Large B Cell Lymphoma

- High grade B cell lymphoma (HGBL) with rearrangements of MYC and BCL2 or BCL6: new category for “double hit” or “triple hit” lymphomas; excludes cases that fulfill criteria for follicular or lymphoblastic lymphoma.

- HGBL, not otherwise specified (NOS): blastoid or intermediate between diffuse large B cell lymphoma (DLBCL) and Burkitt morphology but lack MYC and BCL2 or BCL6 rearrangement.

- Double expressor phenotype: expression of MYC (> 40%) with BCL2 (> 50%), often without MYC / BCL2 translocation; may be more aggressive than DLBCL, NOS but generally less than HGBL.

- Burkitt-like lymphoma with 11q aberration: lacks characteristic MYC rearrangements; has chromosome 11q alterations and more cytologic pleomorphism than Burkitt; frequently nodal.

- DLBCL, NOS: cell of origin subclassification is required.

Mantle Cell Lymphoma (MCL)

- Classically aggressive, now two clinically indolent variants recognized:
  - Leukemic nonnodal MCL: has IGHV mutated SOX11+ B cells; usually involves blood, bone marrow, often spleen; indolent but secondary abnormalities (e.g. TP53 mutation) may result in aggressive disease.
  - In situ mantle cell neoplasia: replaces “in situ MCL”; often incidental; cyclin D1+ cells in the inner mantle zones of follicles but lacks other features to suggest MCL.

Revised Follicular Lymphoma (FL) Variants

- In situ follicular neoplasia: replaces in situ FL; has low rate of progression, often associated with prior or synchronous overt lymphomas; distinguish from partial involvement by FL.

Duodenal type FL (Fig. 1): now recognized as distinct from other GI tract FL; features overlap with in situ follicular neoplasia and MALT lymphoma; has excellent outcome, often with a watch and wait strategy.


- EBV+ DLBCL, NOS: “elderly” term now dropped but typically affects immunocompetent patients > 50 years old; generally worse prognosis than EBV− cases; excludes specific EBV+ subtypes (e.g. lymphomatoid granulomatosis).

Pediatric type FL: now a definite entity affecting children and young adults; is a localized nodal disease with low malignant potential; has expansile, highly proliferative follicles but no BCL2, BCL6 or MYC rearrangements.

Other Low Grade B Cell

- Hairy cell leukemia: BRAF V600E mutations in almost all cases.

- Hairy cell leukemia variant: MAP2K1 mutations, preferential IGHV4 - 34 gene family usage.

- Splenic diffuse red pulp small B cell lymphoma (Fig. 2): provisional entity; uncommon; diffuse involvement of splenic red pulp and bone marrow sinusoids by small, monomorphic lymphocytes and circulating villous lymphocytes.
T Cell Lymphomas (TCL)

- **Peripheral T cell lymphoma (PTCL), NOS:** very heterogeneous group actively studied to better subclassify.
- **Nodal lymphomas of T follicular helper (TFH) cell origin:**
  - Angioimmunoblastic T cell lymphoma (AITL) remains a distinct entity with characteristic morphologic findings and systemic disease.
  - Follicular TCL: morphology resembles follicular lymphoma or progressive transformation of germinal centers; lacks the vascular proliferation and expanded dendritic meshworks of AITL.
- **Node based EBV+ PTCL:** associated with immunodeficiency; most neoplastic cells are EBV+; no angioinvasion or necrosis as seen in extranodal NK / TCL.
- **ALK+ Anaplastic Large Cell Lymphoma (ALCL):** no longer provisional, improved criteria to distinguish from CD30+ PTCL, NOS; rearrangements at DUSP22 and IRF4 locus (6p25) provide superior prognosis; TP63 rearrangements (small subset) are very aggressive.
- **Breast implant associated ALCL:** usually confined to seroma / fibrous capsule enabling conservative management.
- **Enteropathy associated TCL:** formerly EATL type I; closely linked to celiac disease; cells are typically polymorphic.
- **Monomorphic epitheliotropic intestinal TCL:** formerly EATL type II; not associated with celiac disease; cells are monomorphic, usually CD8+, CD56+ and CD5+ with gains in chromosome 8q24 (MYC).
- **Primary cutaneous CD4+ small / medium T cell lymphoproliferative disease:** indolent, localized, TFH phenotype which lacks the genetic profile of nodal TFH lymphomas.
- **New provisional entities are indolent T cell lymphoproliferative disorder of the GI tract and primary cutaneous acral CD8+ TCL:** first identified on ear; both are clonal, usually CD8+ and indolent.
- **Systemic EBV+ TCL of childhood:** no longer “lymphoproliferative disorder” due to fulminant clinical course usually associated with a hemophagocytic syndrome.

**Lymphoblastic Lymphoma**

- **Early T precursor acute lymphoblastic leukemia (ALL):** retains some myeloid and stem cell features by immunophenotype and gene expression profile; CD7+, CD1a+, CD8+; positive for at least one myeloid / stem cell marker.
- **B lymphoblastic leukemia / lymphoma BCR-ABL1-like:** new provisional category with similar gene expression as ALL with BCR-ABL; often has translocations of other tyrosine kinases such as ETV6-JAK2 or BCR-JAK2 or involving CRLF2; has poor prognosis.

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**Meet the Author**

Genevieve Crane, MD, PhD is an Assistant Professor at Weill Cornell Medicine/ NY Presbyterian Hospital in the Division of Hematopathology. She received a B.S. summa cum laude in Chemical Engineering from Rice University, a M.Phil. from University College London as a British Marshall Scholar and M.D. and Ph.D. degrees from the University of Michigan. She did postdoctoral work at MIT before completing her AP residency and a Hematopathology fellowship at Johns Hopkins Hospital.

Dr. Crane has authored more than 30 journal articles and has 2 related patents. She is Section Editor for Hematopathology at Arch Pathol Lab Med and PathologyOutlines.com, a reviewer for multiple pathology journals and is on the Education Committee for the Society of Hematopathology. Follow her on twitter @evemariecrane.