Approach to lymphadenopathy with/without hepatosplenomegaly

By:

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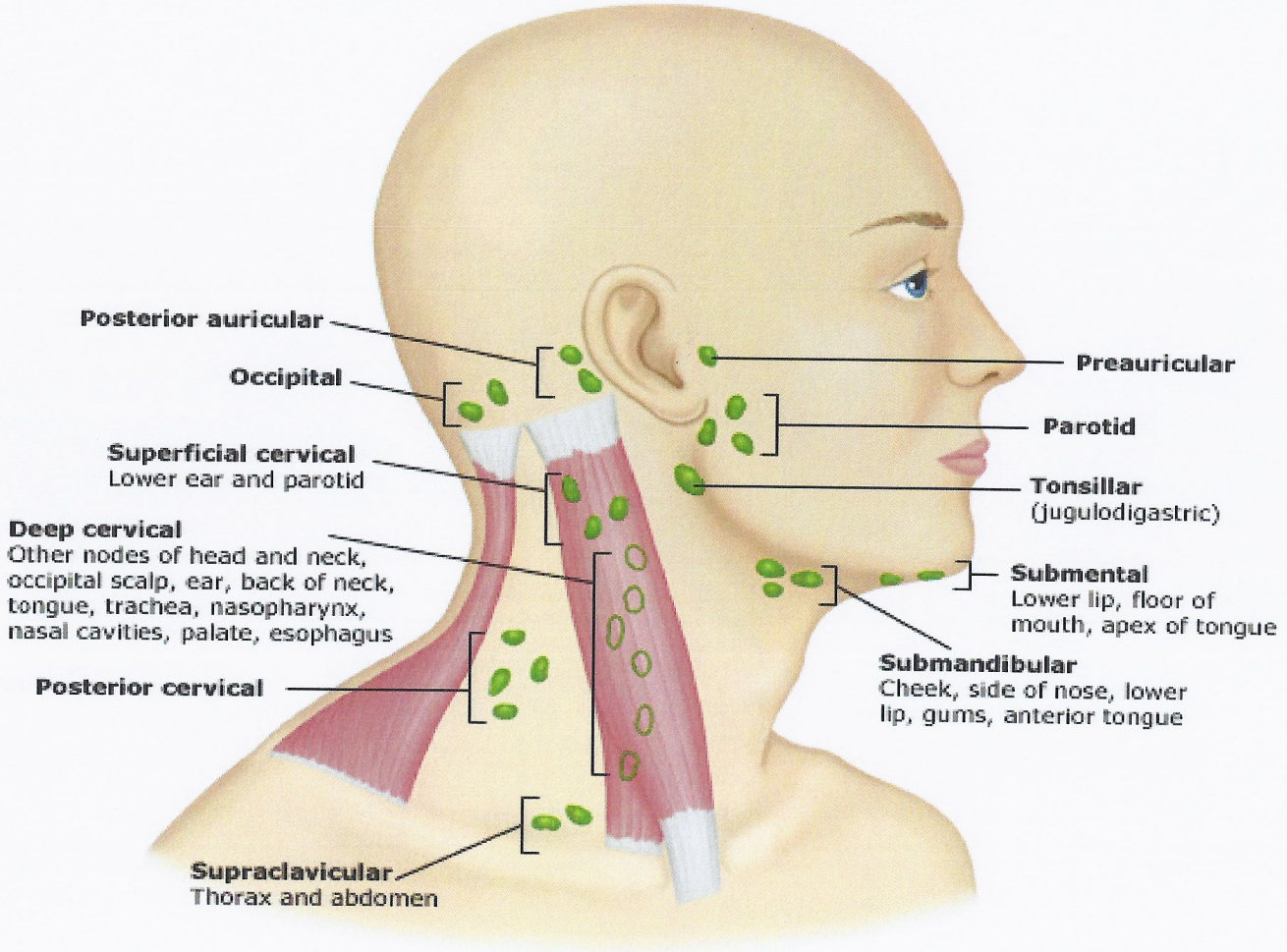
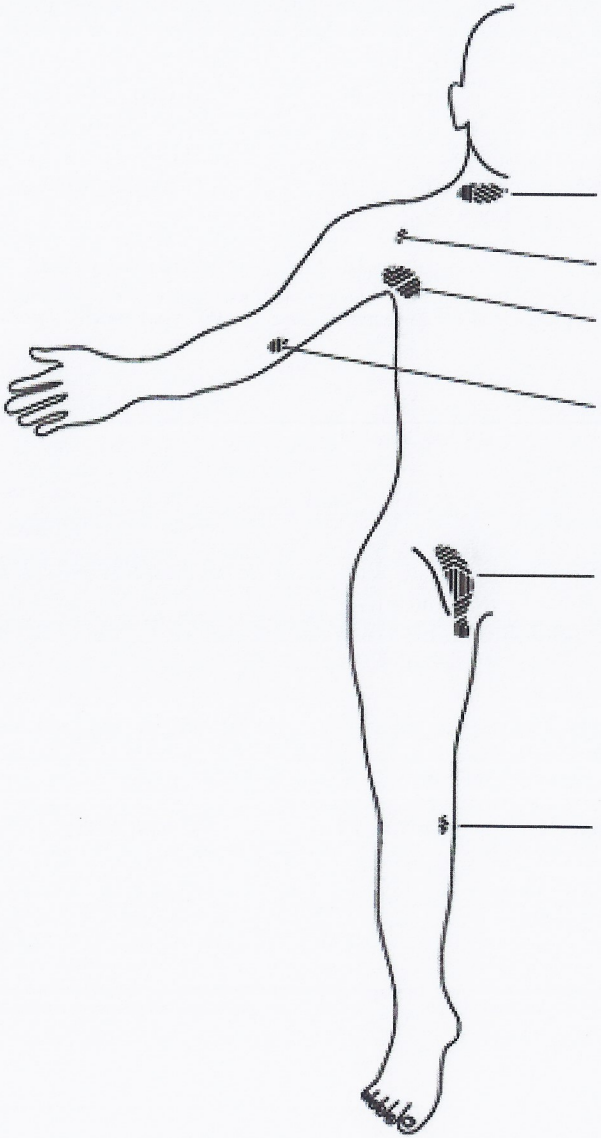
LN Head and neck



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

- 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

Cause	Examples
Infections	
Bacterial	
Localized	Streptococcal pharyngitis; skin infections; tularemia; cat scratch disease; diphtheria;
Generalized	Brucellosis; leptospirosis; typhoid fever.
Viral	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	SLE, JRA, serum sickness
Drugs	phenytoin, Hydralazine, Allopurinol, Pyrimethamine, Isoniazide
Miscellaneous	Sarcoidosis; lipid storage diseases; amyloidosis; histiocytosis; chronic granulomatous diseases

Infectious causes of cervical lymphadenitis in children

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	*Staphylococcus aureus* Group A streptococcus Anaerobic bacteria	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.

Causes of localized lymphadenopathy in children

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.

Location

- Localized -likely to be infectious
- Generalized -more likely pathologic (e.g. malignancy, autoimmune, etc.)
- Head and Neck -likely infectious
- Mediastinal -likely pathologic
- Abdominal -likely pathologic
- Inguinal -likely infectious

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
- Myalgia/arthralgia
- Rashes
- Malaise

Other history

- Pets - especially cats for Cat Scratch Disease
- Travel - including Tuberculosis exposure
- Possible immunodeficiency risk such as HIV
- Family history of similar problems
- Previous treatments (such as antibiotics and how patient responded)
- What do parents think might be going on? What are parents most worried about?

Physical Examination

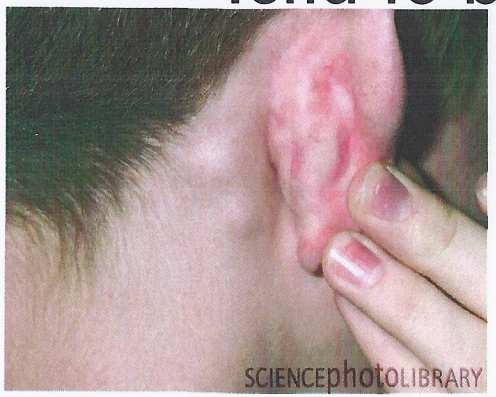
Nodes

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

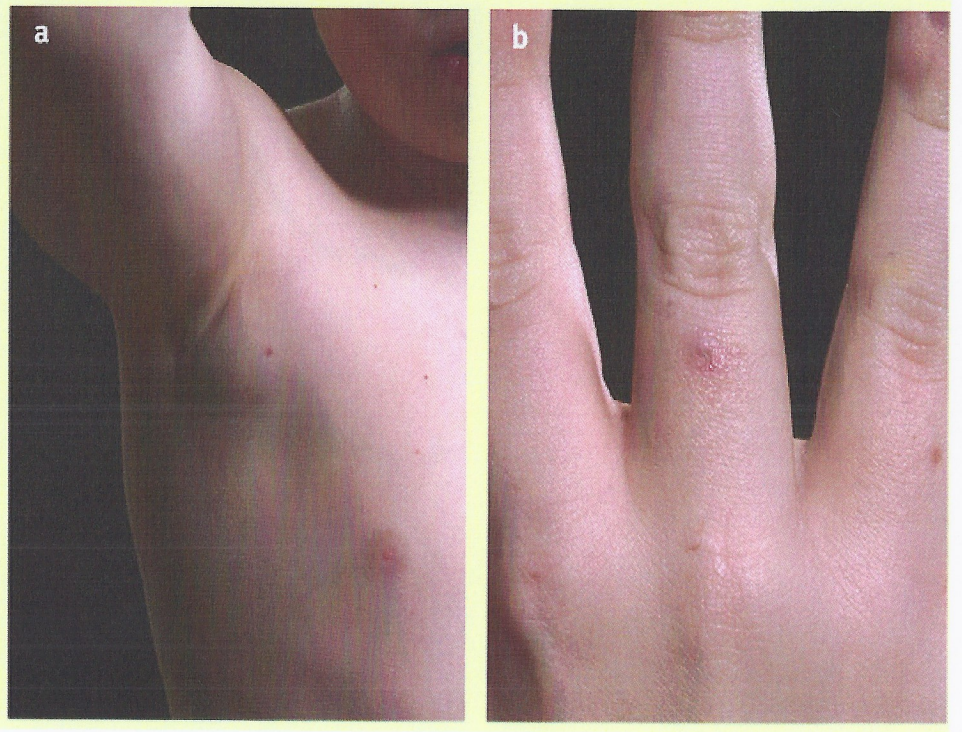
Note:

- 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



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

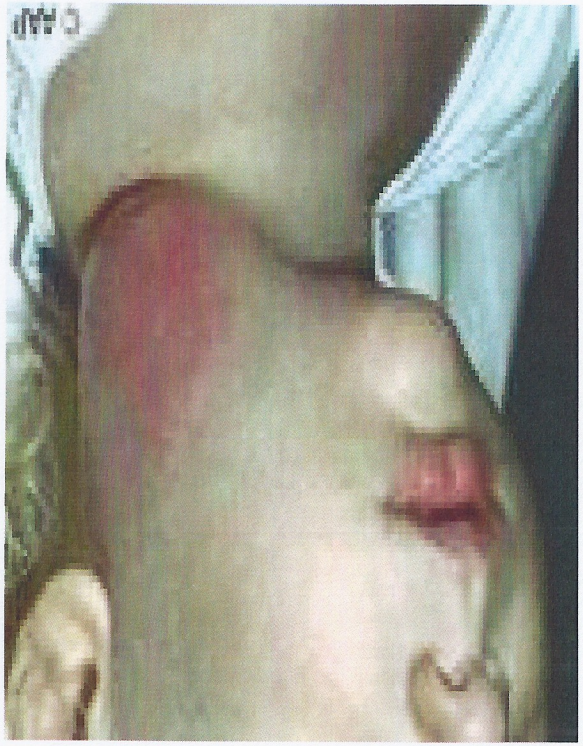


Worrying Signs

- lymphadenopathy of more than 3 cm in size
- more than 4 weeks in duration
- supraclavicular, post. cervical involvement
- Skin tethering/ulceration
- Fixed nodes
- 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



Facial Papule with Adenopathy

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.
Hemangioma	Mass is presents after birth, rapidly grows, plateaus, and is red or bluish in color
Cystic Hygroma	Transilluminates and is compressible
Sternocleidomastoid Tumor	Presents with torticollis, lymphadenopathy does not
Mumps	Mass palpated superior to jaw line, not just inferior to it.

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
- ESR/CRP
- Throat swab
- Serology
  - EBV
  - Bartonella
  - CMV
  - Toxoplasmosis
- PPD (Mantoux test)
- LDH
- Uric acid
- LFT

Imaging Workup

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

Suggested approach to generalized adenopathy in children