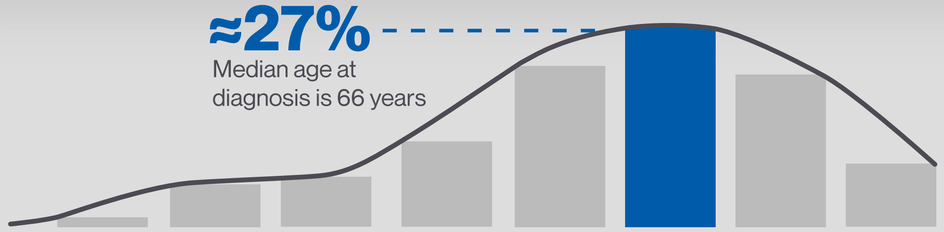
DIFFUSE LARGE B-CELL LYMPHOMA

THE MOST COMMON ADULT LYMPHOMA WORLDWIDE, WHICH IS AGGRESSIVE AND FATAL IF LEFT UNTREATED[1,2]

DLBCL is the most common form of B-cell NHL[1]

DLBCL accounts for 25-45% of NHL cases[2]



DLBCL is **most frequently diagnosed in middle-aged or older adults**; most commonly in the 65-74 years age group[3,a]

65-74 years

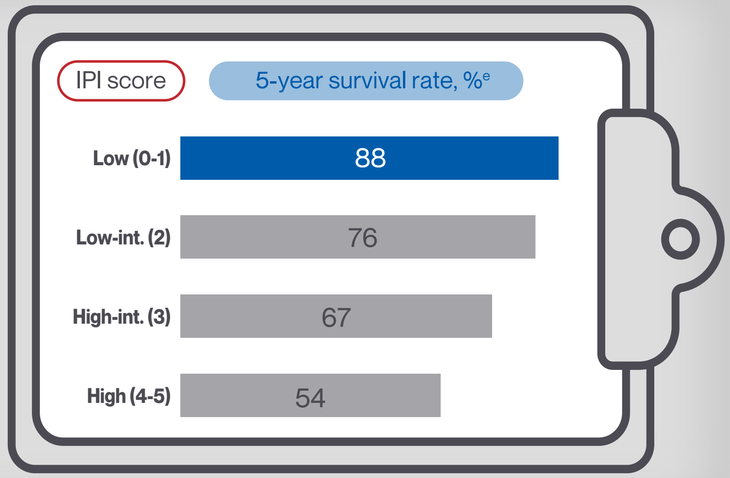
Epidemiology

DLBCL is more frequent in men than in women[3]

Rate per 100,000 persons (age-adjusted incidence)[b]

Low-risk IPI score is associated with favorable survival outcomes[4]

5-year survival rate is lower in patients with high-intermediate or high risk versus low or low-intermediate risk[4,c,d,e]



[a] Data from the U.S., between 2016 and 2020, all races, both sexes. [b] Data from the U.S., between 2016 and 2020, all races. [c] IPI risk categories. [d] Data from 2,124 patients with DLBCL enrolled in 7 multicenter randomized clinical trials and treated with R-CHOP between 1998 and 2009. [e] Based on Kaplan-Meier estimates.

DLBCL, diffuse large B-cell lymphoma; IPI, International Prognostic Index; NHL, non-Hodgkin lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

1. Sehn LH, Gascoyne RD. *Blood*. 2015;125:22-32. **2.** International Agency for Research on Cancer. Accessed Oct 2023. https://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-Cancer-Research-For-Cancer-Prevention-2020. **3.** National Cancer Institute. Accessed Oct 2023. https://seer.cancer.gov/statfacts/html/dlbcl.html. **4.** Ruppert AS, et al. *Blood*. 2020;135:2041-2048.

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The causes of DLBCL are mostly unknown[1,2]

DLBCL is **not an inherited disease**, but ~9% of patients have a first-degree relative[a] with lymphoma or CLL[3]

Factors **known to increase risk** of DLBCL:[3-5]

- **Age**
- **Immunosuppression**
- **Caucasian ethnicity**
- **Male**

Factors **suspected to increase risk** of DLBCL:[6]

- **UV radiation**
- **Pesticides**
- **Diet**
- **EBV**

DLBCL often presents as a rapidly enlarging mass

(typically a lymph node)

Patients may exhibit B symptoms:[7,8,b]

Fever
>38°C lasting ≥3 consecutive days

Weight loss
of >10% during the 6 months prior to diagnosis

Night sweats

Clinical Characteristics

The diagnosis of DLBCL relies on biopsy[9]

Excisional or incisional biopsy is the preferred type of biopsy[9]

Alternative procedures:[9]
Needle biopsy (eg, fine needle aspiration biopsy or core needle biopsy)

IPI criteria are used for risk evaluation in patients with DLBCL[10]

5

- Ann Arbor stage III-IV
- Age >60 years
- ECOG PS ≥2
- >1 extranodal site
- LDH >ULN

Patients are stratified into **low** (score 0-1), **low-intermediate** (2), **high-intermediate** (3), and **high** (4-5) prognostic risk groups[10]

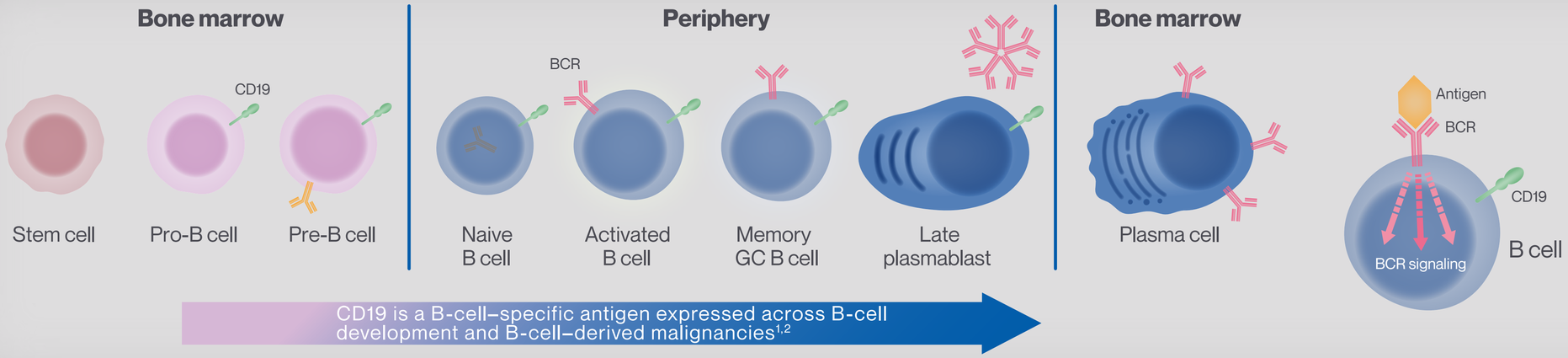
Tests for DLBCL include:[9]

- **Blood tests**
- **Imaging**
- **Heart and lung function**

[a] Parent or sibling. [b] As per Ann Arbor staging system.

CLL, chronic lymphocytic leukemia; EBV, Epstein–Barr virus; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; ULN, upper limit of normal; UV, ultraviolet.

1. Habermann TM. Accessed Oct 2023. https://www.cancertherapyadvisor.com/home/decision-support-in-medicine/hematology/diffuse-large-b-cell-lymphoma/. **2.** Lymphoma Action. Accessed Oct 2023. https://lymphoma-action.org.uk/types-lymphoma-non-hodgkin-lymphoma/diffuse-large-b-cell-lymphoma. **3.** Freedman AS, Friedberg JW. Accessed Oct 2023. https://www.uptodate.com/contents/diffuse-large-b-cell-lymphoma-in-adults-beyond-the-basics. **4.** Barlow B, Behring S. Accessed Oct 2023. https://www.healthline.com/health/diffuse-large-b-cell-lymphoma. **5.** National Cancer Institute. Accessed Oct 2023. https://seer.cancer.gov/statfacts/html/dlbcl.html. **6.** Friedberg JW, Fisher RI. He*matol Oncol Clin North Am*. 2008;22:941-952. **7.** Martelli M, et al. *Crit Rev Oncol Hematol*. 2013;87:146-171. **8.** Kumar V, et al. Recent advances in diffuse large B cell lymphoma. In: *Hematology - Latest Research and Clinical Advances*: IntechOpen; Published online 2018. **9.** American Cancer Society. Accessed Oct 2023. https://www.cancer.org/cancer/types/non-hodgkin-lymphoma/detection-diagnosis-staging/how-diagnosed.html. **10.** International Non-Hodgkin's Lymphoma Prognostic Factors Project. *N Engl J Med*. 1993;329(14):987-994.

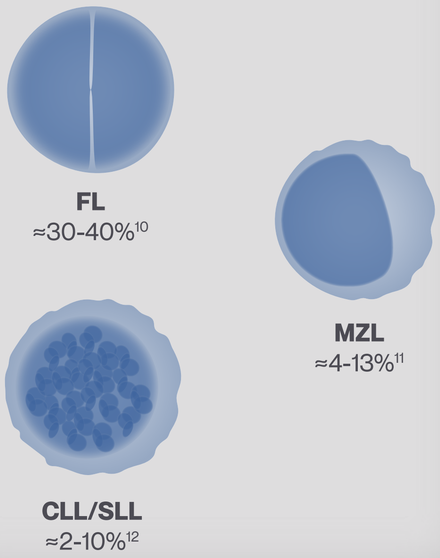


DLBCL **can arise de novo during B-cell differentiation**[6,7]
CD19 enhances BCR signaling and tumour cell proliferation[1,3-5]

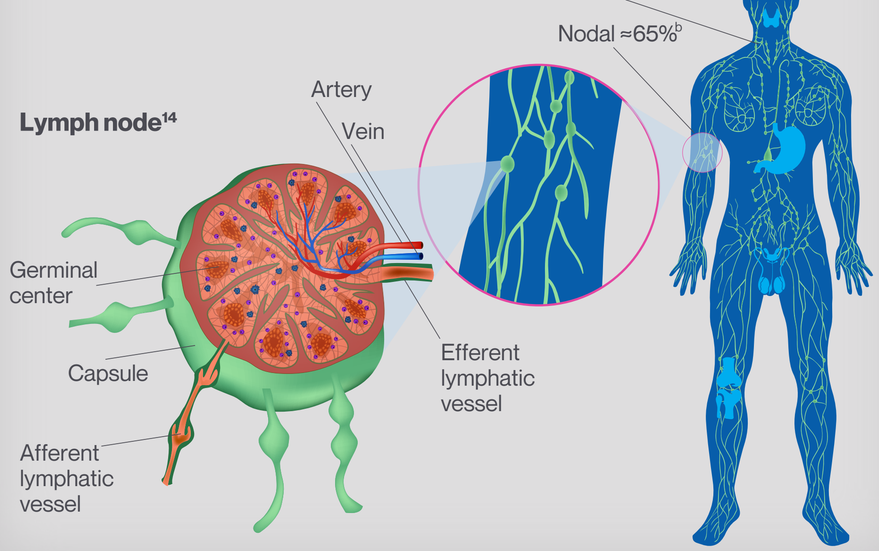
≈150 mutated genes have been identified as genetic drivers of DLBCL[8]

Development and Subtypes

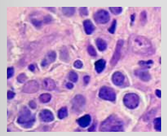
DLBCL can also result from **transformation of indolent lymphomas**[6,9,a]



Most DLBCLs occur in **lymph nodes, but some initially present in extranodal sites**[6,13]

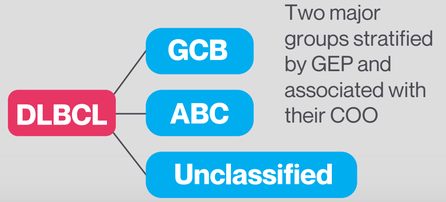


DLBCL has a **diffuse growth pattern** and cell nuclei more than twice the size of normal lymphocyte nuclei[15]



DLBCL has a **highly variable** cell morphology and nuclear appearance[16]

DLBCL subtypes can be distinguished by **genetic features**[7,17-19]



[a] Percentage of patients with the indicated histologies who develop transformation to DLBCL. [b] From a site-specific survival analysis of 93,638 patients with DLBCL aged ≥18 years in the SEER database, between 2000 and 2015.

ABC, activated B-cell–like; BCR, B-cell receptor; CD19, cluster of differentiation 19; COO, cell of origin; FL, follicular lymphoma; GC, germinal center; GCB, germinal center B-cell–like; GEP, gene expression profile; MZL, marginal zone lymphoma; SEER, Surveillance, Epidemiology, and End Results; SLL, small lymphocytic lymphoma.

1. Blanc V, et al. *Clin Cancer Res*. 2011;17:6448-6458. **2.** Del Nagro CJ, et al. *Immunol Res*. 2005;31:119-131. **3.** Cyster JG, Allen CDC. *Cell*. 2019;177:524-540. **4.** Wang K, et al. *Exp Hematol Oncol*. 2012;1:36. **5.** Poe JC, et al. *J Immunol*. 2012;189:2318-2325. **6.** Martelli M, et al. *Crit Rev Oncol Hematol*. 2013;87:146-171. **7.** Schneider C, et al. *Semin Diagn Pathol*. 2011;28:167-177. **8.** Pasqualucci L, Dalla-Favera R. *Blood*. 2018;131:2307-2319. **9.** Lossos IS, Gascoyne RD. *Best Pract Res Clin Haematol*. 2011;24:147-163. **10.** Bargetzi M, et al. *Swiss Med Wkly*. 2018;148:w14635. **11.** Alderuccio JP, Lossos IS. *Ann Lymphoma*. 2020;4:6. **12.** Broadway-Duren J. *Adv Pract Oncol*. 2022;13:535-538. **13.** Gupta V, et al. *J Hematol*. 2022;11:45-54. **14.** Blum KS, Pabst R. *J Anat*. 2006;209:585-595. **15.** Mey U, et al. *Swiss Med Wkly*. 2012;142:w13511. **16.** Gatter K, Pezzella F. *Diagn Histopathol*. 2010;16:69-81. **17.** Alaggio R, et al. *Leukemia*. 2022;36:1720-1748. **18.** Rosenwald A, et al. *N Engl J Med*. 2002;346:1937-1947. **19.** Brown JR, et al. Accessed Oct 2023. https://www.uptodate.com/contents/pathobiology-of-diffuse-large-b-cell-lymphoma-and-primary-mediastinal-large-b-cell-lymphoma.