# Lymph Node Assessment Primary Care Pathway

Quick links: Pathway primer | Expanded details | Provider resources | Patient resources

## Features of Lymphadenopathy Concerning for Lymphoma

### On Clinical Examination

**Presence of all three features below are indications for referral to the Lymphoma Diagnosis Program**

- Size >1cm supraclavicular, >2cm neck, >3cm axilla/groin
- Persistent or enlarging node(s) >2 weeks
- Nodes are not explained by signs or symptoms of:
  - autoimmune disease (arthritis, morning stiffness, rash, Raynaud's)
  - infection (chills, morning/afternoon fever, sore throat, nasal congestion, cough, diarrhea, skin ulcers/lesions, recent travel or other exposures)

**Features particularly concerning for lymphoma**

- Age >40 years
- Fixed or Matted (non-mobile)
- Supraclavicular location
- Lymphadenopathy that is only mildly- or non-tender
- Generalized lymphadenopathy (two or more regions involved)
- Systemic signs and symptoms: "B" symptoms (fever, drenching night sweats, >10% weight loss), hepatosplenomegaly, pruritis

### On Imaging

(Assuming no other malignancy/condition to explain findings)

**Presence of any features below are indications for biopsy**

- Single enlarged lymph node >3cm short axis and abnormal morphology suggestive of lymphoma
- Multiple enlarged lymph nodes with abnormal morphology suggestive of lymphoma and with some nodes usually reaching a size ≥ 2cm in short axis
- A conglomerate nodal mass (neck, mediastinum, mesentery, retroperitoneum)
- A mass where the primary imaging concern is lymphoma
- Splenomegaly with multiple focal solid abnormalities

Essential labs (CBCD, Lytes, Creatinine, LFTs, LDH) and Chest X-Ray (AP/Lateral)
**AND**
Refer to Lymphoma Diagnosis Program for expedited access to urgent whole body CT scan, image-guided core biopsy (FNA strongly discouraged as it does not provide adequate tissue for diagnosis) and cancer centre appointment

LYMPHOMA DIAGNOSIS PROGRAM
Edmonton: 780-432-8681 (fax) Calgary: 403-521-3245 (fax)

Referral Form Link: Alberta Referral Directory (search: "lymphoma")

**BEWARE OF EMERGENT PRESENTATIONS:**
**NOT APPROPRIATE FOR OUTPATIENT LYMPHOMA DIAGNOSIS PROGRAM REFERRAL**

- **AIRWAY COMPROMISE**
- **SUPERIOR VENA CAVA COMPRESSION**

→ **SEND TO EMERGENCY DEPARTMENT FOR STABILIZATION / URGENT ASSESSMENT BY THORACIC SURGERY FOLLOWING USUAL PROCEDURES***

**CALGARY - ADVISE HEMATOLOGIST ON-CALL**

- **SPINAL CORD COMPRESSION**

→ **SEND TO EMERGENCY DEPARTMENT FOR STABILIZATION / URGENT ADMISSION FOLLOWING USUAL PROCEDURES***

**EDMONTON - ADVISE MALIGNANT HEMATOLOGY SERVICE AT CROSS CANCER INSTITUTE**
**CALGARY - ADVISE HEMATOLOGIST ON-CALL**

* Family physicians communicate with Emergency when sending patients as per local standards.

## PATHWAY PRIMER

- Lymphoma is the 5th most common cancer in Canada. Early diagnosis can allow for cure, but in 2016-17 at least 30% of new lymphoma patients were diagnosed only after admission to hospital – 80% of those being urgent admissions. The Lymphoma Diagnosis Program has since been created to minimize diagnostic and treatment delay for patients with suspicious lymphadenopathy.
- The pathway's objectives are to expedite and support patients with highly suspicious presentations that have high likelihood of being a lymphoma diagnosis from the point of suspicion through diagnostic work-up and staging to a consult with a hematologist/oncologist.
- Other problems being addressed are: 1) psychosocial and symptom management support, 2) patient education, 3) reduction in multiple, non-diagnostic biopsy investigations, and, 4) delayed staging investigations
- Two intake points have been identified. These criteria are high specificity based on clinical consensus and available evidence:
    - **Symptomatic presentations in primary care or emergency department** - For suspicious symptomatic presentations, patients would be referred to the cancer centre and flagged for lymphoma triage nurses to coordinate diagnostic and staging investigations including whole body CT and core needle biopsy instead of excisional biopsy, to organize consults with oncologist/hematologist and to deliver patient support education.
    - **Suspicious findings on incidental imaging (Ultrasound and CT)** - Patients with suspicious findings on ultrasound or CT scan would have their imaging results notified to both ordering provider and the cancer centre, which would get flagged for lymphoma triage nurses to close the loop with the ordering provider and ensure the patient gets a timely referral to the cancer centre and coordination of further diagnostic and staging investigations
- For the few patients with a negative biopsy, there will be follow-up with primary care including information resources. The operational model for triage and case review for uncertain cases or cases with delayed referrals or diagnostic or staging tests would be a team-based approach that includes rotating hematologist/oncologist and lymphoma triage nursing staff

## EXPANDED DETAILS

### 1. Clinical Assessment of Lymphadenopathy

- History (Think MIAMI; see section 3)
    - Age?
    - Duration and progression – persistence beyond 2 weeks?
    - Characteristics of concerning lymph nodes – mobility, consistency, sensation?
    - Site(s) of lymphadenopathy – spreading? abnormalities of surrounding skin/mucosa?
    - Autoimmune and/or systemic symptoms?
    - Travel history or sick contacts?
    - Culprit medications (*Allopurinol, Atenolol, Captopril, Carbamazepine, Gold, Hydralazine, Penicillins, Phenytoin, Primidone, Pyrimethamine, Quinidine, Trimethoprim/sulfamethoxazole, Sulindac)?
- Physical Exam
    - Fever
    - Weight loss (unintentional loss of >10% of usual body weight in <6 months)
    - Full-body lymph node exam with further attention to associated lymph node drainage area for areas of concern
    - Abdominal exam focused on assessment for organomegaly
    - Skin and joint exam focusing on assessment of autoimmune features

## 2. Possible Etiology Based on Clinical Assessment

**Table 1**

| Malignancy | Infection | Autoimmune | Other |
|---|---|---|---|
| • Enlarging node(s) > 2 weeks<br>• Supraclavicular location<br>• Fixed or Matted<br><br><u>Size:</u><br>≥ 1cm supraclavicular<br>≥ 2 cm neck<br>≥ 3 cm axilla/groin<br><br><u>Increased risk:</u><br>• Age > 40 yrs<br>• Generalized, non-tender Hepatosplenomegaly<br>• Fever, >10 % weight loss<br>• Drenching night sweats | • Fever, chills<br>• Sore throat<br>• Nasal congestion<br>• Cough<br>• Diarrhea<br>• Skin lesions<br>• Travel, bites, STDs, other exposures<br>• Malaise, fatigue | • Arthritis<br>• Morning stiffness<br>• Rash<br>• Raynaud's<br>• Dry eyes/mouth | • Medications<br>• Sarcoidosis (hilar) Granulomatous<br>• Reactive<br>• Rare conditions<br>• Unexplained |
| **Action:** | **Action:** | **Action:** | **Action:** |
| • CBC&diff, Electrolytes, Creatinine, LFTs, LDH<br>• CXR PA/Lat<br>• **Refer to Lymphoma Diagnosis Program for CT scan and Core needle biopsy** | • Specific testing according to suspected Infection (see Table 2) such as CBC&diff, Monospot, LFTs, Cultures, Serologies<br>• Seek advice from Infectious Disease | • Specific testing according to suspected disorder, such as CBC&diff, creatinine, LFTs, CRP, ANA, RF, CK, Urine R&M, EMG, Muscle biopsy<br>• Seek advice from Rheumatology | • Observe x1 month if low risk.<br>• Hold suspected medications<br>• Re-assess other causes & consider biopsy if node persists |

## 3. Causes of Lymphadenopathy

MIAMI

- Malignancy
    - Lymphoma, metastatic carcinoma/melanoma, Kaposi sarcoma, leukemias
- Infections
    - Bacterial: cutaneous infections or abscess (staphylococcal or streptococcal), tuberculosis, lymphogranuloma venereum, syphilis, brucellosis, cat-scratch disease (Bartonella), chancroid, tularemia, typhoid fever
    - Fungal: coccidioidomycosis, cryptococcosis, histoplasmosis
    - Viral: infectious mononucleosis (Epstein-Barr virus), adenovirus, cytomegalovirus, human immunodeficiency virus, hepatitis, herpes zoster, rubella
    - Other: helminthic, Lyme disease, rickettsial, scrub typhus, toxoplasmosis
- Autoimmune disorders
    - Rheumatoid arthritis, Systemic lupus erythematosus, Sjögren syndrome, Still disease, Dermatomyositis

- Miscellaneous/unusual conditions
    - Angiofollicular lymph node hyperplasia (Castleman disease), berylliosis, silicosis histiocytosis, Kawasaki disease, Kikuchi lymphadenitis, Kimura disease, sarcoidosis
- Iatrogenic causes
    - Medications (Allopurinol, Atenolol, Captopril, Carbamazepine, Gold, Hydralazine, Penicillins, Phenytoin, Primidone, Pyrimethamine, Quinidine, Trimethoprim/sulfamethoxazole, Sulindac)
    - Serum sickness

## 4. Presentations Suggesting Causes of Lymphadenopathy and Initial Testing

**Table 2**

| Symptoms | Suggested Diagnoses | Initial Testing |
|---|---|---|
| Fever, drenching night sweats, weight loss, or nodes located in supraclavicular, popliteal, or iliac region, matted/fixed/large nodes, bruising, splenomegaly | Lymphoma, leukemia, solid tumor metastasis | CBC, nodal biopsy, imaging with ultrasonography or computed tomography (imaging should not delay referral for biopsy) |
| Fever, chills, malaise, sore throat, nausea, vomiting, diarrhea; fatigue | Bacterial or viral pharyngitis, influenza, mononucleosis, tuberculosis, hepatitis, rubella | Limited illnesses may not require any additional testing; depending on clinical assessment, consider CBC, monospot test, liver function tests, cultures, and disease- specific serologies as needed |
| High-risk sexual behavior | Chancroid, HIV infection, lymphogranuloma venereum, syphilis | HIV-1/HIV-2 immunoassay, rapid plasma reagin, culture of lesions, nucleic acid amplification for chlamydia, migration inhibitory factor test |
| Animal Contact: Cats | Cat-scratch disease (*Bartonella*)<br><br>Toxoplasmosis | Serology and polymerase chain reaction<br><br>Serology |
| Animal Contact: Rabbits, Sheep or Cattle (Wool, Hair, Hides, Undercooked Meat) | Brucellosis<br><br>Tularemia | Serology and polymerase chain reaction<br><br>Blood culture and serology |
| Recent Travel or Insect Bites | Diagnosis based on endemic region | Serology and testing as indicated by suspected exposure |
| Arthralgias, rash, joint stiffness, fever, chills, muscle weakness | Rheumatoid arthritis, Sjögren syndrome, dermatomyositis, systemic lupus erythematosus | Antinuclear antibody, anti- doubled-stranded DNA, erythrocyte sedimentation rate, CBC, rheumatoid factor, creatine kinase, electromyography, or muscle biopsy as indicated |

*Adapted from:* Gaddey, H.L. & Riegel, A.M. (2016). Unexplained Lymphadenopathy: Evaluation and Differential Diagnosis. *Am Fam Physician*, 94(11), 896-903.

# BACKGROUND

## About this Pathway

- The creation of the Lymphoma Diagnosis Pathway builds on the success of previous pathways including lung, breast and prostate cancer. Building out multiple cancer diagnosis pathways has begun to create end-to-end pathways for cancer patients in Alberta on a provincial scale with the goals of expedited cancer diagnosis and providing better support to patients through that process.
- Initial work on this pathway was started in May 2019 and is being implemented over two years. Patients, providers and administrators from relevant areas were brought together to gather information on current experiences with lymphoma diagnosis, collect data on how the system is performing and review best practice evidence. Provincial principles of care, strategic areas for improvement in Alberta and a provincial measurement and reporting framework were defined.
- Primary Care, diagnostic imaging and lab providers were engaged to co-design pathways with patients, hematologists/oncologists and lymphoma triage nurses. Local implementation teams engaged in work around planning and pathway roll-out, determination of barriers and facilitators, and shared learnings with other sites.
- Performance dashboard reports will be developed and disseminated to provide feedback to clinical teams on pathway performance and outcomes. Sustainability planning will be initiated early with implementation teams to ensure successful transition of pathways to operations at the end of the initiative.

## Authors & Conflict of Interest Declaration

This pathway was reviewed and revised under the auspices of the Cancer Strategic Clinical Network (CSCN) in 2019 by a multi-disciplinary team led by family physicians and hematologists/oncologists. For more information, contact the CSCN at Cancer.SCN@ahs.ca.

## Pathway Review Process

Primary care pathways undergo scheduled review every three years, or earlier, if there is a clinically significant change in knowledge or practice. The next scheduled review is June 2023. However, we welcome feedback at any time. Please email comments to Cancer.SCN@ahs.ca

## Copyright Information



## Disclaimer

This pathway represents evidence-based best practice, but does not override the individual responsibility of health care professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

## PROVIDER RESOURCES

### Advice Options

Non-urgent advice is available to support family physicians.

- Hematology advice is available across the province via Alberta Netcare eReferral Advice Request (responses are received within five calendar days). Visit www.albertanetcare.ca/documents/Getting-Started-Advice-Requests-FAQs.pdf for more information.
- Non-urgent telephone advice connects family physicians and specialists in real time via a tele-advice line. Family physicians can request non-urgent advice from a hematologist/oncologist:
    - In the Calgary Zone at specialistlink.ca or by calling 403-910-2551. This service is available from 8:00 a.m. to 5:00 p.m., Monday to Friday (excluding statutory holidays). Calls are returned within one hour.
    - In the Edmonton Zone by calling 1-844-633-2263 or visiting www.pcnconnectmd.com. This service is available from 8:00 a.m. to 6:00 p.m., Monday to Friday (excluding statutory holidays and Christmas break). Calls are returned within two business days.

### Resources and References


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|---|
| Gaddey, H.L. & Riegel, A.M. (2016). Unexplained Lymphadenopathy: Evaluation and Differential Diagnosis. *Am Fam Physician*, 94(11), 896-903. |
| Mohseni, S.H., Shojaiefard, A., Khorgami, Z., et al. (2014). Peripheral Lymphadenopathy: Approach and Diagnostic Tools. *Iran J Med Sci*, 39(2), 158-170. |

## PATIENT RESOURCES

### Information

| Description | Website |
|---|---|
| Superficial lymph node biopsy | https://myhealth.alberta.ca/Alberta/Pages/superficial-lymph-node-biopsy-care-instructions.aspx |