Approach to lymphadenopathy with/without hepatosplenomegaly

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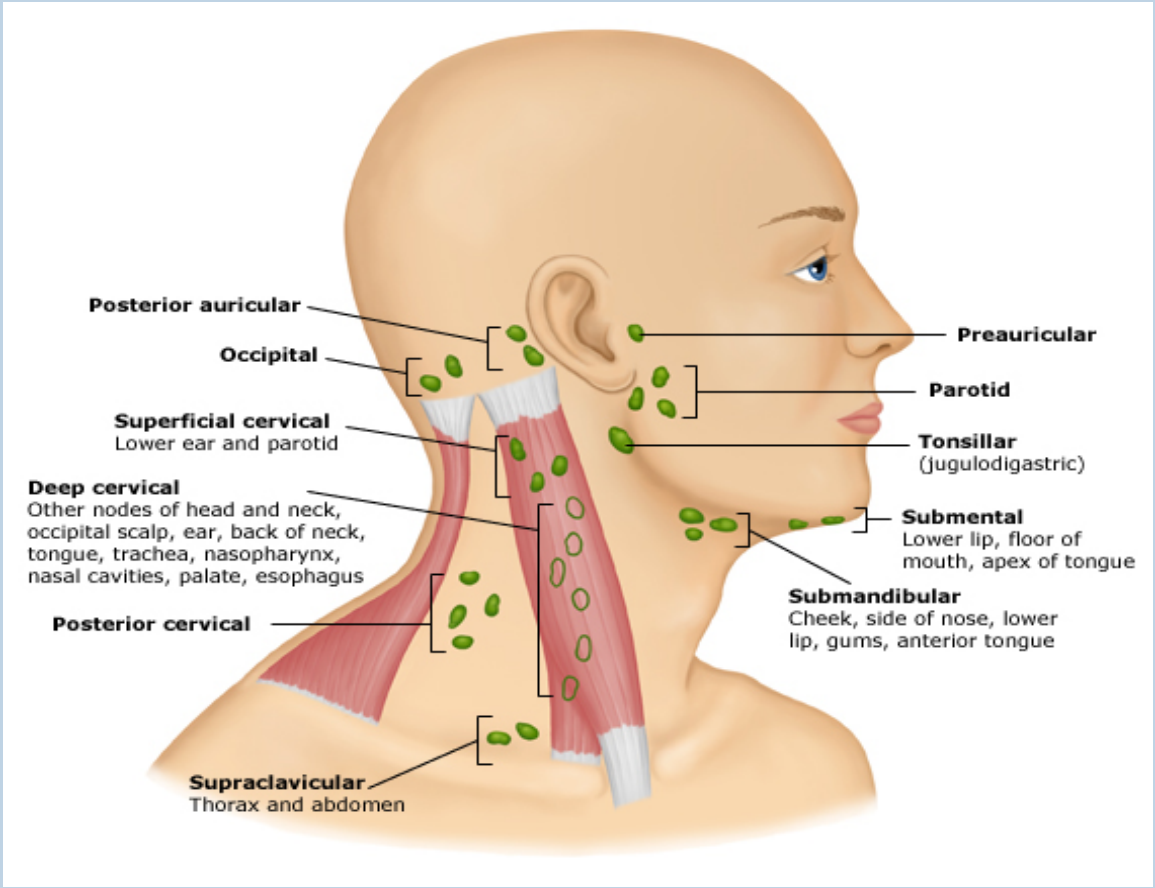
Dr. Elham gave the same slides, the only difference is some pictures
Dr. Sara read almost everything in this ppt
I dont recommend going over the recording

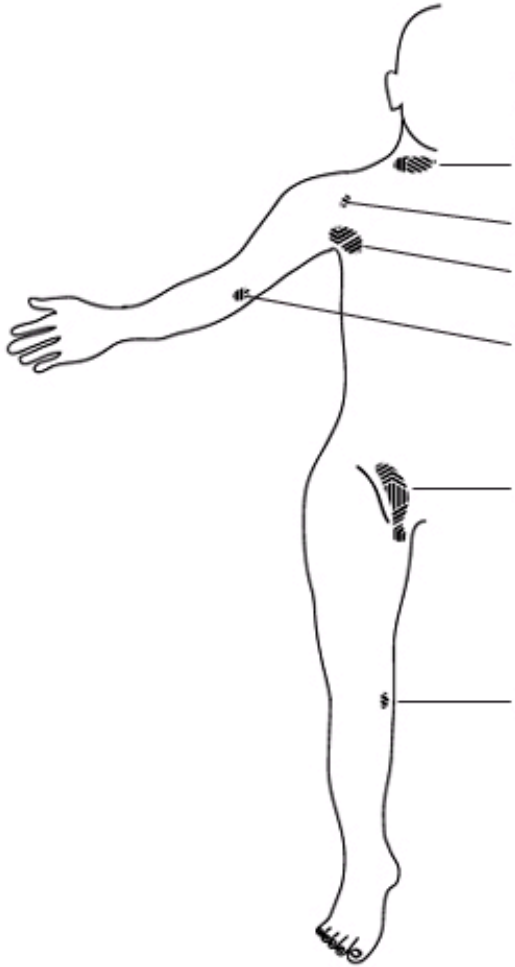
Deema Alfaris

Doctors notes - extra from Nelson

LN Head and neck



Lymph node regions in the body



Node group, number	Drainage
Supraclavicular (2-4)	Right side: Mediastinum, lungs Left side: Abdomen
Deltopectoral (1-2)	Arm
Axillary (20-30)	Arm, breast, thorax, neck
Epitrochlear (1-2)	Medial side of arm below elbow
Inguinal (12-20)	Lower extremity, genitalia, buttock, and abdominal wall below umbilicus
Popliteal (6-7)	Lower leg

Its important to know the drainage of each group

Posterior is usually pathologic

- Palpable lymph nodes are normal in anterior cervical, axillary and inguinal regions in healthy children
- Lymphadenopathy: enlargement of the lymph nodes beyond this normal state. Practically this is any node >1.0 cm in greatest diameter
- Certain nodes should be considered enlarged at different sizes (i.e. epitrochlear nodes > 0.5 cm, inguinal nodes >1.5 cm, submandibular nodes > 1.5 cm)

Definitions

- Acute Lymphadenopathy
  - < 2 weeks duration
- Subacute Lymphadenopathy
  - 2-6 weeks duration
- Chronic Lymphadenopathy
  - > 6 weeks duration

Generalized lymphadenopathy is enlargement of two or more noncontiguous lymph node groups
regional lymphadenopathy involves one lymph node group only.

Cause	Examples
Infections (Most common)	
Bacterial	
– Localized	Streptococcal pharyngitis; skin infections; tularemia; cat scratch disease; diphtheria;
– Generalized	Brucellosis; leptospirosis; typhoid fever.
Viral (Very common)	Epstein-Barr virus; herpes simplex virus; cytomegalovirus; mumps; measles; rubella; HIV, hepatitis B; dengue fever
Mycobacterial	Mycobacterium tuberculosis; atypical mycobacteria
Fungal	Histoplasmosis; coccidioidomycosis; cryptococcosis
Protozoal	Toxoplasmosis; Leishmaniasis
Neoplastic diseases	leukemia metastatic; lymphoma; Hemophagocytic lymphohistiocytosis
Autoimmune (Usually generalizes)	SLE, JRA, serum sickness
Drugs	phenytoin, Hydralazine, Allopurinol, Pyrimethamine, Isoniazide
Miscellaneous	Sarcoidosis; lipid storage diseases; amyloidosis; histiocytosis; chronic granulomatous diseases

Caused by bartonella, you dont need to know the name, just the disease

Primary HIV presents with flulike Sx and lymphadenopathy

You dont need to remember those by name, just know their classification

- Cervical lymphadenitis is the most common regional lymphadenitis among children and is associated most commonly with pharyngitis caused by group A streptococcus, respiratory viruses, and Epstein-Barr virus (EBV).
- EBV primarily affects B lymphocytes and is the cause of infectious mononucleosis, a clinical syndrome characterized by fever, fatigue and malaise, cervical or generalized lymphadenopathy, tonsillitis, and pharyngitis.
- CMV, Toxoplasma, adenoviruses, hepatitis B virus, hepatitis C virus, HIV infection, known as acute retroviral syndrome, can cause an infectious mononucleosis-like syndrome with lymphadenopathy.

Infectious causes of cervical lymphadenitis in children

You dont need to know this

Presentation	Common	Uncommon	Rare
Acute bilateral	Rhinovirus Epstein-Barr virus*• Cytomegalovirus*• Herpes simplex virus Adenovirus Enterovirus *Mycoplasma pneumoniae* Group A streptococcus Influenza	Roseola• Parvovirus B19•	*Corynebacterium diphtheriae* Rubella• Measles Mumps•
Acute unilateral Common	*Staphylococcus aureus* Group A streptococcus Anaerobic bacteria Seen with dental issues like carries	Group B streptococcus Tularemia* Alpha streptococcus *Pasteurella multocida* *Yersinia pestis*• Gram-negative bacilli	*Yersinia enterocolitia** Anthrax
Chronic unilateral	Nontuberculous *Mycobacterium* Cat scratch disease	Toxoplasmosis• Tuberculosis• Actinomycosis	*Nocardia brasiliensis* Aspergillosis Sporotrichosis
Chronic bilateral	Epstein-Barr virus Cytomegalovirus•	HIV• Toxoplasmosis• Tuberculosis• Syphilis•	Brucellosis• Histoplasmosis•

HIV: human immunodeficiency virus.
* Infection can persist and become more chronic in appearance.
• Often associated with generalized lymphadenopathy.

UpToDate®

- Extra tables

Table 99-1 | Infectious Causes of Generalized Lymphadenopathy

VIRAL
Epstein-Barr virus (infectious mononucleosis)
Cytomegalovirus (infectious mononucleosis-like syndrome)
HIV (acute retroviral syndrome)
Hepatitis B virus
Hepatitis C virus
Varicella
Adenoviruses
Rubeola (measles)
Rubella
BACTERIAL
Endocarditis
Brucella (brucellosis)
Leptospira interrogans (leptospirosis)
Streptobacillus moniliformis (bacillary rat-bite fever)
Mycobacterium tuberculosis (tuberculosis)
Treponema pallidum (secondary syphilis)
FUNGAL
Coccidioides immitis (coccidioidomycosis)
Histoplasma capsulatum (histoplasmosis)
PROTOZOAL
Toxoplasma gondii (toxoplasmosis) *Trypanosoma cruzi* (Chagas disease)

Table 99-2 | Infectious Causes of Regional Lymphadenopathy

NONVENEREAL ORIGIN
Staphylococcus aureus
Group A streptococcus
Group B streptococcus (in infants)
Bartonella henselae (cat-scratch disease)
Yersinia pestis (plague)
Francisella tularensis (glandular tularemia)
Mycobacterium tuberculosis
Nontuberculous mycobacteria
Sporothrix schenckii (sporotrichosis)
Epstein-Barr virus
Toxoplasma gondii
SEXUALLY TRANSMITTED INFECTIONS (PRIMARILY INGUINAL LYMPHADENOPATHY)
Neisseria gonorrhoeae (gonorrhea)
Treponema pallidum (syphilis)
Herpes simplex virus
Haemophilus ducreyi (chancroid)
Chlamydia trachomatis serovars L_{1-3} (lymphogranuloma venereum)
LYMPHOCUTANEOUS SYNDROMES
Bacillus anthracis (anthrax)
F. tularensis (ulceroglandular tularemia)
B. henselae (cat-scratch disease)
Pasteurella multocida (dog or cat bite) Rickettsialpox
Spirillum minus (spirillary rat-bite fever)
Y. pestis (plague)
Nocardia (nocardiosis)
Cutaneous diphtheria (*Corynebacterium diphtherial*)
Cutaneous coccidioidomycosis (*Coccidioides immitis*)
Cutaneous histoplasmosis (*Histoplasma capsulatum*) Cutaneous leishmaniasis
Cutaneous sporotrichosis (*S. schenckii*)

Causes of localized lymphadenopathy in children

The doctor skipped this slide

Doctor elham mentioned those to her group

Lymph node group	Area of drainage	Causes
Occipital	Posterior scalp, neck	Common: Scalp infections (including tinea capitis, lice), insect bites, seborrhea, roseola (human herpesvirus 6, HHV6) Less common: Rubella, acute lymphoblastic leukemia
Posterior auricular	Temporal and parietal scalp	Rubella, roseola (HHV6, HHV7)
Anterior auricular (preauricular)	Anterior and temporal scalp, anterior ear canal and pinna, lateral conjunctiva and eyelids	Common: Eye or conjuctival infections (eg, adenovirus, oculoglandular syndrome) Less common: Cat scratch disease, tularemia, listeriosis
Submental	Central lower lip, floor of mouth	Tongue, gum, buccal mucosal, and dental infections (eg, gingivostomatitis), group B streptococcal infection (in infants <2 months of age)
Submaxillary (submandibular)	Cheek, nose, lips, anterior tongue, submandibular gland, buccal mucosa	Tongue, gum, buccal mucosal, and dental infections; dental caries; chronically cracked lips
Cervical	Cranium, neck, oropharynx	**Anterior:** Common: Viral upper respiratory infections, infections of pharynx, oral cavity, or head and neck; primary bacterial adenitis, tuberculosis, Epstein-Barr virus, cytomegalovirus, cat scratch disease, tularemia, nontuberculous mycobacterium, mycobacterium tuberculosis Less common: Kawasaki disease, tularemia, toxoplasmosis, non-infectious causes (eg, Hodgkin's disease, lymphosarcoma, neuroblastoma, rhabdomyosarcoma, sarcoidosis) **Posterior:** Toxoplasmosis, Epstein-Barr virus, rubella
Supraclavicular	Right: Inferior neck and mediastinum Left: Inferior neck, mediastinum, and upper abdomen	Malignancy (lymphoma or metastatic disease)
Axillary	Greater part of arm, shoulder, superficial anterior and lateral thoracic and upper abdominal wall	Common: Cat scratch disease, pyogenic infections of upper arms, brucellosis, reactive response to disruption in skin integrity Less common: Brucellosis, Yersinia pestis, rat-bite fever, toxoplasmosis, rheumatologic disease of the hand or wrist
Epitrochlear	Hand, forearm, elbow	Common: Viral diseases, sarcoidosis, tularemia, infection of hands Less common: Cat scratch disease, tularemia, secondary syphilis, rheumatologic disease of the hand or wrist
Inguinal	Leg and genitalia	Common: Genital herpes, primary; syphilis, gonococcal infection, lymphoma Less common: Yersinia pestis, chancroid, lymphogranuloma venereum
Popliteal	Posterior leg and knee	Local infection

Data from:

1. *Segal GB, Hall CB. Lymphadenopathy. In: Primary Pediatric Care, 4th ed, Hoekelman RA (Ed), Mosby, St. Louis 2001. p.1192.*
2. *Perkins SL, Segal GH, Kjeldsberg CR. Work-up of lymphadenopathy in children. Semin Diagn Pathol 1995; 12:284.*
3. *Malley R. Lymphadenopathy. In: Textbook of Pediatric Emergency Medicine, 5th ed, Fleisher GR, Ludwig S, Henretig FM (Eds), Lippincott Williams and Wilkins, Philadelphia 2006. p.421.*

History & Physical Exam

The history and physical examination are particularly important in determining the differential diagnosis and ultimately the timing, workup and treatment of lymphadenopathy.

History

Duration

Short (< 2 weeks) -likely to be infectious

Long (> 2 weeks but < 1 year) -likely to be infectious, malignancy, autoimmune, drug reaction.

Like TB

We always like to classify starting with the most common and in pediatrics, causes of prolonged lymphadenopathy goes:

1. Infectious
2. Autoimmune
3. Malignancies
4. Miscellaneous

Location

Localized -likely to be infectious

Generalized -more likely pathologic (e.g. malignancy, autoimmune, etc.) Or even infectious

Head and Neck -likely infectious

Mediastinal -likely pathologic Never overlook a mediastinal node as normal. Always investigate.

Abdominal -likely pathologic

Inguinal -likely infectious

Always examine the draining area

Associated symptoms-each may be associated with infectious, malignant, autoimmune, or immunodeficiency diseases:

- Pain
- Sore Throat
- URI
- Toothache
- Ear pain
- Fever
- Weight loss (> 10% over 6 months)
- Night sweats
- Pruritis Think of lymphoma
- Myalgia/arthralgia Autoimmune
- Rashes
- Malaise

Other history

- Pets - especially cats for Cat Scratch Disease
- Travel - including Tuberculosis exposure
  Which countries are a TB concern? Philippines, Indonesia and especially Ethiopia. It is thus important to ask about housemaids
- Possible immunodeficiency risk such as HIV
- Family history of similar problems
- Previous treatments (such as antibiotics and how patient responded)
- What are parents most worried about?

Physical Examination

Nodes

- Location -local, regional, generalized
- Size
- Character- e.g. firm,soft, etc. (may be subjective)
- Fixed or non-fixed
- Erythema and tenderness

We used to see this a lot 1–2 months after BCG vaccination, now they modified it and we no longer see this

Note:

- Generalized, firm, discrete, non-tender, fixed tend to be more ominous causes such as malignancy
- Localized, warm, tender, matted, erythematous -tend to be associated with infections

Preauricullar
- Lymph nodes of viral infections are usually soft

General
    Febrile or toxic appearing
Skin
    Cellulitis, impetigo, rash
HEENT
    Otitis, pharyngitis, teeth, and nasal cavity
Lungs
    Consolidations suggesting TB
Abdomen
    Hepatosplenomegaly

This is cat scratch disease, sometimes even the preauricular nodes get involved

Worrying Signs

- lymphadenopathy of more than 3 cm in size more than 4 weeks in duration
- supraclavicular, post. cervical involvement
- Skin tethering/ulceration
- Fixed nodes Why? Because it means the process is infiltrative, reaching the subcutaneous tissue or even skin
- Firm/rubbery consistency
- abnormal laboratory and radiological findings

Other Signs

Signs of anemia -tachycardia, pale conjunctiva -may be associated with malignancy, autoimmune diseases

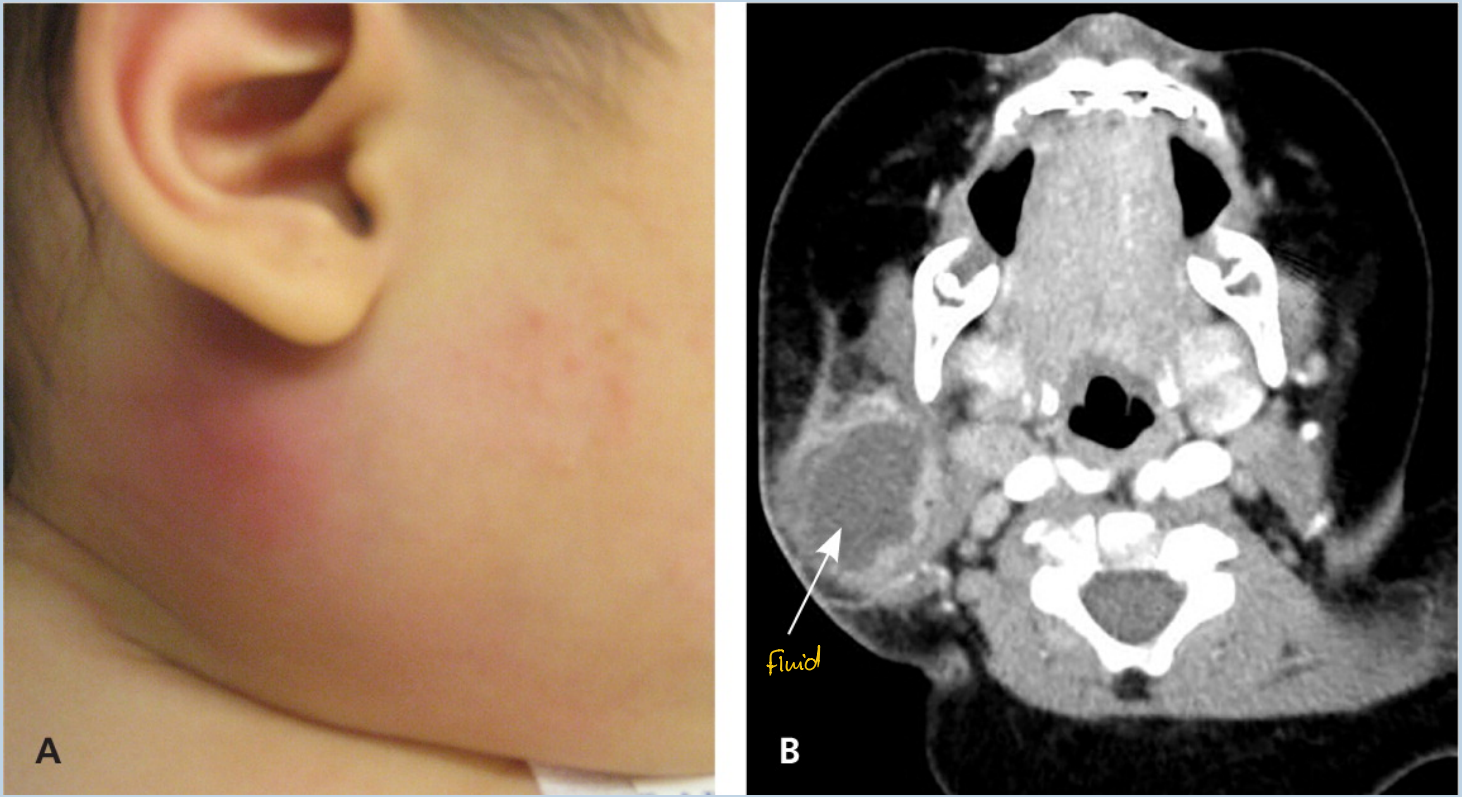
Dermatological changes -petechiae, bruising, bleeding -may be associated with malignancy

Weight/growth -poor growth may be associated with malignancy

Acute suppurative lymphadenitis

This is most likely submandibular, the surrounding area is diffusely swollen

You can see fluid in this CT scan, so this is acute suppurative lymphadenitis, we dont usually order a CT scan unless we're looking for something else. Ultrasound is enough, you can also feel for fluctuation. If you see fluid in US call surgery immediately. This is the most common cause of lymphadenopathy in pediatrics that we see



Acute suppurative lymphadenitis

- Suppurative cervical lymphadenitis, frequently caused by S. aureus or group A streptococcus, shows erythema and warmth of the overlying skin with moderate to exquisite tenderness.

Atypical mycobacteria

This is a more localized process, not surrounded by swelling or edema, in an older child. This is a case of atypical mycobacteria. It is not painful, occurs in older children (>5), no constitutional symptoms.

- The local reaction is circumscribed, and overlying skin may develop a violaceous discoloration without warmth. Fever and systemic symptoms are minimal or absent.
- The recommended treatment of cervical lymphadenitis caused by nontuberculous mycobacteria is complete surgical excision. Antimycobacterial drugs are necessary only if there is recurrence or inability to excise infected nodes completely, or if M. tuberculosis is identiied, which requires 6 months of antituberculous chemother- ap
- Mycobacterium species commonly causing lymphadenitis in children includes M. avium complex, M. scrofulaceum, and M. kansasii.

Facial Papule with Adenopathy

Cat scratch disease

This is another example of cat scratch disease, the scratch can be on hands, face or not visible.
Here you can see a papule an an enlarged draining cervical node.

- The cause of cat-scratch disease is B. henselae, a gram-negative bacillus that stains with War- thin-Starry silver stain. It is transmitted to humans by bites and scratches. B. henselae also causes bacillary angiomatosis and peliosis hepatis in persons with HIV infection.
- Cat-scratch disease typically presents with a cutaneous papule or conjunctival granuloma at the site of bacterial inoculation, followed by lymphadenopathy of the draining regional nodes. The nodes are tender, with suppuration in approximately 10% of cases.
- Cat-scratch disease usually does not require treatment because the lymphadenopathy resolves in 2 to 4 months without sequelae.
- Azithromycin may hasten resolution and reduces node size at 30 days but no benefit is evident at 90 days. Aspiration is indicated for suppurative nodes.

Mimickers of lymphadenopathy

- Thyroglossal duct cyst — Moves with tongue protrusion and is midline.
- Dermoid Cyst — Midline and often has calcifications on plain films.
- Branchial Cyst — Smooth and fluctuant along SCM border. Present with repeated pneumonias
- Hemangioma — Mass is presents after birth, rapidly grows, plateaus, and is red or bluish in color
- Cystic Hygroma — Transilluminates and is compressible Dilated lymphatics
- Sternocleidomastoid Tumor — Presents with torticollis, lymphadenopathy does not
  Not a true tumor, it is usually secondary to birth trauma to the sternocleidomastoid then the area gets fibrosed and presents as a lump
- Mumps — Mass palpated superior to jaw line, not just inferior to it.
  We frequently get ER calls for mums then we only find the swelling to be submandibular. In mumps you should feel it above the jawline

When to Investigate ?

Patients generally should be considered for investigation and/or referral if:

- Unexplained generalized lymphadenopathy
- Any palpable supraclavicular or popliteal node
- Significant constitutional symptoms
- Hepatic or splenic enlargement
- Anemia or bleeding
- Unresponsiveness to antibiotic treatment
- Not decreasing in size after appropriate period of observation

Laboratory Workup

- CBC with Differential — Looking for anemia and bone marrow involvement
- ESR/CRP — CRP is more specific, ESR is an acute phase reactant seen even in autoimmune processes, whereas CRP is more specific to bacterial infection
- Throat swab
- Serology
  - EBV
  - Bartonella — Cat scratch disease
  - CMV
  - Toxoplasmosis
- PPD (Mantoux test)
- Malignancy
  - LDH
  - Uric acid
- LFT — In the case of hepatosplenomegaly, changes in LFTs are seen with CMV and EBV but only in hundreds, unlike the thousands seen with viral hepatitis

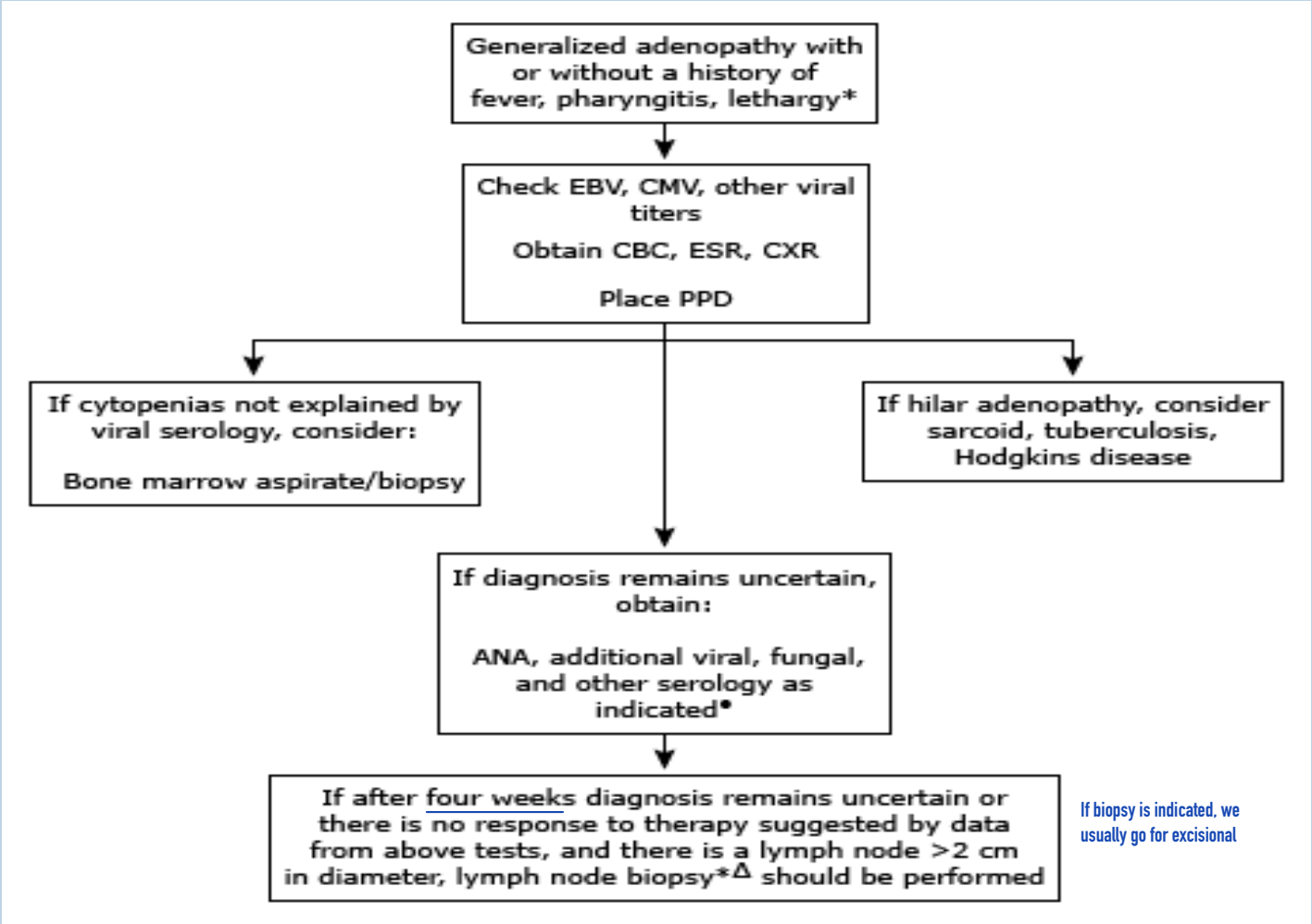
Imaging Workup

- CXR Hilar lymphadenopathy is diagnosed by either X ray or CT, we start with CXR
  - To look for mediastinal lymphadenopathy
- Ultrasound
  - To evaluate for or follow progress of an abscess
  - To assess the consistency
- CT- scan Other lymphadenopathy
- Biopsy
  - FNA or Excisional
  - Early biopsy is indicated in children with supraclavicular, mediastinal, or massively enlarged nodes or groups of nodes >3 cm.

Table 3. Indications for Ordering Clinical Laboratory or Imaging Studies in the Workup of a Child with a Neck Mass

Test	*Indication*
Bartonella henselae titers	Recent exposure to cats
Complete blood count	Serious systemic disease suspected (e.g., leukemia, mononucleosis)
Computed tomography	Imaging study for retropharyngeal or deep neck abscess, or suspected malignancy
Magnetic resonance imaging	Preferred if vascular malformation is suspected
Purified protein derivative (PPD) test for tuberculosis	Exposure to tuberculosis, young child in rural community (atypical tuberculosis)
Ultrasonography	Recommended initial imaging study for a developmental mass, palpable mass, or suspected thyroid problem
Viral titers (cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, toxoplasmosis)	If history suggests exposure or a suspected inflammatory mass is not responding to antibiotics

Suggested approach to generalized adenopathy in children



If biopsy is indicated, we usually go for excisional


CM
1
2
3
4
5
6
7

EXTRA

Acute cervical lymphadenitis

- Acute cervical lymphadenitis as a complication of group A streptococcal infection parallels the incidence of streptococcal pharyngitis
- Empirical treatment targeting S. aureus and group A streptococcus includes a penicillinase-resistant penicillin (e.g., oxacillin) or first-generation cephalosporin (e.g., cefazolin). For patients with hypersensitivity to β-lactam antibiotics, or if community-acquired methicillin resistant S. aureus is suspected, clindamycin is appropriate.

Infectious mononucleosis

- Infectious mononucleosis is characterized by lymphocytosis with atypical lymphocytes; thrombocytopenia and elevated hepatic enzymes are common.
- The most reliable test for diagnosis of acute EBV infection is the IgM antiviral capsid antigen. Heterophil antibody is also diagnostic but is not reliably positive in children younger than 4 years with infectious mononucleosis.
- There is no specific treatment for infectious mononucleosis
- Infectious mononucleosis usually resolves in 2 to 4 weeks, but fatigue and malaise may wax and wane for several weeks to months.
- Corticosteroids have been used for respiratory compromise resulting from tonsillar hypertrophy, which responds rapidly, and for thrombocytopenia, hemolytic anemia, and neurologic complications.

Case #1

A 2- year- old boy brought to the clinic with fever and ® sided neck swelling for 3 days.

What are the likely etiologies? Acute unilateral, most likely infectious. Could be viral or bacterial.
What points in history will be suggestive of each etiology?
What points in physical examination relevant to each possible etiology?
What are the appropriate investigations helpful in reaching a diagnosis?

Case #2

An 8 – year – old patient with left cervical lymphadenopathy for the past 4 weeks.

Subacute, older child, you'll need to obtain a full Hx

What are the likely etiologies? (mention at least 3)
What points in history will be suggestive of each etiology?
What points in physical examination relevant to each possible etiology?
What are the appropriate investigations helpful in reaching a diagnosis?

Case #3

10 years old girl presented with history of fever, pallor , cervical and axillary lymphadenopathy for the past 8 weeks.

What are the likely etiologies? (mention at least 3)
What points in history will be suggestive of each etiology?
What points in physical examination relevant to each possible etiology?
What are the appropriate investigations helpful in reaching a diagnosis?

Again always go by the most common

1. Infection (chronic like brucellosis)
2. Autoimmune
3. Malignancy