Approach to lymphadenopathy in children
Components of the Lymphatic System

- **Lymph**
- **Lymphatic Vessels**
  - Lymphatic Capillaries
  - Lymphatic Vessels
  - Lymphatic Trunks
  - Lymphatic Ducts
- **Lymphatic Organs**
  - Thymus
  - **Lymph Nodes**
  - Spleen
  - Tonsils
- **Lymphatic cells**
Components of the Lymphatic System

- **Lymph**: a fluid similar to plasma—does not have plasma proteins
- **Lymphatic vessels**: network that carries lymph from peripheral tissues to the venous system
- **Lymphatic cells**: Lymphocytes, phagocytes, and other immune system cells
- **Lymphoid tissues and lymphoid organs**: found throughout the body
Function of the Lymphatic System

- **Reabsorbs excess interstitial fluid:**
  - returns it to the venous circulation
  - maintain blood volume levels

- **Absorption & transport of fatty acids and fats**
  - drain into larger lymphatic vessels
  - eventually into the bloodstream.

- **Lymphocyte development, and the immune response.**
Lymph nodes

Lymph nodes are

- bean shaped organs
- found in clusters.
- over 800 lymph nodes
- 300 are located in the head and neck
Lymphadenopathy

- refers to enlargement of the lymph nodes.

- Lymphadenitis refers to enlarged lymph nodes that are inflamed
Lymphadenopathy

- is common

- is an early indicator of some diseases.

- Early recognition of disease improves prognosis for recovery.
Lymphadenopathy

- **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
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*
Lymph nodes of the head and neck

- Posterior auricular
- Occipital
- Superficial cervical
  - Lower ear and parotid
- Deep cervical
  - Other nodes of head and neck, occipital scalp, ear, back of neck, tongue, trachea, nasopharynx, nasal cavities, palate, esophagus
- Posterior cervical
- Supraclavicular
  - Thorax and abdomen
- Preauricular
- Parotid
- Tonsillar (jugulodigastric)
- Submental
  - Lower lip, floor of mouth, apex of tongue
- Submandibular
  - Cheek, side of nose, lower lip, gums, anterior tongue
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
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
Lymphadenopathy

- **Localized**: Only one area is involved
- **Generalized**: 2 or more noncontiguous areas are involved
Lymphadenopathy

* Generalized lymphadenopathy (enlargement of >2 noncontiguous node regions) is caused by **systemic disease**

* Regional lymphadenopathy is most frequently the result of **infection** in the involved node and/or its drainage area
Lymphadenopathy

- Distinguishing between localized and generalized LAP is important.

- In primary care patients with unexplained LAP
  
  75% localized lymphadenopathy
  25% generalized lymphadenopathy.
Presentation of lymphadenopathy

- Unexplained lymphadenopathy
  - 3/4 presents with localized
  - 1/4 present with generalized
INITIAL EVALUATION

History

1. lymph node enlargement
2. associated symptoms (local and systemic)
3. potential exposures
4. past medical history
associated symptoms

- **Local symptoms of infection**
  - Cough: pneumonia (bacterial, viral, fungal)
  - Sore throat: GAS, adenovirus, diphtheria
  - Skin lesions Staphylococcus aureus, HSV, cat scratch disease

- **Constitutional symptoms**
  - May indicate malignancy, *Mycobacterium tuberculosis*, rheumatologic disease
Exposures

- Ill contacts
- Viral respiratory infections, CMV, EBV, GAS
- Unpasteurized animal milk
- Brucellosis
- Undercooked meats
- Toxoplasmosis
- Animals
- Cat scratch disease
- Travel
- Sexual activity
- Sexually transmitted infections; hepatitis B infection
Past medical history

Medication history

1. allopurinol
2. atenolol
3. captopril
4. carbamazepine
5. cephalosporins
6. gold
7. hydralazine
8. penicillin
9. phenytoin
10. sulfonamides
Past medical history

- recurrent infections, skin abscesses, suppurative adenitis
- Chronic granulomatous disease

- Autoimmune disease
  - Autoimmune lymphoproliferative syndrome

- Immunization status
  - Diphtheria, measles, rubella
Physical examination

- General examination
- Systemic examination
- Lymph nodes
Physical examination

General examination

- **Vital signs**
  - Weight loss of >10 percent of body weight may be indicative of malignancy.
  - Fever indicative of infection.

- **Head, eyes, ears, nose, throat**
  - Conjunctival injection – Kawasaki disease

- **Oropharynx** – Dental problems, pharyngitis, herpangina
Systemic examination

Chest and CVS

Abdomen

- Hepatosplenomegaly

Skin

- Localized lesions (cat scratch disease)
- Generalized rash (viral illness)
Lymph nodes

Remember:

- Normal lymph nodes are not palpable
- Examine the draining lymph nodes area of any lesion
- Examine the area drained by affected lymph nodes
Lymph nodes

- An examination of the lymph nodes forms part of the routine for most body systems.

- No need to percuss or auscultate, examination involves inspection followed by palpation
Lymph nodes

The following groups of lymph nodes are to be examined:

1- Cervical groups
2- Axillary groups
3- Inguinal groups
4- Epitrochlear lymph nodes.
5- Remember that the liver and spleen are parts of the lymphoid tissue
Lymph nodes

- **SSSSS (5S):**
  
  1- Site.
  2- Shape.
  3- Size.
  4- Surface: Smooth, nodular, irregular.
  5- Skin overlying the swelling
Lymph nodes

Confirm your inspection

- Size
- Temperature
- Tenderness
- Consistency
- Mobility
- Draining area
Lymph nodes Location

Localized lymphadenopathy

✓ present in only one region generally suggests local causes
✓ search for pathology in the area of node drainage

Generalized adenopathy

✓ present in two or more noncontiguous regions
✓ usually is a manifestation of systemic disease
Lymph nodes Size

- normal lymph nodes are <1 cm in diameter.

- epitrochlear region usually are less than 0.5 cm in diameter.

- normal lymph nodes in the inguinal region usually are less than 1.5 cm in diameter.

- The risk of malignancy is increased in lymph nodes >2 cm in diameter.
Consistency

- Fluctuance usually indicates infection usually S. aureus or group A Streptococcus
- Hard nodes generally are due to cancer or previous inflammation.
- Firm, rubbery nodes may indicate lymphoma or chronic leukemia
- Matting
A group of lymph nodes that feel connected and move as a unit is said to be matted.

**Nodes that are matted could be**

- Malignant
  - Metastatic carcinoma
  - Lymphomas
- Benign
  - Tuberculosis
  - Sarcoidosis
Fixation

- Normal lymph nodes are freely movable
- Fixed to adjacent tissues (e.g., deep fascia)
  - Invading cancers
  - Inflammation in tissue surrounding the nodes.
Tenderness

- Indication of rapid increase in size: stretch of capsular shell
- NOT useful in determining benign vs malignant state
- Inflammation, suppuration, hemorrhage
GENERAL PRINCIPLES

- Urgency and extent of evaluation
- Step-wise approach
- Worrisome features
- glucocorticoids
Urgency and extent of evaluation

- generally is benign and self-limited.
- It is not necessary to identify the underlying etiology in every patient.
- is determined by how ill the patient appears.
- the lymphadenopathy resolves without explanation before invasive diagnostic testing is undertaken.
- the evaluation of LAP in children occurs in stages over approximately four weeks.
Step-wise approach

- **The first stage**
  treat conditions that appear obvious based upon the history and examination eg, throat culture for group A streptococcal pharyngitis.

- **the second stage**
  provide a two-week trial of antibiotic therapy or a two- to three week period of observation.
Step-wise approach

- If the cause remains uncertain, less common causes and causes that require specific treatment (e.g., tuberculosis) are evaluated.

- After four weeks, the diagnosis remains uncertain and the lymph node has not regressed in size, biopsy may be warranted.
Worrisome features

- **Systemic symptoms**
  - fever >1 week
  - night sweats
  - weight loss [>10 percent of body weight]

- **Supraclavicular nodes**
- **Fixed, nontender nodes**
- **Lymph nodes >2 cm in diameter that have increased in size**
Worrisome features

- Abnormal chest radiograph particularly mediastinal mass or hilar adenopathy

- Abnormal CBC and differential lymphoblasts, cytopenias in more than one cell line

- Persistently elevated ESR/CRP rising ESR/CRP despite antibiotic therapy
**glucocorticoids**

- must be avoided before a definitive diagnosis is established.
- mask or delay the histologic diagnosis of leukemia
- may exacerbate an infectious disease.
Generalized lymphadenopathy

differential diagnosis
Generalized

- Inflammation
  - Infective
  - Autoimmune
  - Primary
  - Secondary

- Malignancy
- Metabolic
- Drug reaction
- Miscellaneous
Infectious

- 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
- Serum sickness

Malignant: leukemia, lymphoma, neuroblastoma

Metabolic Storage diseases: Neimenn-Pick disease, Gaucher disease

Drug reaction: phenytoin, allopurinol

Miscellaneous Sarcoidosis  Hemophagocytic lymphohistiocytosis  Hyperthyroidism
Initial tests

generalized lymphadenopathy

- CBCD, ESR, and CRP
- Serology for CMV and EBV
- Tuberculin skin testing (TST)
- Chest radiograph (CXR)
- Serology for other viral illnesses as warranted by the history and examination
Initial tests

generalized LAP in whom the diagnosis remains uncertain after the initial evaluation, Serologic testing for

- B. henselae, toxoplasmosis, histoplasmosis, brucellosis, syphilis, (HIV)
- Antinuclear antibody as a screen for vasculitis syndromes (eg, SLE, rheumatoid arthritis)
Indications for biopsy

a biopsy of the most abnormal node within four weeks if:

- Any lymph nodes increase in size
- There is a lymph node $\geq 2$ cm in diameter and either of the following:
  - The diagnosis remains uncertain after four weeks
  - There is no response to therapy
Approach to Lymphadenopathy

Reassure Family

Lymphadenopathy

Yes

Significant Physical Signs or Symptoms?

e.g. Weight loss, Hepatosplenomegaly ...

No

Observe : 2-3 Weeks

Node(s) Resolving

Observe & Follow

Node(s) : Increase in size

Not Resolving

Investigate : (CBC, ESR ...)

Yes

Observe : 2-3 Weeks

Node(s) Resolving
Localized adenopathy

The causes of localized adenopathy vary with the lymph node region
Localized adenopathy

- benign clinical history
- an unremarkable physical examination
- no constitutional symptoms

should be reexamined in three to four weeks
Localized adenopathy

- constitutional symptoms or signs
- risk factors for malignancy
- lymphadenopathy that persists for three to four weeks should undergo a biopsy.
Cervical lymphadenopathy

DEFINITIONS

- Cervical lymphadenopathy – Enlarged lymph node(s) of the neck, including preauricular, parotid,

- Acute lymphadenitis – Develops over a few days

- Subacute/chronic lymphadenitis – Develops over weeks to months.
<table>
<thead>
<tr>
<th>Acute unilateral cervical lymphadenitis</th>
<th>Subacute/chronic unilateral lymphadenitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute bilateral cervical lymphadenitis</td>
<td>Subacute/chronic bilateral lymphadenitis</td>
</tr>
</tbody>
</table>
# Infectious causes of cervical lymphadenitis in children

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
</tr>
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<tbody>
<tr>
<td>Acute bilateral</td>
<td>Rhinovirus</td>
<td>Roseola</td>
<td>Corynebacterium diphtheriae</td>
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<tr>
<td></td>
<td>Epstein-Barr virus*</td>
<td>Parvovirus B19*</td>
<td>Rubella*</td>
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<tr>
<td></td>
<td>Cytomegalovirus*</td>
<td></td>
<td>Measles*</td>
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<tr>
<td></td>
<td>Herpes simplex virus</td>
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<td>Mumps*</td>
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<tr>
<td></td>
<td>Adenovirus</td>
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<tr>
<td></td>
<td>Enterovirus</td>
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<tr>
<td></td>
<td>Mycoplasma pneumoniae</td>
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<tr>
<td></td>
<td>Group A Streptococcus</td>
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<tr>
<td></td>
<td>Arcanobacterium haemolyticum</td>
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<td></td>
<td>Influenza</td>
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<tr>
<td>Acute unilateral</td>
<td>Staphylococcus aureus</td>
<td>Group B</td>
<td>Yersinia enterocolitica*</td>
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<tr>
<td></td>
<td>Group A Streptococcus</td>
<td>Streptococcus</td>
<td>Anthrax*</td>
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<tr>
<td></td>
<td>Anaerobic bacteria</td>
<td>Tularemia*</td>
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<td></td>
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<td>Alpha streptococcus</td>
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<tr>
<td></td>
<td></td>
<td>Pasteurella multocida</td>
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<tr>
<td></td>
<td></td>
<td>Yersinia pestis*</td>
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<tr>
<td></td>
<td></td>
<td>Gram-negative bacilli</td>
<td></td>
</tr>
<tr>
<td>Chronic unilateral</td>
<td>Nontuberculous mycobacteria</td>
<td>Toxoplasmosis*</td>
<td>Nocardia brasiliensis</td>
</tr>
<tr>
<td></td>
<td>Cat scratch disease</td>
<td>Tuberculosis*</td>
<td>Aspergillosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actinomycosis</td>
<td>Sporotrichosis</td>
</tr>
<tr>
<td>Chronic bilateral</td>
<td>Epstein-Barr virus*</td>
<td>HIV</td>
<td>Brucellosis*</td>
</tr>
<tr>
<td></td>
<td>Cytomegalovirus*</td>
<td>Toxoplasmosis*</td>
<td>Histoplasmosis*</td>
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<tr>
<td></td>
<td></td>
<td>Tuberculosis*</td>
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<tr>
<td></td>
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<td>Syphilis*</td>
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</tbody>
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Acute bilateral cervical lymphadenitis

Caused by self-limited viral upper respiratory infection

- enterovirus
- adenovirus
- influenza virus

The LN(reactive LN) typically are
- small, rubbery
- mobile, discrete
- minimally tender
- No erythema or warmth
Acute unilateral cervical lymphadenitis

is usually caused by bacteria

- S. Aureus
- GAS
S. aureus and GAS

- occur in children younger than 5 years of age
- history of a recent URI or impetigo
- Submandibular nodes are affected in more than 50%
- The lymph node usually is
  - 3 to 6 cm in diameter
  - tender
  - warm
  - erythematous
  - poorly mobile
- One-fourth to one-third of infected nodes suppurate and become fluctuant
Subacute/chronic bilateral cervical lymphadenitis

- Most often caused by EBV or CMV infection
- EBV causes infectious mononucleosis
  - manifest as
    - Fever,
    - exudative pharyngitis
    - lymphadenopathy
    - hepatosplenomegaly
Subacute/chronic unilateral cervical lymphadenitis

- Nontuberculous mycobacteria (NTM) infections
- Bartonella henselae-cat scratch disease (CSD)
- TB
- Toxoplasmosis
Axillary lymphadenopathy

- Local infection
- Cat scratch disease
- Brucellosis
- Reactions to immunizations
- Non Hodgkin lymphoma
- Juvenile rheumatoid arthritis
Inguinal lymphadenopathy

- Local infection
- Diaper dermatitis
- Syphilis
- Genital herpes
## Localized lymphadenopathy

<table>
<thead>
<tr>
<th>Location</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submaxillary and submental</td>
<td>• Oral and dental infections&lt;br&gt;• Acute lymphadenitis</td>
</tr>
<tr>
<td>Occipital</td>
<td>• Pediculosis capitis (lice)&lt;br&gt;• Tinea capitis/local skin infection&lt;br&gt;• Rubella&lt;br&gt;• Roseola</td>
</tr>
<tr>
<td>Preauricular (rarely palpable in children)</td>
<td>• Local skin infection&lt;br&gt;• Chronic ophthalmic infection</td>
</tr>
</tbody>
</table>
Investigations

- Complete blood count  CRP, ESR
- R/o infectious causes:  CMV, EBV
toxoplasma, Bartonella titres
TB skin test, HIV test
- Hepatic and renal profile + urinalysis (systemic disorders that can cause lymphadenopathy)
- Lactate dehydrogenase, uric acid, calcium, phosphate, magnesium if malignancy suspected
DIAGNOSTIC TESTS

CBCD

- Cytopenias in more than one cell line – Leukemia
- Isolated leukopenia or neutropenia – Viral infection
- Leukocytosis with left shift – Bacterial infection
- Atypical lymphocytes – EBV, CMV
- Eosinophilia – Parasitic infection
- Anemia – SLE, M. tuberculosis
- Thrombocytosis – Kawasaki disease
DIAGNOSTIC TESTS

ESR and CRP

- acute phase reactants
- a nonspecific marker of inflammation
- Persistent or increasing elevation may warrant biopsy
DIAGNOSTIC TESTS

- **Tuberculin skin test**
  TST is indicated to screen for *M. tuberculosis* infection.

- **Chest radiograph**
  (CXR)s in children with peripheral LAP are made on a case-by-case basis.
DIAGNOSTIC TESTS

generally obtain chest radiographs in children with:

- Generalized LAP at the time of presentation
- Supraclavicular LAP at the time of presentation
- Cervical or inguinal adenopathy ≥2 cm in diameter who do not have signs or symptoms of infection
DIAGNOSTIC TESTS

Ultrasonography

- the lymph node may be helpful in the presence and extent of an abscess

- Abdominal ultrasonography may be warranted in children with unexplained inguinal adenopathy
Lymph node biopsy

Lymph node cultures material may be obtained via

- excisional biopsy
- needle aspiration
- incision and drainage

Abscess fluid should be sent for

1. Gram stain
2. Bacterial culture (aerobic and anaerobic), mycobacterial stain and culture
3. Fungal stain and culture.
Lymph node biopsy

- indicated in patients with worrisome features
- prefer open biopsy to fine needle aspiration
- Largest node
- Avoid inguinal & axillary
- Supra clavicular-highest diagnostic yield
Management

- Treat the underlying cause.

- If no specific cause – Antibiotic (10 day course), if still persist- give another course of other antibiotic

- anti-TB

- Chemotherapy- for malignancy

- Incision & drainage – nodes with suppuration
Acute bilateral LN

- self-limited viral illness.
Acute unilateral LN

- well-appearing children: monitoring it over time
- children with moderate symptoms: oral antimicrobial therapy is recommended
- children with severe symptoms: parenteral antimicrobial therapy after incision and drainage of the inflamed node is recommended
Initial regimen

- generally provide initial empiric coverage for group A Streptococcus and S. aureus.
- The antibiotic choice is influenced by the prevalence of (CA-MRSA):
  - High CA-MRSA prevalence ➔ **Clindamycin**
  - Low CA-MRSA prevalence ➔ **cephalexin** or **amoxicillin-clavulanate**
  - exposure to cats ➔ **azithromycin**.
Infectious Mononucleosis (Glandular Fever)

Caused by Epstein Barr Virus

Signs/Symptoms
1. Prolong fever
2. Exudative pharyngitis
3. Painless generalized lymphadenopathy
4. Splenomegaly

Diagnosis
50% lymphocytosis with >10% Atypical lymphocytes on peripheral
Positive monospot test (Paul Bunnell test)
Serum heterophile Antibody definitive (positive at 2-6 weeks)

Complication: splenic rupture, respiratory obstruction, encephalitis

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% patients.
Mononucleosis

Whitish coating on the tonsils

Visual Photophobia

Swelling lymph nodes

Respiratory Cough

Gastric Nausea

Spleen Enlarged

Atypical white blood cell

Systemic:
- Chills
- Fever
- Aches
- Headache
Kawasaki Disease

- Five Characteristics of Disease
  - Fever >5 days
  - Cervical lymphadenopathy (usually unilateral)
  - Erythema and edema of palms and soles with desquamation of skin
  - Nonpurulent Bilateral Conjunctivitis
  - Strawberry Tongue

- Complications
  - Coronary artery aneurysms
  - Coronary artery thromboses
  - Myocardial infarction

- Treatment
  - IVIG and Aspirin
Kawasaki Disease

Signs & Symptoms of Kawasaki Disease