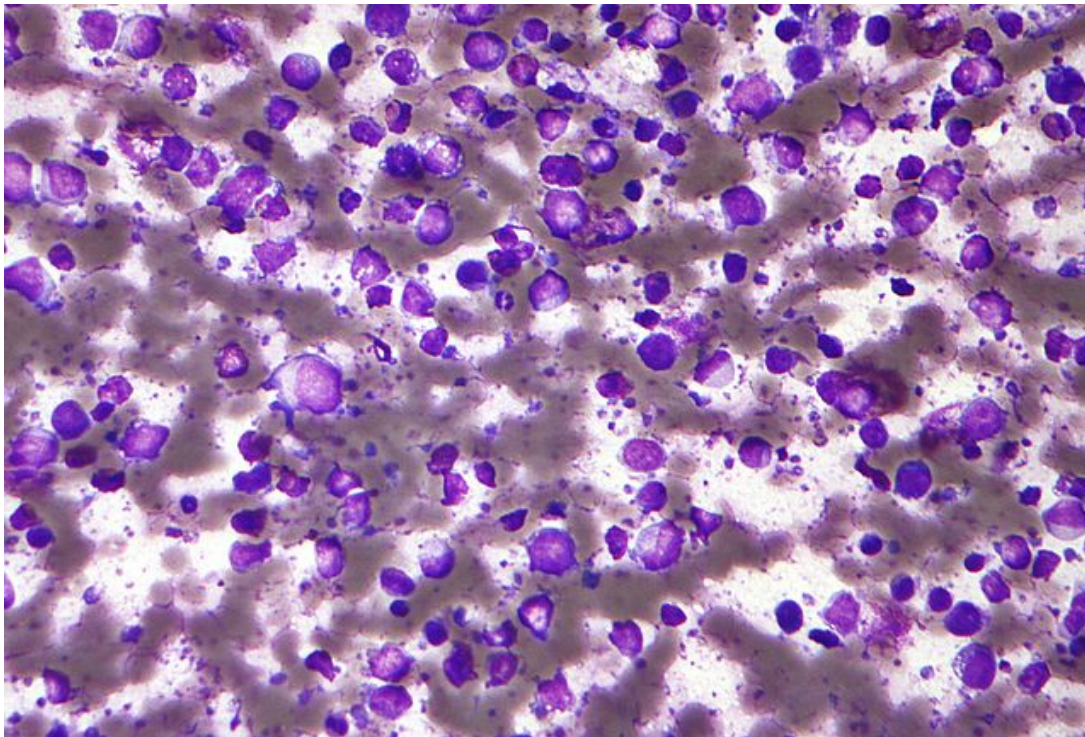


## Diffuse Large B-Cell Lymphoma (DLBCL; DLBL) — Classification and Prognosis

[See online here](#)

**Diffuse Large B-Cell Lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL), accounting for one-third of all NHLs in the western world. It is a very aggressive, fast-growing neoplasm unless diagnosed and treated timely (survival is less than one year without a cure). This illness is characterized by painless enlarged lymph nodes. It has a very close affiliation with genetic issues, Epstein-Barr virus (EBV) and immunocompromised conditions (congenital and acquired: HIV, AIDS).**



### Introduction to Diffuse Large B-Cell Lymphoma

The diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin's lymphoma (NHL). It is an aggressive, rapid-growing type of NHL that is rapidly fatal if untreated.

### Epidemiology of Diffuse Large B-Cell Lymphoma

DLBCL is the most common type of NHL in the United States, accounting for 25 % to 35 % of all NHLs. The incidence rate of DLBCL is approximately 4.7 cases per 100,000 persons annually in the US, and it is constantly increasing. The incidence increases with age and

the mean age at the time of diagnosis is 64 years. Men are slightly more susceptible.

## Etiology of Diffuse Large B-Cell Lymphoma

The exact etiology of DLBCL has not been determined precisely yet. However, the following possible risk factors are identified for this disease:

- Infections (EBV, Kaposi sarcoma-associated human herpes virus 8 [HHV 8], [Helicobacter pylori](#), *Chlamydia psittaci* and hepatitis C virus)
- Chronic inflammation
- Immunosuppression
- Familial
- [Obesity](#)
- [Autoimmune diseases](#)
- Environmental factors
- Long-term chemical exposure (herbicides, insecticides and oxidative dye)
- [Organ transplantation](#)

## Classification of Diffuse Large B-Cell Lymphoma

The World Health Organization (WHO) has classified DLBCL into following different subtypes depending upon specific clinical, morphologic and molecular characteristics.

- DLBCL, not otherwise specified (NOS)
- T-cell/Histiocyte-rich large B-cell lymphoma
- Primary DLBCL of the central nervous system (CNS)
- Primary cutaneous DLBCL, leg type
- Epstein-Barr virus (EBV)-positive DLBCL of the elderly
- Germinal center B-cell (GCB)-DLBCL
- Activated B-cell (ABC)-DLBCL

## Clinical Presentation of Diffuse Large B-Cell Lymphoma

The clinical presentation of patients with DLBCL is very similar to other NHLs or other types of blood cancer. Most cases are accompanied by painless enlarged and swollen lymph nodes. Moreover, over 40 % of the patients have the extranodal manifestation of the disease, namely, skin, gastrointestinal tract, central nervous system, respiratory system, genitourinary tract, or the bones.

**The common clinical features are as follows:**

- Rapidly enlarged painless lymph nodes
- Pelvic lymphadenopathy leads to pedal edema due to the blockage of the lymph outflow
- Fever, night sweats and weight loss (so-called B-symptoms)
- Itchiness
- Breathlessness
- Fatigue

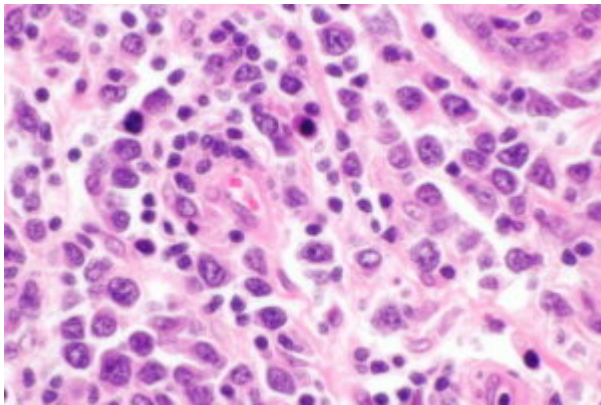
The cancerous cells typically target the reticuloendothelial system (lymph nodes, spleen, liver and bone marrow); hence the common physical findings are lymphadenopathy

(often involving cervical, axillary and inguinal lymph nodes) and hepatosplenomegaly.

## Diagnosis of Diffuse Large B-Cell Lymphoma

### Laboratory studies

**Histological examination:** The microscopic examination of the excisional biopsy of the nodes is the gold standard for the diagnosis. It shows a diffuse spread of abnormally enlarged cells with an equal number of small and large cells, with a cleaved or indented nucleus and coarse chromatin in them.



By Nephron - Own work CC BY-SA 3.0,  
<https://commons.wikimedia.org/w/index.php?curid=42936324>

**Complete blood counts:** Anemia, thrombocytopenia, and/or leukopenia may occur with the bone marrow involvement

#### Comprehensive metabolic panel:

- Serum electrolytes
- Lactic dehydrogenase (LDH)
- Renal function
- Hepatic function
- Serum  $\beta_2$  microglobulin (B-cell lymphoma) testing

#### Flow cytometry

**Bilateral iliac crest bone marrow biopsies** (staging) determines the rate of the bone marrow involvement.

**Lumbar puncture** in advanced cases (cytologic and chemical analysis of the cerebrospinal fluid).

### Imaging studies

**CT scan** of neck, chest, abdomen, and pelvis to know the extent of the disease and aids in the staging of DLBCL.

**Positron emission tomography (PET)** in higher grades of the malignant process.

**Bone imaging and bone marrow biopsy** are needed if there is a history of unexplained bone pain, elevated alkaline phosphatase levels and/or pancytopenia.

# Staging of Diffuse Large B-Cell Lymphoma

The staging of DLBCL is done, like other NHLs, by the Ann-Arbor classification.

Stage	Criteria
I	Involvement of a single lymph node region (I/N), or of a single or localized extra nodal site (I/E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II/N), or involvement of an extranodal site or organ (II/E) and one or more lymph node regions on the same side of the diaphragm (II/N/E)
III	Involvement of two or more lymph node regions on both sides of the diaphragm (III/N), or involvement of localized extranodal foci and affected lymph nodes on both sides of the diaphragm (III/E or III/N/E)
IV	Diffuse or disseminated involvement of one or more extralymphatic organs, with or without lymph node involvement

Table: "DLBCL Ann Arbor staging" by biooncology.com.

## Management of Diffuse Large B-Cell Lymphoma

Since DLBCL is a highly aggressive tumor and rapidly fatal if untreated, the treatment has to commence immediately. **The following treatment options are available:**

- Chemotherapy: The most common chemotherapy regimen for advanced DLBCL is called **R-CHOP**. R-CHOP includes **Rituximab**, **Cyclophosphamide**, **Hydroxydaunorubicin** (doxorubicin), **Oncovin** (vincristine) and **Prednisone**.
- Radiotherapy
- Chemotherapy coupled with stem cell transplantation (autologous or allogeneic) in the case of relapse of the disease.
- Regular check-up

## Prognosis of Diffuse Large B-Cell Lymphoma

The NHL international prognostic index is used to predict the prognosis of patients with DLBCL. It consists of the following five risk factors.

- > 4 affected lymph node regions
- Lactate dehydrogenase > normal
- Age > 60 years
- Ann-Arbor stage III or IV
- Hemoglobin <12g/dl

The 5-year survival rate depends upon the presence of a number of these risk factors, which is given:

Number of Risk Factors	Risk of Relapse	5-Year Survival Rate in %
0 - 1	Low	73
2 - 3	Intermediate	50
4 - 5	High	26

## Review Questions

The correct answers can be found below the references.

**1. A 67 year-old-man, plumber complains of multiple swellings in the neck, easy fatigability and bone pain at rest. On exam, his temperature is 38.9°C and he is sweaty and weak. CBC reveals a low hemoglobin and platelet count. Serum biochemistry reveals hypercalcemia. The biopsy report of the neck node is given: There are equal numbers of big and small cells mixture which have coarse chromatin in the cleaved nucleus. What is the most probable diagnosis?**

- A. Follicular lymphoma.
- B. Tuberculosis.
- C. Sarcoidosis.
- D. Diffuse large B-cells lymphoma.
- E. Mantle cell lymphoma

**2. Diffuse large B-cells lymphoma is:**

- A. Fast growing and ruthless if there is no timely treatment neoplasm, triggered by cancerous B-lymphocytes, NHL.
- B. Slow growing regardless treatment neoplasm, triggered by cancerous lymphocytes, NHL.
- C. Moderately growing on the background of proper chemotherapy neoplasm, triggered by cancerous B-lymphocytes NHL.
- D. Fast growing regardless treatment neoplasm, triggered by T-lymphocytes.
- E. None of the above.

**3. What are the most informative methods of diagnostics of DLBCL?**

- A. CBC, Flow cytometry, calcium in blood serum, LDH, serum  $\beta 2$  microglobulin (B-cell lymphoma) testing biopsy of the affected node or the organ tissue, CT.
- B. CBC, Potassium and folate in the blood serum, serum  $\beta 2$  microglobulin (B-cell lymphoma) testing CT, kidney tests and X-ray.
- C. CBC, Calcium in the blood serum, CT (bone scan), ECG, urine examination, serum  $\beta 2$  microglobulin (B-cell lymphoma) testing.
- D. CBC, Cholesterol, serum  $\beta 2$  microglobulin (B-cell lymphoma) testing, X-ray, ECG, flow cytometry, potassium in the blood serum.
- E. None of above.

## References

[Improving Outcomes for Patients with Diffuse Large B-Cell Lymphoma](http://onlinelibrary.wiley.com) via <http://onlinelibrary.wiley.com>

[Diffuse large B-cell lymphoma](http://lymphomas.org.uk) via [lymphomas.org.uk](http://lymphomas.org.uk)

[Diffuse Large B-Cell Lymphoma](http://ncbi.nlm.nih.gov) via [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov)

[Diffuse Large Cell Lymphoma Clinical Presentation](http://emedicine.medscape.com) via [emedicine.medscape.com](http://emedicine.medscape.com)

[Management of diffuse large B-cell lymphoma \(DLBCL\)](http://ncbi.nlm.nih.gov) via [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov)

**Correct answers:** 1D, 2A, 3A

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