## Causes of lymphadenopathy with splenomegaly

| Overview | • Enlarged lymph nodes or a palpable spleen tip are exceptionally common physical findings and are not always signs of disease.  
• Lymphadenopathy or splenomegaly may also be the first sign, or even the only sign, of a serious or life-threatening condition.  
• It also can be detected in symptomatic or asymptomatic patients.  
• The possible causes of each finding are diverse, with a broad differential diagnosis ranging from:  
  1. nonmalignant conditions (inflammatory disorders or acute or chronic infections)  
  2. malignant processes (hematologic malignancies or metastatic carcinomas) |
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| Mechanism of lymphadenopathy | 1. Physical enlargement of a lymph node can occur via several processes:  
  a) Polyclonal lymphocyte proliferation due to a reaction to a specific group of antigens.  
  b) Mono-clonal proliferation from malignant transformation of a lymphoid cell can increase the size and number of lymph node follicles, thereby expanding the node.  
  2. It can also occur due to infiltration of the node by nonlymphoid cells, e.g:  
  • Inflammatory reaction by neutrophils in lymphadenitis  
  • Metastatic spread of cancer cells from a primary site of neoplasia.  
  3. Systemic processes can cause a release of cytokines resulting in edema of lymph nodes, e.g:  
  • Cytokine-mediated edema is usually diffuse and not localized to a single node or nodal group.  
  4. In metabolic storage disorders, engorged macrophages can accumulate in a lymph node, causing enlargement. |
| Causes | • Because the splenic white pulp serves as an active immune organ with efferent lymphatic vessels, the mechanisms by which splenomegaly can occur overlap with the mechanisms that cause lymphadenopathy.  
• Because the spleen is also a phagocytic organ with mechanical filtration capability (e.g., for senescent erythrocytes) as well as a potential site of hematopoiesis, there are additional mechanisms for splenomegaly, including brisk hemolysis and extramedullary hematopoiesis.  
• Furthermore, splenomegaly can also occur due to disruption of venous blood flow from the organ, such as splenic or portal vein thrombosis, or portal hypertension due to intrinsic hepatic disease. |
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### Infection  
- Localized infection: cellulitis, abscess  
- Mycobacterial: TB  
- Zoonotic infections  
- Fungal: histoplasmosis  
- Viral: HIV  
- Parasitic: Toxoplasmosis  
### Malignancies  
- Hematologic: lymphoma  
- Solid tumors  
### Immunologic disorder  
- Connective tissue disorders  
- Serum sickness  
- Sarcoidosis  
### Miscellaneous  
- Castleman’s disease (LN hyperplasia)  

## Causes of splenomegaly

| Causes of splenomegaly | 1. Excessive antigenic stimulation: Infection:  
  a. Viral (most common in children), bacterial, protozoal, and fungal (Common causes include Epstein-Barr virus infection, tuberculosis, malaria  
  2. Autoimmune disorders  
  3. Collagen vascular disorders  
  4. Sarcoidosis  
  5. Amyloidosis  
  6. Excessive destruction of abnormal blood cells  
  a. Hemolysis (e.g., hereditary spherocytosis, thalassemia major)  
  7. Chronic myeloproliferative disorders  
  a. Especially myelofibrosis and chronic myelogenous leukemia  
  8. Malignancy  
  a. ALL  
  b. Non-Hodgkin lymphoma, Hodgkin lymphoma  
  c. Acute or chronic myelogenous leukemia  
  9. Obstruction of venous flow  
  a. Cirrhosis  
  b. Portal vein thrombosis,  
  c. Congestive heart failure  
  10. Storage diseases  
  a. Gaucher disease  
  b. Niemann-Pick disease  

## Summary

• Lymphadenopathy and splenomegaly are important findings that may be noted by the patient.  
• It also detected on a physical examination, or uncovered during an imaging study.  
• Enlargement of lymph nodes or the spleen has a broad differential diagnosis, including infectious causes, autoimmune and inflammatory disorders, and a variety of hematologic malignancies and solid tumors.  
• Pathologic diagnosis from excisional lymph node biopsy and supplemental laboratory studies are usually necessary to obtain a correct diagnosis.  
• Lymphadenopathy and splenomegaly should be followed up closely and evaluated promptly because most causes, including hematologic malignancies, are treatable and potentially curable.