GUIDELINE FOR THE INVESTIGATION AND REFERRAL OF ADULT PATIENTS WITH LYMPHOCYTOSIS.	
Guideline Number & Full Title	**3278 - GUIDELINE FOR THE INVESTIGATION AND REFERRAL OF ADULT PATIENTS WITH LYMPHOCYTOSIS**
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Directorate & Speciality	Clinical Haematology, CAS
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Date on which guideline must be reviewed (this should be one to three years)	03/02/26
Explicit definition of patient group to which it applies	Adult patients with isolated lymphocytosis in the primary care setting.
Version History	1.0 (January 2021)
Abstract	This guideline describes the investigation of adult patients with lymphocytosis, along with criteria for referral to haematology.
Key Words	Lymphocytosis, flow cytometry, CLL.
Evidence base of the guideline – Peer Review	Evidence level 6 - recommended best practise based on the clinical experience of the guideline developer. This guideline has been reviewed by fellow Haematology consultants who care for patients with Chronic Lymphocytic Leukaemia (CLL).
Consultation Process	Consultant Haematologists Dr. Christopher Fox Dr. Amber Hodgson Dr.. Dean Smith
Target Audience	Primary care physicians/ANP, NUH medical staff.

This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

GUIDELINE FOR THE INVESTIGATION AND REFERRAL OF ADULT PATIENTS WITH LYMPHOCYTOSIS.

Purpose

To provide clear guidance for the effective investigation of adult patients with lymphocytosis, including criteria for referral of patients to the haematology department.

Individual patient circumstances must be assessed as the guidelines may not be appropriate to all patients and alternative investigations and approaches may sometimes be required.

Background

Clinically relevant lymphocytosis is defined as a lymphocyte count > 5.0 x 10^9/l. Causes of a lymphocytosis include reactive and primary haematological causes:

Reactive causes

- Acute viral infection when the lymphocytosis is transient. Most commonly Epstein-Barr virus (glandular fever). Other viral causes include cytomegalovirus, influenza, herpes simplex and mumps (Grove et al, 2009).

- Chronic infections: Tuberculosis, brucellosis, secondary syphilis and chronic viral infections (including HIV and hepatitis B/C).

- Smoking

Haematological causes

Chronic lymphocytic leukaemia (CLL) is the most common primary haematological cause for a persistent lymphocytosis. The incidence of CLL peaks between 60 and 80 years of age, with an average age at diagnosis of 72 years. However, younger patients can be affected with 11% diagnosed under the age of 55 (Howlader et al, 2012). Early stage CLL is often asymptomatic and requires no therapy, hence, no direct clinical benefit of early diagnosis is expected in CLL. Rate of progression to symptomatic CLL is low (<1% per year).

Hairy cell leukaemia and low-grade B-cell non Hodgkin lymphoma are less common neoplastic causes of lymphocytosis (Grove et al, 2009).

Investigations and procedures

Local NUH threshold for normal lymphocytes in 4.0 x10/^{9}L, however only lymphocytosis above 5 x10/^{9}L is considered to be clinically relevant for the purpose of this guideline.

Any lymphocytosis below 5 x10/^{9}L is unlikely to represent relevant pathology and can be safely monitored in primary care. In case of any clinical concerns, patients could be discussed with Haematology via Advice and Guidance system.

Patients with a clinically significant lymphocytosis (>5 x10/^{9}L) should be assessed by a clinician with a full history, physical examination and a review of other full blood count parameters. The guidance for investigations is provided in the flowchart below (See page 4)

A. History.

- History of viral symptoms in the last 12 weeks.
- Smoking history
- B symptoms: Weight loss >10%, unexplained fevers, drenching night sweats.
- Anaemia (HB <100 g/L).
- Thrombocytopenia (Platelets <100 x10/^{9}L)
- Neutropenia (Neutrophils <1.0 x10/^{9}L)
- Chronic inflammatory/autoimmune conditions

B. Examination

- Lymphadenopathy (lymph nodes >1.5cm)

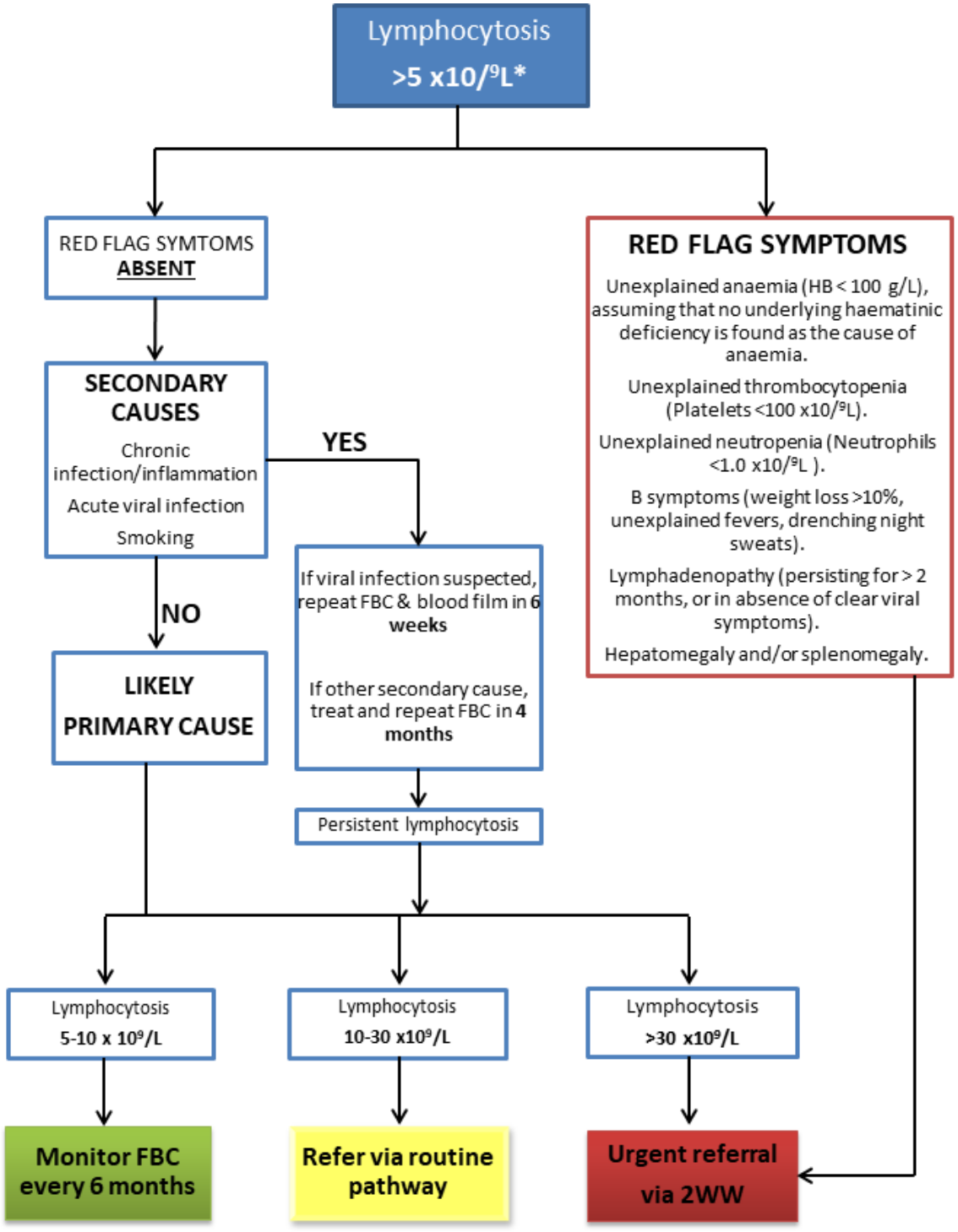
  If yes, how long has it been present for? Is it painful?
- Hepatomegaly and/or splenomegaly?

C. Further investigations

- Glandular fever screen if any symptoms suggestive of this
- Screening for other chronic viral aetiologies
- Blood film

Lymphocytosis >5 x10/^{9}L, who do not meet the criteria from Table 1 can be safely monitored in the community. FBC and clinical visit are recommended every 6 months. Criteria for referral should be evaluated in every visit.

Flowchart of investigations



* Lymphocytosis below 5x 10^9/L can be safely monitored in the community. Repeat FBC every 6 months.

Table 1. Summary of criteria for immediate referral to haematology
✓ Any lymphocytosis above 30 x10/^{9}L should be immediately referred via **2WW pathway**.
✓ Any persistent asymptomatic lymphocytosis (> 12 weeks) above 10 x10/^{9}L should be referred via **routine pathway**.
✓ Any lymphocytosis between 5-30 x10/^{9}L with any of the following should be referred via **2WW pathway**: o Unexplained anaemia (HB < 100 g/L), assuming that no underlying haematinic deficiency is found as the cause of anaemia. o Unexplained thrombocytopenia (Platelets <100 x10/^{9}L) o Unexplained neutropenia (Neutrophils <1.0 x10/^{9}L) o B symptoms (weight loss >10%, unexplained fevers, drenching night sweats) o Lymphadenopathy (persisting for > 2 months, or in absence of clear viral symptoms) o Hepatomegaly and/or splenomegaly

Further investigations for patients who do not meet criteria for immediate referral

- Patients with mild anaemia, thrombocytopenia or neutropenia who do not meet thresholds for referral should have monitoring with FBC and clinical evaluation every 4-6 months, this can be safely done in the community if none of the criteria from table 1 are met. If any clinical concern please use the Haematology Advice and Guidance system.

- Advise stop smoking if appropriate and repeat FBC in 4 – 6 weeks

Contact information

For urgent queries Haematology SpR and consultant can be contacted via NUH switchboard.

References

Howlader et al, SEER Cancer Statistics Review 1975-2009 (Vintage 2009 Populations). National Cancer Institue, Bethesda, MD. http://seer.cancer.gov

Grove et al, Incidental finding of lymphocytosis in an asymptomatic patient. *BMJ* 2009; 338:b2119