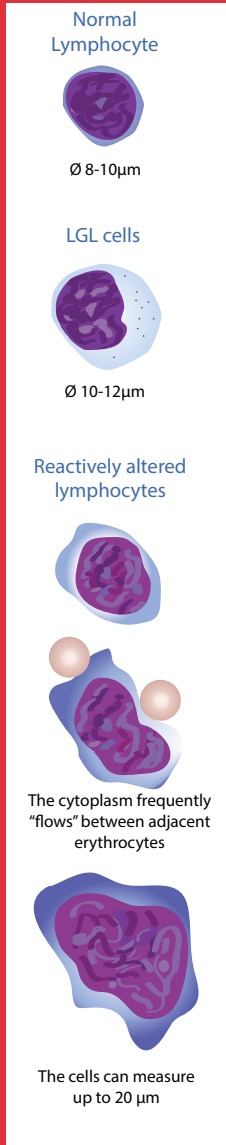




Possible changes in lymphocyte morphology in reactive lymphocytes



Reactively modified lymphocytes are characterized by the following changes:

- Increased cell size (initially plasma volume)
- Nuclear shape tending towards oval, cleft, occasionally irregular nuclear contours
- Increasing cytoplasmic basophilia
- with heaviest staining in the periphery and paler zone in the vicinity of the nucleus
- Some nucleoli in large reactive lymphocytes
- The cytoplasm of reactive lymphocytes frequently "flows" between adjacent erythrocytes.

Introduction

An absolute increase in the lymphocyte count which occurs in response to an external trigger, and is reversible if the trigger regresses, is referred to as a reactive (secondary) lymphocytosis (e.g. a viral infection).

For some causes of a reactive lymphocytosis, the appearances are morphologically more characteristic and the reactive lymphocytes distinctive. These can be very variable in the details of their changes and thus lead to the typical pleomorphic (protean, "variegate") cell picture. Reactive lymphocytes must be differentiated from primary lymphocytosis (malignant lymphoproliferation). Here again, the primary assessment is the lymphocyte morphology under the microscope. In contrast to reactive lymphocytosis, there is, as a rule, a monomorphic cell picture, reflecting the clonal origin of the cells (e.g. CLL-lymphocytes). Additional details on the expanded lymphocyte population can be derived from an analysis of the surface markers (immunophenotyping).

Our inter-laboratory test preparation 2018-H3b is derived from a 22-year-old male with a serologically confirmed EBV infection.

Reactive lymphocytoses with reactive lymphocyte morphology.

The clinical picture of "mononucleosis" is one of a proliferation of large, mononuclear, reactively changed lymphocytes as an expression of the immune response. The cause of this illness in 90% of cases is an infection with the Epstein-Barr virus (EBV), the additional 10% of similar illness patterns being due to other agents (EBV-negative "mononucleosis syndromes").

EBV - Epstein-Barr virus

This agent is very widespread (seroconversion rate of around 98% in adults). Many infections run an asymptomatic course. In adolescents and young adults, there are frequently typical symptoms of "mononucleosis syndrome". Symptoms include symmetrical lymph node enlargement (classical Pfeiffer glandular fever), splenomegaly, tonsillo-pharyngitis, fever and generalized weakness, all of which may persist for several weeks.

CMV - cytomegalovirus

A new cytomegalovirus infection in an immunocompetent adult generally presents asymptotically. If there are symptoms, they resemble those of an EBV infection. However, lymph nodes and splenomegaly are found less often. There is generally no tonsillo-pharyngitis.

HIV - acute primary infection

Around 50% of subjects with new HIV infections suffer for 8-12 weeks following the primary infection with flu-like symptoms or those similar to mononucleosis. Therefore, with similar symptoms and negative serology for EBV, the possibility of infection should be raised and corresponding laboratory tests performed. Since the symptoms more commonly develop prior to seroconversion, proof should be sought from PCR testing for HIV-p24 antigen or HIV-RNA. In this way, the "diagnostic gap" prior to the development of antibodies is reduced.

EBV-negative "mononucleosis syndrome"

Additional agents, which may more rarely be associated with mononucleosis syndrome, include infections with toxoplasma, herpes virus HHV-6 or adenovirus type 12.

Reactive lymphocytes without reactive lymphocyte morphology

The following agents/ conditions lead to a reactive lymphocytosis without also provoking any significant lymphocyte morphological changes.

Infectious	Non-infectious
Viruses: <ul style="list-style-type: none"> • Coxsackie virus B2 • Poliiovirus • Enteroviruses Bacteria: <ul style="list-style-type: none"> • Bordetella pertussis (lymphocytes with nuclear clefts, analogous to T-cells) • Bartonella henselae (cat-scratch disease) Protozoa: <ul style="list-style-type: none"> • Babesioses (transmitted by ticks) 	<ul style="list-style-type: none"> • Medication-induced hypersensitivity reactions (in combination with eosinophilia) • Stress-induced e.g. following heart attack, trauma, epileptic attack (followed by neutrophilia) • Persistent polyclonal B-cell lymphocytosis with binucleate lymphocytes (predominantly young to middle-aged female smokers) • Post-splenectomy lymphocytosis with an elevated proportion of LGL-cells (large-granular-lymphocytes)



Spotlight on hematology

Diagnostics of reactive lymphocytosis

Reference ranges for lymphocytes in adults:

Lymphocyte # 1.50-4.00 G/l

A reactive lymphocytosis with mild reactive changes in the lymphocytes is often seen in toddlers and young children in the setting of infections.

The simultaneous occurrence of large lymphocytes with extensive reactive changes is, by contrast, exclusively found in the “mononucleosis syndrome”.

As a rule, these cells are relatively readily identified in microscopic examination of the blood picture. In individual cases though, differentiation from neoplastic cells can be more difficult.

The recognition of atypical lymphocytes in the histograms of hematology analyzers can be helpful here. There is variable success, depending upon the numbers of, and degree of change in, the abnormal cells, as well as the lysis, staining and measurement techniques used by the apparatus.

Evidence for reactive lymphocytosis with various hematologic analyses

Orphee Mythic (3-Part Diff)

Normale Leukozytenhistogramme	MQ 2018-3 H3B EBV
Mythic uses fixed discriminators. The lymphocyte peak is narrow and below the left discriminator.	Large reactive lymphocytes broaden the lymphocyte population towards the right.

ABX Microsemi (3-Part Diff)

In Microsemi, the discriminators are fixed. In this normal histogram, nearly all the lymphocytes lie to the left of the lower discriminator.	Large reactive lymphocytes lead to a double peak in the lymphocyte population. The curves intersect the lower discriminator at half height.

Sysmex XP300 (3-Part Diff)

Sysmex uses variable discriminators. In this normal histogram, the line between the lymphocytes of the MXD population is to the left of 100.	Large lymphocyte population, wider, shifted to the right towards the MXD population. The variable discriminator is to the right of 100.

Sysmex XE-5000 (5-Part Diff)

	Various events are counted in the “atypical lymph” domain.

Siemens ADVIA 2120 (5-Part Diff)

	Multiple elements are measured in the “LUC” (large unstained cells) domain.

About

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