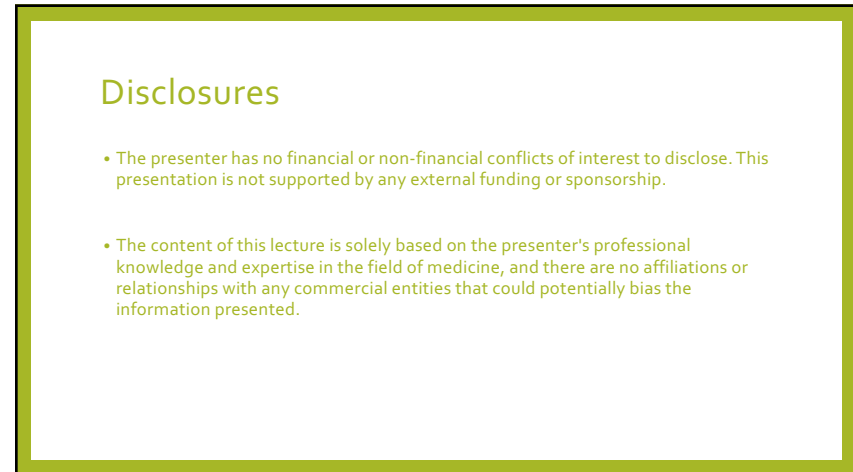
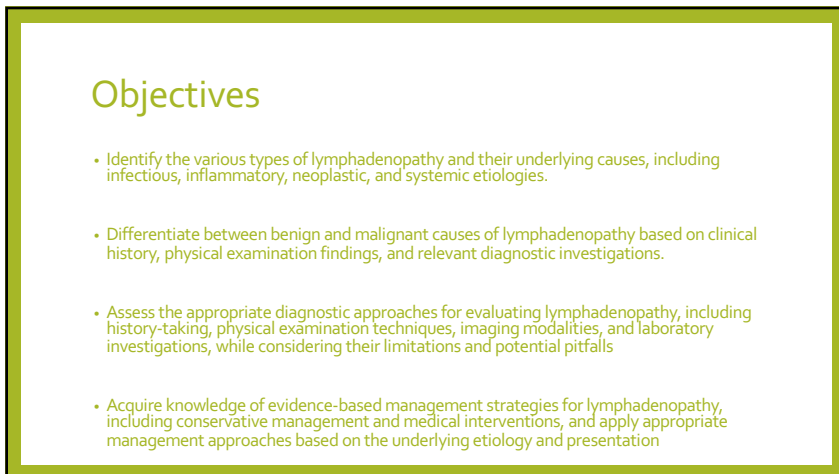


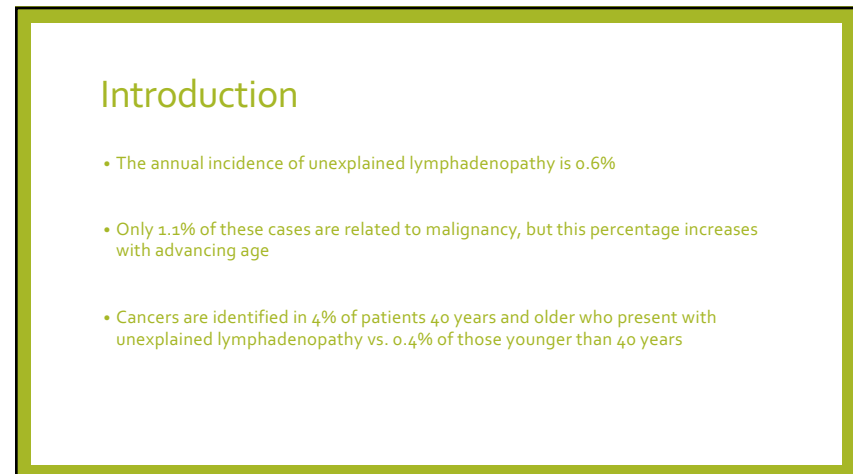
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4

Etiologies

- In most cases, the history and physical examination alone identify the cause

5

Etiologies

- In most cases, the history and physical examination alone identify the cause
- Etiologies of lymphadenopathy can be remembered with the MIAMI mnemonic:
 - Malignancies
 - Infections
 - Autoimmune disorders
 - Miscellaneous and unusual conditions
 - Iatrogenic causes

Table 1. MIAMI Mnemonic for Differential Diagnosis of Lymphadenopathy

Malignancies
Kaposi sarcoma, leukemias, lymphomas, metastases, skin neoplasms
Infections
Bacterial: brucellosis, cat-scratch disease (<i>Bartonella</i>), chancroid, cutaneous infections (staphylococcal or streptococcal), lymphogranuloma venereum, primary and secondary syphilis, tuberculosis, tularemia, typhoid fever
Granulomatous: berylliosis, coccidioidomycosis, cryptococcosis, histoplasmosis, silicosis
Viral: adenovirus, cytomegalovirus, hepatitis, herpes zoster, human immunodeficiency virus, infectious mononucleosis (Epstein-Barr virus), rubella
Other: fungal, helminthic, Lyme disease, rickettsial, scrub typhus, toxoplasmosis
Autoimmune disorders
Dermatomyositis, rheumatoid arthritis, Sjögren syndrome, Still disease, systemic lupus erythematosus
Miscellaneous/unusual conditions
Angiofollicular lymph node hyperplasia (Castleman disease), histiocytosis, Kawasaki disease, Kikuchi lymphadenitis, Kimura disease, sarcoidosis
Iatrogenic causes
Medications, serum sickness
<small>Information from references 2 and 3.</small>

6

History

- Factors that can assist in identifying the etiology of lymphadenopathy include:
 - Patient age
 - Duration of lymphadenopathy
 - Exposures
 - Associated symptoms
 - Location (localized vs. generalized)
 - B symptoms
- Other historical questions include asking:
 - Time course of enlargement, tenderness to palpation, recent infections, recent immunizations, and medications

7

History

- Fever, night sweats, weight loss, or node located in supraclavicular, popliteal, or iliac region, bruising, splenomegaly
 - Leukemia, lymphoma, solid tumor metastasis
- Fever, chills, malaise, sore throat, nausea, vomiting, diarrhea; no other red flag symptoms
 - Bacterial or viral pharyngitis, hepatitis, influenza, mononucleosis, tuberculosis (if exposed), rubella
- High-risk sexual behavior
 - Chancroid, HIV infection, lymphogranuloma venereum, syphilis

8

History

- Cat exposure
 - Cat-scratch disease (Bartonella), Toxoplasmosis
- Rabbits, or sheep or cattle wool, hair, or hides
 - Anthrax, Brucellosis, Tularemia
- Undercooked meat
 - Anthrax, Brucellosis, Toxoplasmosis
- Arthralgias, rash, joint stiffness, fever, chills, muscle weakness
 - Rheumatoid arthritis, Sjögren syndrome, dermatomyositis, systemic lupus erythematosus

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History – Age and Duration of Symptoms

- About one-half of otherwise healthy children have palpable lymph nodes at any one time
- Most lymphadenopathy in children is benign or infectious in etiology
- In adults and children, lymphadenopathy lasting less than two weeks or greater than 12 months without change in size has a low likelihood of being neoplastic.
- Exceptions include low-grade Hodgkin lymphomas and indolent non- Hodgkin lymphoma, although both typically have associated systemic symptoms

10

History – Exposures

- Environmental, travel-related, animal, and insect exposures should be questioned in your history taking
- Chronic medication use, infectious exposures, immunization status, and recent immunizations should be reviewed as well
- Tobacco and alcohol use and ultraviolet radiation exposure increase concerns for neoplasm
- An occupational history that includes mining, masonry, and metal work may elicit work-related etiologies of lymphadenopathy, such as silicon or beryllium exposure
- Asking about sexual history to assess exposure to genital sores or participation in oral intercourse is important, especially for inguinal and cervical lymphadenopathy
- Which Rx's can lead to lymphadenopathy?

11

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- Which Rx's can lead to lymphadenopathy?
 - Allopurinol, Atenolol, Captopril, Carbamazepine, Gold, Hydralazine, Penicillin, Phenytoin, Primidone, Pyrimethamine, Quinidine, Trimethoprim/Sulfamethoxazole, Sulindac

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History – Associated Symptoms

- A thorough review of systems aids in finding any red flag symptoms

13

History – Associated Symptoms

- A thorough review of systems aids in finding any red flag symptoms
- Arthralgias, muscle weakness, and rash suggest an auto-immune etiology
- Constitutional symptoms of fever, chills, fatigue, and malaise indicate an infectious etiology
- In addition to fever, drenching night sweats and unexplained weight loss of greater than 10% of body weight may suggest Hodgkin lymphoma or non-Hodgkin lymphoma

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Examination

- Overall state of health and height and weight measurements may help identify signs of chronic disease, especially in children
- A complete lymphatic examination should be performed to rule out generalized lymphadenopathy, followed by a focused lymphatic examination with consideration of lymphatic drainage patterns
- Lymph node qualities include warmth, overlying erythema, tenderness, mobility, fluctuance, and consistency
- A skin examination should be performed to rule out other lesions that would point to malignancy and to evaluate for erythematous lines along nodal tracts or any trauma that could lead to an infectious source of the lymphadenopathy
- Finally, abdominal examination focused on splenomegaly, although rarely associated with lymphadenopathy, may be useful for detecting infectious mononucleosis, lymphocytic leukemias, lymphoma, or sarcoidosis

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Examination - What is Abnormal?

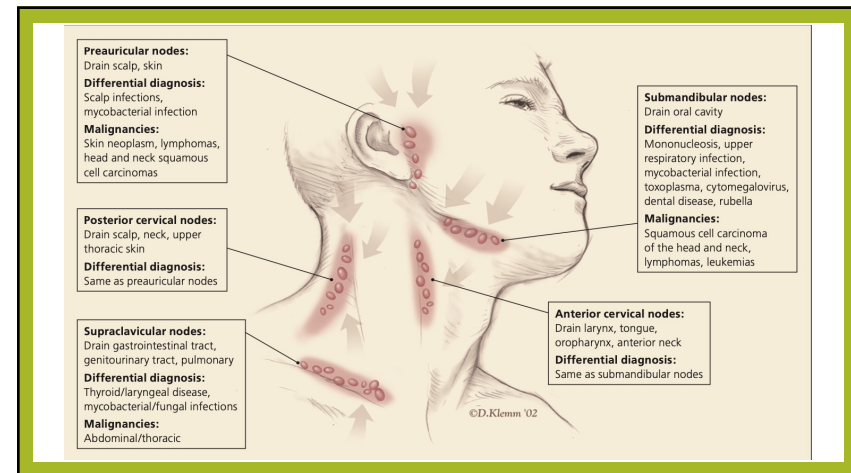
- Refers to lymph nodes that are abnormal in size (e.g., greater than 1-2 cm depending on location); No specific nodal size is indicative of malignancy
- Palpable supraclavicular, popliteal, and iliac nodes, and epitrochlear nodes greater than 5 mm, are considered abnormal
- Hard or matted lymph nodes may suggest malignancy or infection
- Shotty lymphadenopathy is the presence of multiple small lymph nodes that feel like "buck shots" under the skin usually implies reactive lymphadenopathy from viral infection.
- A painless, hard, irregular mass or a firm, rubbery lesion that is immobile or fixed may represent a malignancy, although in general, qualitative characteristics are unable to reliably predict malignancy
- Painful or tender lymphadenopathy is nonspecific and may represent possible inflammation caused by infection, but it can also be the result of hemorrhage into a node or necrosis.

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Lymphadenopathy – Cervical and Head

- Head and neck lymphadenopathy can be classified as submental, submandibular, anterior or posterior cervical, preauricular, and supraclavicular
- Infection is a common cause of head and cervical lymphadenopathy; in children, acute and self-limiting viral illnesses are the most common etiologies of lymphadenopathy
- Inflamed cervical nodes that progress quickly to fluctuation are typically caused by staphylococcal and streptococcal infections
- Persistent lymphadenopathy lasting several months can be caused by atypical mycobacteria, cat-scratch disease, sarcoidosis, and Kawasaki disease
- Supraclavicular adenopathy in adults and children is associated with high risk of intra-abdominal malignancy and must be evaluated promptly
 - Studies found that 34% to 50% of these patients had malignancy, with patients older than 40 years at highest risk

17



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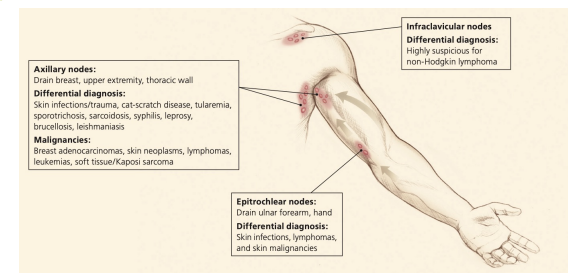
Lymphadenopathy – Axillary

- Infections or injuries of the upper extremities are a common cause of axillary lymphadenopathy
- Common infectious etiologies are cat-scratch disease, tularemia, and sporotrichosis due to inoculation and lymphatic drainage
- Absence of an infectious source or traumatic lesions is highly suspicious for a malignant etiology such as Hodgkin lymphoma or non-Hodgkin lymphoma
- Breast, lung, thyroid, stomach, colorectal, pancreatic, ovarian, kidney, and skin cancers (malignant melanoma) can metastasize to the axilla
- Silicone breast implants may also cause axillary lymphadenopathy because of an inflammatory reaction to silicone particles from implant leakage

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Lymphadenopathy – Epitrochlear

- Epitrochlear lymphadenopathy (nodes greater than 5 mm) is pathologic and usually suggestive of lymphoma or melanoma
- Other causes include infections of the upper extremity, sarcoidosis, and secondary syphilis

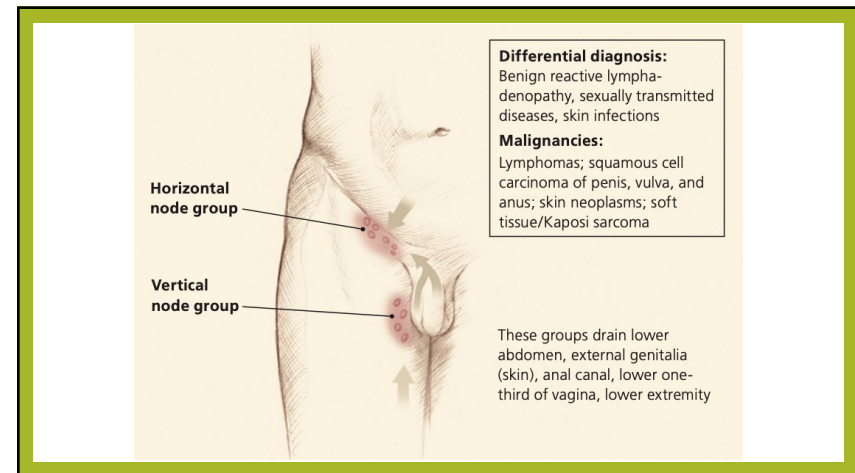


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Lymphadenopathy - Inguinal

- Inguinal lymphadenopathy, with nodes up to 2 cm in diameter, is present in many healthy adults
- It is more common in those who walk outdoors barefoot, especially in tropical regions
- Common etiologies include sexually transmitted infections such as herpes simplex, lymphogranuloma venereum, chancroid, and syphilis, and lower extremity skin infections
- Lymphomas, both Hodgkin and non-Hodgkin, typically do not present in the inguinal region
- Other inguinal lymphadenopathy-associated malignancies are penile and vulvar squamous cell carcinomas and melanoma
 - Inguinal lymphadenopathy is present in about one-half of penile or urethral carcinomas

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Lymphadenopathy - Generalized

- Generalized lymphadenopathy is the enlargement of more than two noncontiguous lymph node groups
- Significant systemic disease from infections, autoimmune diseases, or disseminated malignancy often causes generalized lymphadenopathy, and specific testing is necessary to determine the diagnosis
- Benign causes of generalized lymphadenopathy are self-limited viral illnesses, such as infectious mononucleosis, and medications
- Other causes include acute HIV infection, activated mycobacterial infection, cryptococcosis, cytomegalovirus, Kaposi sarcoma, and systemic lupus erythematosus.
- Generalized lymphadenopathy can occur with leukemias, lymphomas, and advanced metastatic carcinomas

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Diagnostic Evaluation

Take your history and complete Physical Exam
(complete L.N. exam as directed by lymphatic
Drainage map (see previous pictures))

Diagnostic of benign
Or self-limited disease

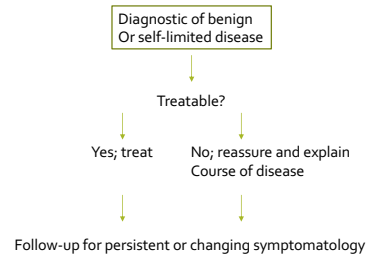
Suggestive of autoimmune
Disease or serious infectious
cause

Suggestive of malignancy

Unexplained

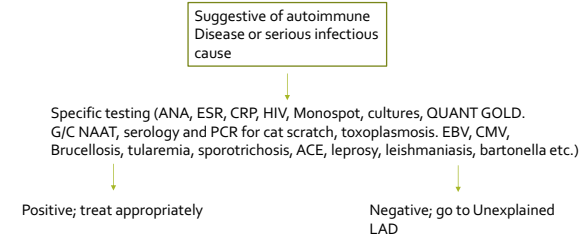
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Diagnostic Evaluation



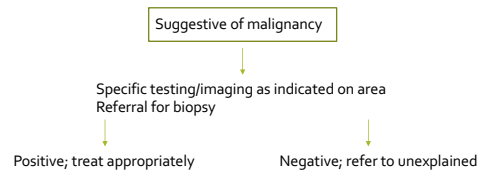
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Diagnostic Evaluation



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Diagnostic Evaluation



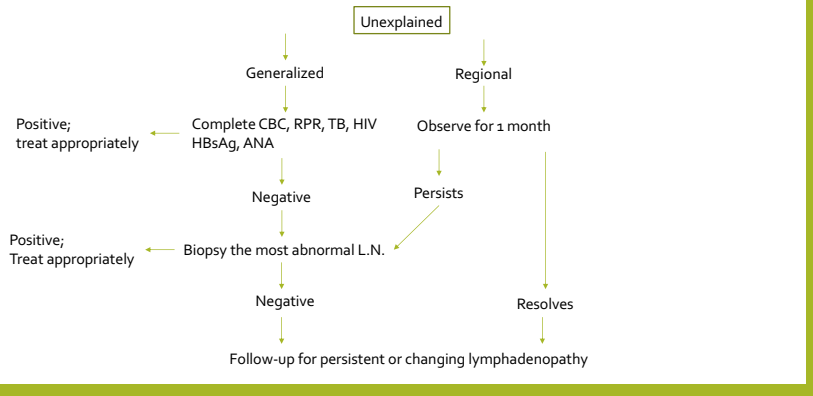
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When To Order Contrast?

- CLOT - Cannot see a PE without contrast
- OBSTRUCTION - It is seen better with IV contrast and even better with both IV and oral contrast
- NEOPLASM - If the word cancer/neoplasm goes with the patient's history, need IV contrast and often oral as well
- TRAUMA - Trauma patients need IV contrast only for the chest, abdomen and pelvis
- RENAL - Yes you can see a stone without IV contrast. But a 60 year old with flank pain who never had a stone before likely does not have one now. If you give contrast you will still be able to see a stone, but will see other things as well
- ABSCESS - Cannot tell if it is an abscess without IV contrast. THIS IS THE MOST COMMON WRONG ORDER. RULE OUT ABSCESS WITHOUT CONTRAST
- SKINNY - Patients that are very skinny, need oral and IV contrast for the abdomen and pelvis. Because of the lack of intraperitoneal fat, everything is bunched together and it is almost impossible to diagnose anything
- THIRTY - We now give IV contrast to patients with GFR equal to or greater than 30

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Diagnostic Evaluation



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Biopsy

- Fine-needle aspiration (FNA) and core needle biopsy can aid in the diagnostic evaluation of lymph nodes when etiology is unknown or malignant risk factors are present

Table 4. Risk Factors for Malignancy

Age older than 40 years
Duration of lymphadenopathy greater than four to six weeks
Generalized lymphadenopathy (two or more regions involved)
Male sex
Node not returned to baseline after eight to 12 weeks
Supraclavicular location
Systemic signs: fever, night sweats, weight loss, hepatosplenomegaly
White race

Information from references 4, 6, and 10.

- FNA cytology is a quick, accurate, minimally invasive, and safe technique to evaluate patients and aid in triage of unexplained lymphadenopathy

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Biopsy

- If a reactive lymph node is likely, core needle biopsy can be avoided, and FNA used alone.
- Combined, FNA and core biopsy, allow cytologic and histopathologic assessment of lymph nodes; however, the use of both techniques may not be needed because the diagnostic accuracy of FNA in adult populations has been reported to approach 90%, with a sensitivity and specificity of 85% to 95% and 98% to 100%, respectively
- False-positive diagnoses are rare with FNA; false-negative results occur secondary to:
 - Early or partial involvement of lymph nodes
 - Inexperience with lymph node cytology
 - Unrecognized lymphomas with heterogeneity, and sampling errors

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Biopsy

- Regardless, FNA may be a useful triage tool for differentiating benign reactive lymphadenopathy from malignancy
- Open excisional biopsy remains a diagnostic option for patients who do not wish to undergo additional procedures
- When selecting nodes for any method, the largest, most suspicious, and most accessible node should be sampled
 - Inguinal nodes typically display the **lowest** yield
 - Supraclavicular nodes have the **highest** yield

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