or PCR
- \* Management: supportive Usually supportive, but if the disease progresses we can give Co-trimoxazole
- \* \*\*Other less common zoonotic causes are tularemia, brucellosis, and anthracosis.



# Kawasaki Disease

- \* Lymphomucocutaneous Disease
- \* Five Characteristics of Disease (4/5 for diagnosis)
  - ? Fever >5 days
  - ? Cervical lymphadenopathy (usually unilateral)
  - ? Erythema and edema of palms and soles with desquamation of skin desquamation in the second week
  - ? Nonpurulent Bilateral Conjunctivitis
  - ? Strawberry Tongue With packed lips and redness in oral cavity
- \* Complications Risk of these complications is 25% without immunoglobulins, but if immunoglobulins given in the first 10 days of presentation this risk decreases to 2.5%
  - ? Coronary artery aneurysms
  - ? Coronary artery thromboses
  - ? Myocardial infarction
- \* Treatment
  - o IVIG and Aspirin You have to continue aspirin until the ESR and echo become normal
- \* \*\*Be sure to get Echo and EKG is Kawasaki disease is suspected

# Systemic Manifestations of Kawasaki Disease



Non purulent conjunctivitis



Desquamation



Strawberry tongue

# Differential Diagnosis

Of lymphadenopathy

## Submaxillary and submental

- Oral and dental infections
- Acute lymphadenitis **And direct involvement of bacteria**

## Occipital

- Pediculosis capitis (lice)
- Tinea capitis/local skin infection
- Rubella
- Roseola

## Preauricular (rarely palpable in children)

- Local skin infection
- Chronic ophthalmic infection



# Differential Diagnosis

Mediastinal (not directly palpable; assess indirectly via presence of supraclavicular adenopathy. Usually discovered by chest x-ray

- May manifest as cough, dysphagia, hemoptysis, or SVC syndrome
  - ALL Acute lymphocytic leukemia SVC = superior vena cava
  - Lymphoma
  - Sarcoidosis
  - Cystic fibrosis
  - Granulomatous disease ( tuberculosis, histoplasmosis, coccidioidomycosis)





## Axillary y

- Local infection
- Cat scratch disease
- Brucellosis
- Reactions to immunizations *In the same limb*
- Non Hodgkin lymphoma
- Juvenile rheumatoid arthritis
- Hidradenitis suppurativa  
*Usually in adolescent or adults rather than children*



# Differential Diagnosis

## Abdominal

- (may manifest as abdominal pain, backache, urinary frequency, constipation, or intestinal obstruction due to intussusception)
- Acute mesenteric adenitis *Usually by adenovirus*
- Lymphoma

## Inguinal

- Local infection
- Diaper dermatitis
- Syphilis
- Genital herpes



# Histor y

- \* Characteristic of LN: onset, size, duration, is it painful or erythematous? Generalized or local? Associated symptom?
- \* Recent infection? URT symptom? Rashes? Changes in bowel movement or voiding patterns? Bone and joint pain?
- \* Constitutional sx? Fever, night sweat, weight loss?
- \* Skin lesion or trauma? Cat scratch? Animal/ insect bites? Open wounds? Dental abscess?

Ingestion of raw milk or raw meet ?

# Histor y

- \* Any ongoing medical condition? Surgery?
- \* Recent travel and exposures? Contact with infected person? Viral respiratory exposures such as EBV/ CMV? TB exposure?
- \* Immunization status? MMR? DTaP? MMR and DTaP can present with lymphadenopathy
- \* Medication? Isoniazide, Allopurinol, Phenylbutazone, Pyrimethamine? Carbamazepine or phenytoin?
- \* Allergies
- \* Adolescence: IVDU or sexual history
- \* Cats: Toxoplasmosis and Bartonella
- \* Foods: Unpasteurized milk (Brucellosis), Undercooked meats (Toxoplasmosis, Tularemia)

# Investigation

## S

Neutrophilia > Group A strept, s.aureus

Atypical lymphocytes or lymphocytosis > EBV, CMV

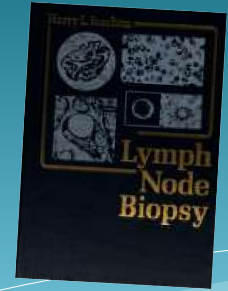
- \* Complete blood count, peripheral blood smear
- \* Erythrocyte sedimentation rate (non-specific)
- \* Rule out infectious causes: Monospot, CMV, EBV, & toxoplasma, Bartonella titres, TB skin test, Anti-HIV test, CRP, ESR
- \* Hepatic and renal function + urinalysis (systemic disorders that can cause lymphadenopathy)
- \* Lactate dehydrogenase, uric acid, calcium, phosphate, magnesium if malignancy suspected
- \* US guided lymph node biopsy If the diagnosis not clear then go for biopsy

Investigations depend on history, you will not order all of these

# Imaging Studies

- \* Chest X-ray. This study will help determine the presence of mediastinal adenopathy and underlying pulmonary diseases including tuberculosis, coccidioidomycosis, lymphomas, and neuroblastoma.
- \* CT of the chest and/or abdomen. Supraclavicular adenopathy is highly associated with serious disease in the chest and abdomen.
- \* Bone marrow, liver biopsies, Bone marrow biopsy in leukemia, neuroblastoma, and lymphoma
- \* Nuclear medicine scanning is helpful in the evaluation of lymphomas.

# Biopsy indications



1. + constitutional sx
2. Very large LN
3. Persistent growing > 2 wk
4. Constant for 6 wks *Constant in size*
5. Fixed lymph nodes *To the underlying tissue*
6. Non responsive after 2 course  
of antibiotic therapy

# Management

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Extra

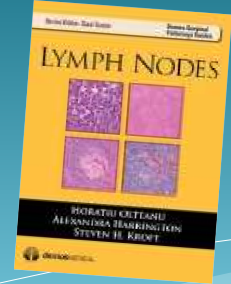
- \* Treatment with antibiotics. Bacterial infection results in large nodes that are warm, erythematous, and tender. Start on antibiotics that cover the bacterial pathogens frequently implicated in lymphadenitis, including staphylococcus aureus and streptococcus pyogenes. Reevaluate in 2-4 weeks. Biopsy if unchanged or larger.
- \* If malignancy is a strong possibility excisional biopsy should be considered immediately.
- \* If lymphadenitis is present, aspirate may be needed for culture.



# Management

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Extra



- \* Treat the underlying cause.
- \* If no specific cause – Antibiotic (10day course), if still persist- give another course of other antibiotic
- \* Antifungal, anti-TB
- \* Chemotherapy- for malignancy
- \* HAART- for HIV
- \* Incision & drainage – nodes with suppuration

# Conclusion

- \* In summary, lymphadenopathy is a sign of a variety of underlying disorders, most of which are benign in children.
- \* Less commonly, there is a more serious cause of lymphadenopathy and thus it is extremely important to think of and rule out malignancy through a thorough history and physical exam.

# Viral Lymphadenitis

## Extra

- \* Most common form of reactive lymphadenopathy
- \* Common virus' involved:
  1. Adenovirus
  2. Rhinovirus
  3. Coxsackie virus A and B
  4. EBV
- \* Lymphadenopathy often bilateral, diffuse, non-tender
- \* Other Signs/Symptoms are consistent with URI
- \* Management is expectant but they are often biopsied due to slow regression
- \* Nodal architecture and hilar vascularity are normal on pathologic examination