This resource has been developed as part of the Implementing PAthways for Cancer Early Diagnosis (I-PACED) project supported by the Victorian Government. It aims to increase GP awareness about critical primary care points for lymphoma. This pathway refers to the Hodgkin and diffuse large B-cell lymphomas Optimal Care Pathway – a nationally endorsed resource.

Summary statistics
- In Victoria 2017 there were 1,030 new cases of lymphoma in males and 795 new cases in females
- The five-year survival for males with Hodgkin’s lymphoma is 89% and 70% for diffuse large B-cell lymphoma
- For females, the five-year survival is 86% for Hodgkin’s lymphoma and 69% for diffuse large B-cell lymphoma.

Risk factors
- Middle-aged to older adults; additional ‘peak’ of incidence of Hodgkin lymphoma in adolescents and young adults
- Intrinsically immunosuppressed patients or those receiving therapeutic immunosuppression (e.g. transplant recipients, HIV-positive patients)
- Epstein-Barr virus (EBV) infection in conjunction with immune deficiency
- Family history of lymphoma
- Past history of lymphoproliferative disorder
- Obesity (modest but modifiable risk factor).

Screening recommendations
- There are no effective screening programs for lymphoma
- Individuals at risk of immunodeficiency-associated lymphoma should be made aware of this increased risk and advised of relevant symptoms.

Signs and symptoms
See Figure 1: Risk assessment tool
- A lump or mass
- Unexplained lymphadenopathy or splenomegaly, particularly persistent lymphadenopathy of up to four weeks
  - or associated with systemic symptoms
  - despite appropriate treatment for presumed infection
  - pain in the lymph nodes following alcohol consumption
- One or more of these systemic symptoms in the absence of lymphadenopathy: fever, drenching sweats, unexplained weight loss, persistent severe itch
- Undiagnosed back or abdominal pain without palpable lymphadenopathy
- Unexplained elevation of lactate dehydrogenase (LDH)
- Unexplained cytopenias.

Sudden onset of new respiratory symptoms may be a presenting feature of mediastinal obstruction, particularly in the paediatric population, and may require urgent imaging.

Persistent or enlarging lumps without other symptoms should be seen within two weeks.

Initial investigations include
See Figure 2: Diagnostic flowchart
- Prompt referral to a specialist centre to facilitate a tissue diagnosis if high likelihood of lymphoma
- Investigations should be completed within four weeks and include:
  - Full blood examination (FBE), urea and electrolytes (U&E), liver function tests, calcium, urate, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), LDH (no laboratory test can exclude lymphomas)
  - Imaging (ultrasound for peripheral lesions, chest radiography and computed tomography (CT) scan)
  - Biopsy (a negative fine-needle aspiration (FNA) does not exclude lymphomas).
- A period of observation of up to six weeks can be appropriate for patients without any significant or progressive symptoms.
Figure 1: Risk assessment tool for non-Hodgkin lymphoma

<table>
<thead>
<tr>
<th>Symptom</th>
<th>PPV as a single symptom</th>
<th>Infection</th>
<th>Shortness of breath</th>
<th>Indigestion</th>
<th>Constipation</th>
<th>Back pain – 2nd occurrence</th>
<th>Fatigue</th>
<th>Vomiting and nausea</th>
<th>Abdominal pain</th>
<th>Malaise</th>
<th>Weight loss</th>
<th>Mass</th>
<th>Head and neck mass</th>
<th>Lymphadenopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.8</td>
<td></td>
<td>2.3</td>
<td>13</td>
</tr>
<tr>
<td>0.2</td>
<td>0.8</td>
<td></td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.7</td>
<td></td>
<td>2.8</td>
<td>&gt;10</td>
</tr>
<tr>
<td>0.3</td>
<td>0.6</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.6</td>
<td>&gt;5</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td>1.0</td>
<td>0.4</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.4</td>
<td>&gt;10</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>0.3</td>
<td>0.9</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>0.2</td>
<td>0.9</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>&gt;10</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>1.3</td>
<td>0.1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>&gt;10</td>
<td></td>
</tr>
<tr>
<td>0.6</td>
<td>2.2</td>
<td>0.6</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>&gt;10</td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td>3.6</td>
<td></td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>&gt;10</td>
<td></td>
</tr>
<tr>
<td>0.3</td>
<td>11</td>
<td></td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>&gt;10</td>
<td>&gt;10</td>
<td></td>
</tr>
</tbody>
</table>

PPV = Positive predictive value (%) or probability of Ca if Sx present

Probability of cancer

- <1%
- 1-2%
- 2-5%
- >5%

*second presentation

Figure 1 shows the probability of non-Hodgkin lymphoma for individual symptoms and pairs of symptoms in people ≥ 60 years.

Figure 2: Diagnostic flowchart

**PREDOMINANT PRESENTATIONS**
- Enlarged, usually painless lymph nodes anywhere in the body (commonly in the neck, axilla or groin)
- Unexplained fever
- Night sweats
- Unintentional weight loss/anorexia

**STILL SUSPECT LYMPHOMA**

**INITIAL INVESTIGATIONS**
- Full medical history (include fevers, sweats, weight loss, malaise)
- Physical examination (particularly of lymph nodes and spleen)
- Full blood count, EUC/LFTs, serological studies
- Chest X-ray (to image the mediastinum)
- CT scan (of chest, abdomen, pelvis, as clinically indicated)

**INDICATORS FOR URGENT EXCISIONAL BIOPSY**
- Spinal cord compression
- Pericardial tamponade
- Superior or inferior vena cava obstruction
- Airway obstruction
- Possible CNS mass lesions
- Intestinal obstruction
- Ureteric obstruction
- Severe hepatic dysfunction
- Patient is unwell

**DEMONSTRATE LYMPHOMA**

**INDICATORS FOR BIOPSY**
- Aged 40 years and over
- Supraclavicular location
- Lymph node >2cm diameter
- Firm/hard texture, mobile, not tender
- Present several weeks
- Abnormal CXR/CT scan
- Significant constitutional symptoms

**INDICATORS FOR SURGICAL BIOPSY**
- Coagulation screen
- Flow cytometry (if lymphocytosis is present)
- Ultrasound of lymph nodes

**PERSISTENT LYMPHADENOPATHY**

**LESS COMMON BUT POSSIBLE PRESENTATIONS**
- Persistent fatigue/loss of energy
- Flu-like illness
- Generalized itching
- Abdominal pain
- Bone pain
- Back pain
- Shortness of breath/protracted cough
- Neurological symptoms

**INDICATORS FOR BIOPSY**
- Aged 40 years and over
- Supraclavicular location
- Lymph node >2cm diameter
- Firm/hard texture, mobile, not tender
- Present several weeks
- Abnormal CXR/CT scan
- Significant constitutional symptoms

**SYSTEMIC PRESENTATIONS**
- Specific organ involvement such as mediastinal enlargement on CXR
- Protracted cough
- Splenomegaly
- Fever or weight loss

**DIFFERENTIAL DIAGNOSES**
- Thymoma
- Metastatic carcinoma
- TB
- Sarcoidosis
- Portal hypertension
- Infiltrative disease of spleen; extramedullary haematopoiesis
- Myeloproliferative disease

**URGENT HOSPITAL REFERRAL**
Rapidly progressive lymphomas may result in acute medical emergencies due to compression of vital internal structures (urethra, trachea or major blood vessels)

**FURTHER INVESTIGATIONS BY GP BEFORE REFERRAL FOR SURGICAL BIOPSY**
- Coagulation screen
- Flow cytometry (if lymphocytosis is present)
- Ultrasound of lymph nodes

**DIFFERENTIAL DIAGNOSES**
- Infectious mononucleosis
- Toxoplasmosis
- Cytomegalovirus
- HIV
- Rubella
- Viral hepatitis and other viral infections
- Cat-scratch disease

**SUSPECT LYMPHOMA**

**ELIMINATE DIFFERENTIAL DIAGNOSES**
- Infections
- Mononucleosis
- Toxoplasmosis
- Cytomegalovirus
- HIV
- Rubella
- Viral hepatitis and other viral infections
- Cat-scratch disease

**REFERRAL**
Refer all patients with suspected lymphoma to a clinical haematologist or medical oncologist or general physician (if appropriate i.e. in regional/rural areas) who works in association with a multidisciplinary team and has appropriate expertise in the management of lymphoma.

This information is reproduced from ‘Is Lymphoma on Your Radar?’ decision support tool for GPs with permission from Leukaemia Foundation. Available at www.leukaemia.org.au/disease-information/health-professionals
**Referral pathway**

- Prior to referral, discuss the cost implications to enable patients to make an informed decision regarding their choice of specialist and health service, including out of pocket costs: for example, radiological tests and specialist appointments.
- Urgent hospital admission for patients with severe symptoms, clinical progression or instability, or presence of or impending mechanical obstruction
- Patients diagnosed with lymphoma should be referred to a haematologist or medical oncologist with professional expertise in lymphoma management linked with a multidisciplinary team (MDT)
- Patients without a histologic diagnosis but suspected of having lymphoma should be referred to an appropriate specialist for diagnostic workup
- Referral information should include relevant psychosocial, medical and family history, current medications, allergies and results of clinical investigations (imaging and pathology results).

**Local referral process and proformas can be found at:**


**Patient resource checklist**

- ✔ Factsheets and resources at [livelighter.com.au](http://livelighter.com.au)
- ✔ For additional practical and emotional support, encourage patients to call Cancer Council 13 11 20 to speak with an experienced oncology nurse or visit [cancervic.org.au](http://cancervic.org.au) for more information about lymphoma
- ✔ For translator assistance call TIS on 13 14 50
- ✔ Leukaemia Foundation – for free information packs, support and resources, visit [leukaemia.org.au](http://leukaemia.org.au) or freecall 1800 620 420

---

The Optimal Care Pathways were developed through consultation with a wide range of expert multidisciplinary teams, peak health organisations, consumers and carers. They are nationally endorsed by the National Cancer Expert Reference Group, Cancer Australia and Cancer Council Australia.