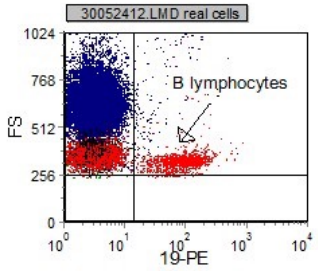
B CELL LYMPHOMAS
Introductory Lecture

Lab Techniques Review

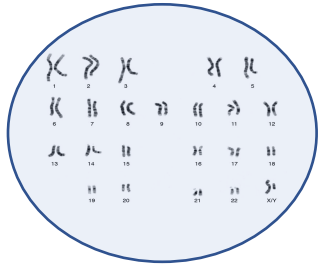
Flow Cytometry



Cell shape/size and CD marker identifies the cell population

Blood or Bone Marrow Flow Cytometry Result:
There is a 20% abnormal CD20+ population

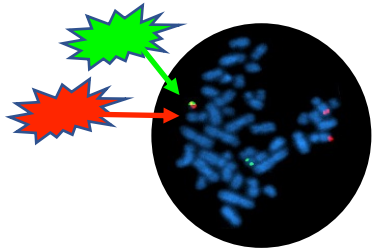
Karyotyping



Visual inspection of metaphase chromosomes reveals large gene changes

Karyotype result:
There is trisomy 8. There is translocation (8;14)

FISH



Fluorescently tagged DNA probes can detect target DNA sequences

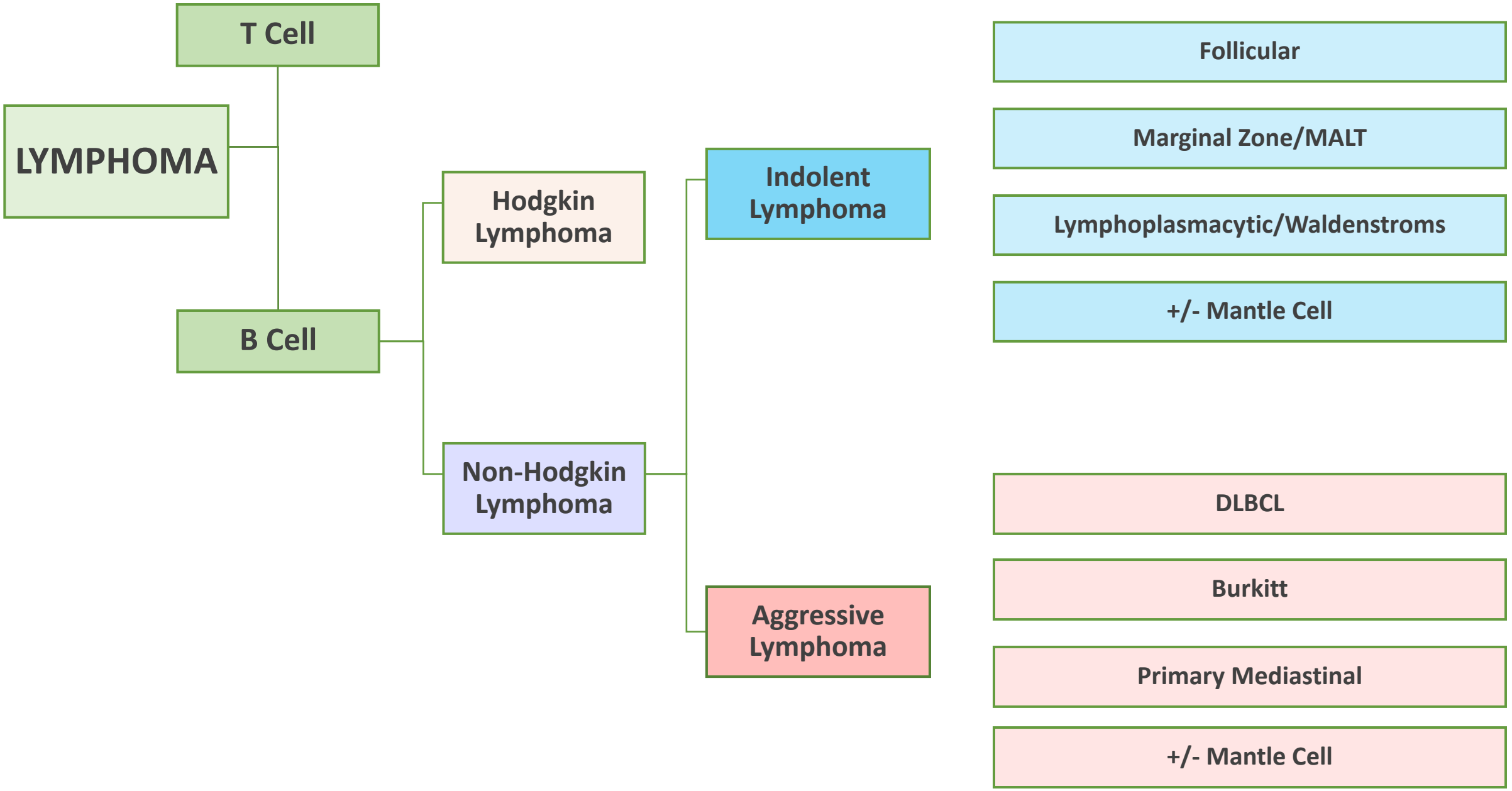
FISH result:
There are X copies of a BCR-ABL translocation

NGS

GGCCTAA → GGTCCAA

Gene Sequencing sequences specific genes and detects ANY gene mutations

NGS result:
There is a FLT3 mutation

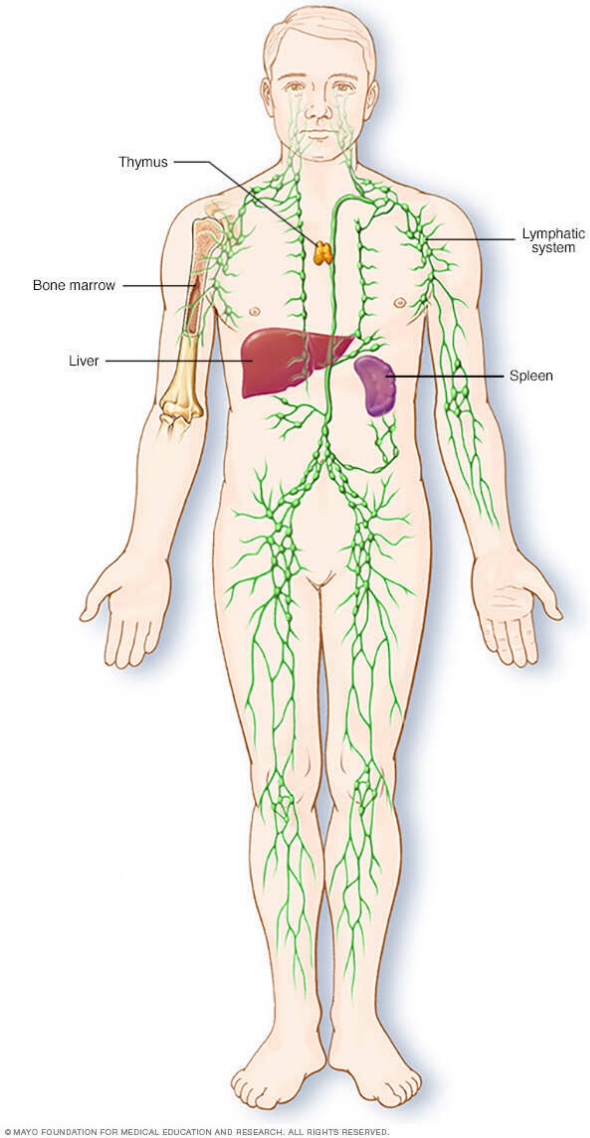

LYMPHOMA
T Cell
B Cell
Hodgkin Lymphoma
Non-Hodgkin Lymphoma
Indolent Lymphoma
Aggressive Lymphoma
Follicular
Marginal Zone/MALT
Lymphoplasmacytic/Waldenstroms
+/- Mantle Cell
DLBCL
Burkitt
Primary Mediastinal
+/- Mantle Cell

B Cell Lymphomas

Hodgkin Lymphoma

+

Non-Hodgkin Lymphoma (NHL)

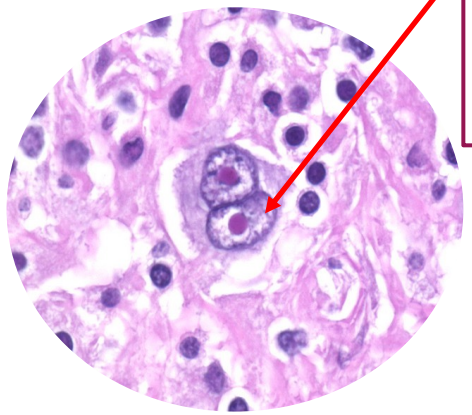


https://www.beaconhealthsystem.org/library/diseases-and-conditions/lymphoma/

B Cell Lymphomas

Hodgkin Lymphoma

Presence of Reed-Sternberg Cells



"Owl Eye" Nuclei = Clearing around nucleoli
- Often bi-lobed nuclei
- Cytoplasm retracts → appearance of cells w/ surrounding lacunae

+

Non-Hodgkin Lymphoma (NHL)

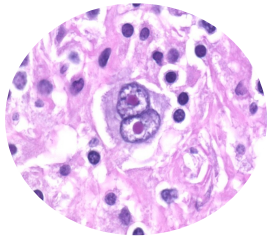
Absence of Reed-Sternberg Cells

https://www.webpathology.com/

B Cell Lymphomas

Hodgkin Lymphoma

→ **Presence of Reed-Sternberg Cells**



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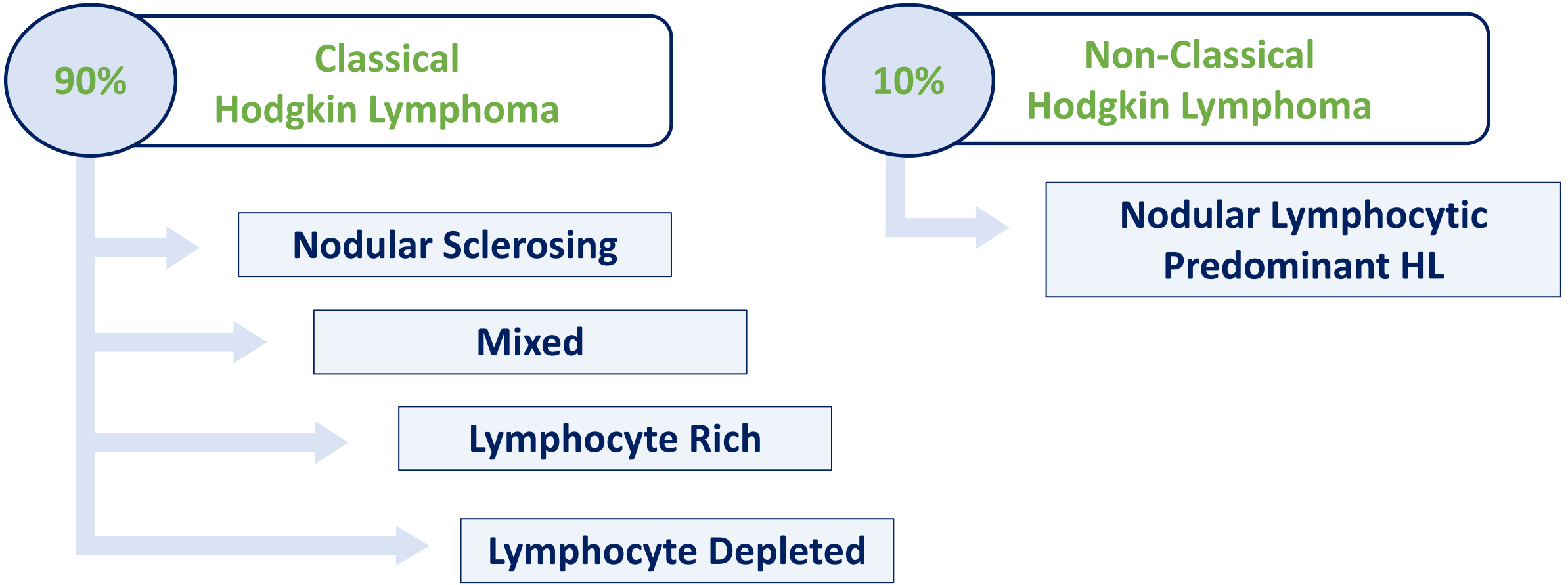
Non-Hodgkin Lymphoma (NHL)

→ **Indolent Lymphomas**

→ **Aggressive Lymphomas**

Hodgkin Lymphoma

Types of HL


90%
Classical
Hodgkin Lymphoma
Nodular Sclerosing
Mixed
Lymphocyte Rich
Lymphocyte Depleted
10%
Non-Classical
Hodgkin Lymphoma
Nodular Lymphocytic
Predominant HL

Risk Factors for HL

Risk Factors
Age (Bi-modal: 20's, 60s)
Immunosuppression
Autoimmune Disease
Infections (HIV, EBV)

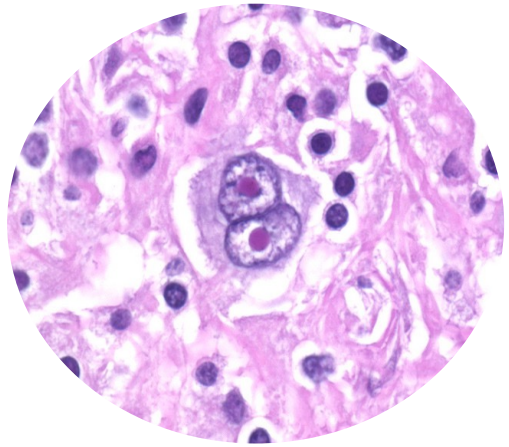
Diagnosis of HL

#1 **Excisional LN Biopsy → <u>DIAGNOSIS</u>**

Flow Cytometry

CD15+/CD30+

* NLPHL sub-type is CD20+, CD15-/CD30-



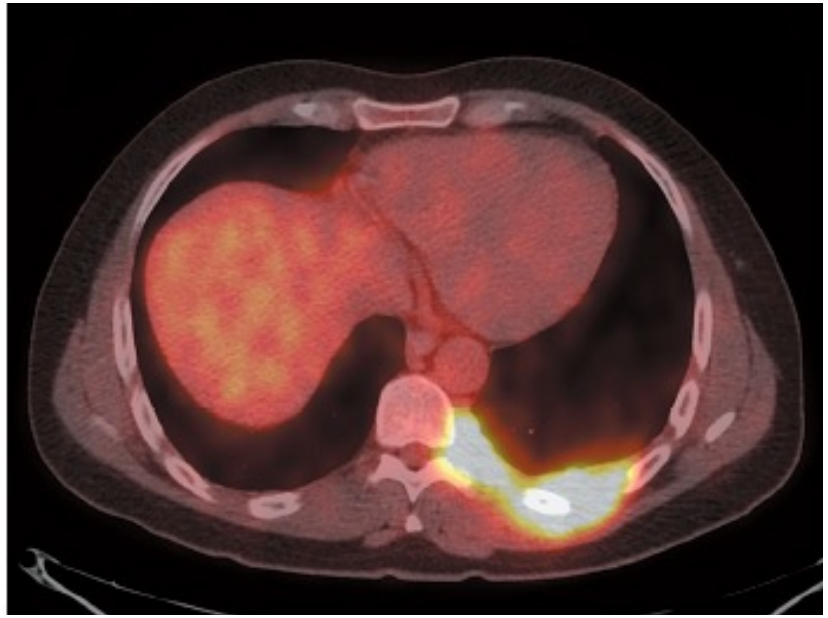
Histology

Reed Sternberg Cells

* Hodgkin Lymphoma is the "**odd**" lymphoma separate from NHLs. **CD15** is odd

Radiographic Staging

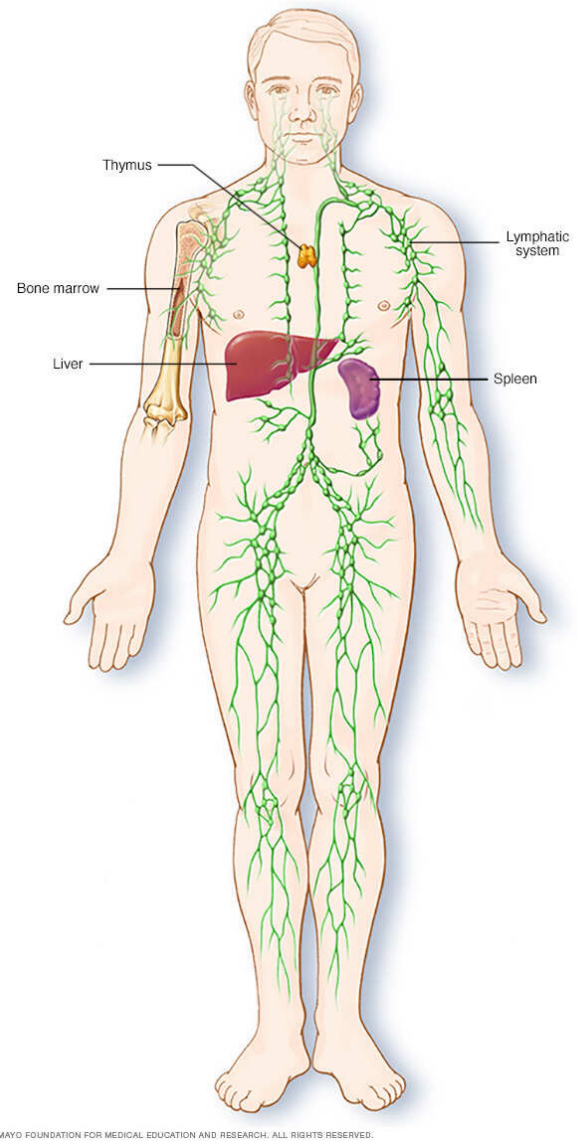
#2 PET Scan → STAGING



Deauville Score	
Score 1	No uptake
Score 2	Uptake < Liver
Score 3	**Uptake similar to Liver**
Score 4	Uptake moderately > Liver
Score 5	Uptake markedly > Liver

https://radiologykey.com/lymphoma-8/

Lymphoma Staging



Ann Arbor Staging	
Stage I	**1 LN** (ex: LN, spleen, thymus, waldeyer's ring)
Stage II	**2+ LN same side diaphragm**
Stage III	**2+ LN both sides diaphragm**
Stage IV	**Extra-Nodal Organ** (ex: liver, bone marrow)
A/B	**A = No B symptoms** **B = Yes B symptoms** (weight loss, night sweats, fevers)
X	**Bulky Disease:** **1. Mediastinal mass > 1/3 diameter thorax** **2. Mass > 10 cm**

Risk Factors for HL

Bad Prognostic Factors	Prognosis
Age >45	Cure > 80% Patients
Male	Early Stage >90% 5 year OS
Stage IV	
WBC > 15 or lymphopenia	Late Stage > 75% 5 year OS
Hemoglobin < 10.5	
Albumin < 4	

* Positive PET after 2 cycles chemotherapy

Chemotherapy Regimens HL

ABVD	notable side effects
A Doxorubicin	* cardiac toxicity
B Bleomycin	* pulmonary toxicity
V Vinblastine	* neurotoxicity
D Dacarbazine	

General Side Effects:
myelosuppression, infertility, secondary malignancy, alopecia

**** ABVD = most common regimen in HL**

BEACOPP
B Bleomycin
E Etoposide
A Adriamycin
C Cyclophosphamide
O Vincristine
P Procarbazine
P Prednisone

Stanford V
MOPP

**** BEACOPP = utilized if poor response to ABVD**

Classic HL Treatment Stage I- IIA

2-4 Cycles ABVD + RT

* 4 cycles if unfavorable
(bulky disease, B symptoms, 3+ LN)

Classic HL Treatment Stage IIB-IV

6 Cycles ABVD +/- RT

* RT if bulky disease

ABVD	
A	Doxorubicin
B	Bleomycin
V	Vinblastine
D	Dacarbazine

TREATMENT RESPONSE MONITORING

* Usually get re-staging PET after cycle 2 to assess response (goal Deauville <3)

PULMONARY CONSIDERATIONS

** Can omit bleomycin in cycle 3-6 if good response on restaging PET

** Can replace bleomycin with brentuximab if bad lung disease

HL Treatment Stage I-IIA

FAVORABLE

2 Cycles ABVD → Restage PET → 20 Gy RT

UNFAVORABLE

- Bulky
- B Symptoms
- 3+ LNs

2 Cycles ABVD → Restage PET → 2 Cycles ABVD + 30 Gy RT

HL Treatment Stage IIB-IV

2 Cycles ABVD → Restage PET → 4 cycles ABVD + RT if bulky disease

*** If Deauville > 3 on restaging PET, consider switch to BEACOPP**

Non-Classical HL = NLPNL

Treat more like NHL

Stage IA-IIA	→	**RT Alone**
Stage IB-IIB	→	**ChemoRT**
Stage III-IV	→	**Observe if asymptomatic, non-bulky** **Rituximab monotherapy** **R-CHOP if advanced**

Non-Hodgkin Lymphoma

Aggressive NH Lymphomas

- DLBCL (Diffuse Large B Cell Lymphoma)
- Primary Mediastinal Large B-Cell Lymphoma
- Burkitt Lymphoma
- Mantle Cell Lymphoma
- Angioimmunoblastic T Cell Lymphoma
- Anaplastic Large Cell Lymphoma
- Peripheral T Cell Lymphoma

Indolent NH Lymphomas

- SLL/CLL
- Follicular Lymphoma
- Marginal Zone Lymphoma
- Mantle Cell Lymphoma
- Lymphoplasmacytic Lymphoma/Waldenstrom's Macroglobulinemia
- Cutaneous T-Cell Lymphoma

* Mantle cell can be indolent or aggressive

Aggressive NH Lymphomas

GENERAL TREATMENT PRINCIPLES

- All stages need aggressive chemotherapy, ex:

  R-CHOP
  R-HyperCVAD
  R-EPOCH
  R-Bendamustine (*old/poor ECOG)

Indolent NH Lymphomas

GENERAL TREATMENT PRINCIPLES

- Early stages (I-II), low-grade or slow growing can:

  Observe if asymptomatic
  RT Monotherapy
  Rituximab

- Advanced Stages (III-IV) often require chemo

AGGRESSIVE NH LYMPHOMAS

Aggressive NH Lymphomas

- DLBCL (Diffuse Large B Cell Lymphoma)
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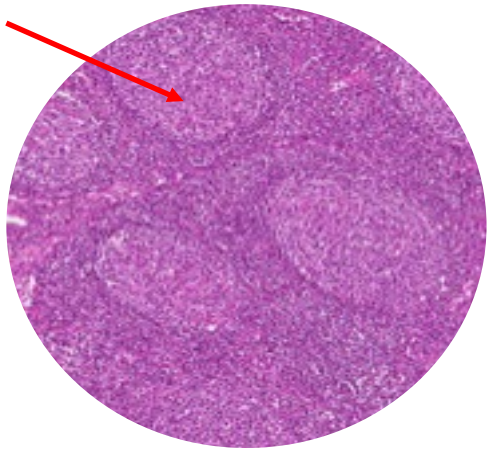
Diffuse Large B Cell Lymphoma = DLBCL

Germinal Center



Normal LN

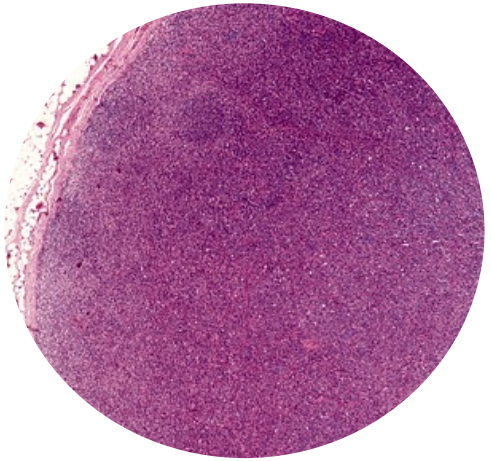
Flow Cytometry

CD10+, CD20+

Cytogenetics

BCL2 = t(14;18), t(3;14)
BCL6 = t(3;V)
C-MYC = t(2;8), t(8;14), t(8,22)

* t(14;18) seen in Follicular Lymphoma
* t(8;14) seen in Burkitt Lymphoma



Diffuse LN involvement
Lack of normal
lymphoid structures

* **DOUBLE HIT** DLBCL = mutations in **MYC** and **BCL2 +/- BCL6**

UpToDate® https://www.proteinatlas.org/learn/dictionary/normal/lymph+node

Diffuse Large B Cell Lymphoma = DLBCL

Epidemiology

- Most common NHL (25%)
- Male > female
- White > blacks
- Primary or Secondary disease
- Secondary: POD from CLL, Follicular lymphoma, MALT, splenic marginal zone

Presentation

- Rapidly enlarging, symptomatic mass
- 60% stage III-IV at presentation
- 30% BM involvement at presentation
- 30% B symptoms

Prognosis

- 5 Year OS 75%

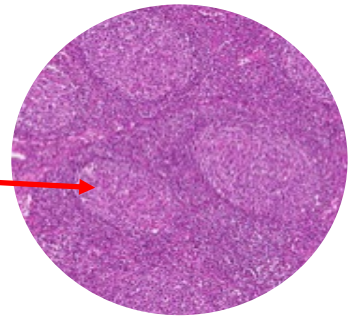
DLBCL

DLBCL Cell of Origin

Germinal B Cell
(better prognosis)

Activated B Cell
(worse prognosis)

Germinal Center



IHC

CD10+

- → BCL6
- \+ → GCB

BCL6

- → Non-GCB
- \+ → MUM1

MUM1

- → GCB
- \+ → Non-GCB

A germinal center is a site within LN or spleen where B cells maturate

DLBCL

Bad Prognostic Factors

- Age > 60
- ECOG >2
- LDH
- Stage III-IV
- >2 Extra-nodal sites

Risk for CNS Involvement

- Elevated LDH
- Extra-Nodal Sites
  (testes, breast, sinus, orbits, BM, kidney, adrenal)
- Double hit, c-MYC

APpLES “Apples” = Age, PS, LDH, Extra-Nodal Sites, Stage

DLBCL

RCHOP **3 cycles stage I-II, non-bulky** **6 cycles stage III-IV or bulky**	**+ RT in limited stage**
R Rituximab	* Hepatitis Reactivation * Infusion Reaction
C Cyclophosphamide	
H Doxorubicin	* Cardiotoxicity
O Vincristine	* Neurotoxicity
P Prednisone	

+ CNS Prophylaxis (all stages)
IT Methotrexate (MTX)
IT Cytarabine (ARAC)
High-dose IV MTX

DOUBLE HIT DLBCL = mutations in **MYC** and **BCL2 +/- BCL6**

Treat with more aggressive chemo: R-EPOCH, R-HyperCVAD, clinical trial

DLBCL

Relapsed/Refractory Treatment

1) Chemotherapy → Auto-SCT: if chemosensitive in 2nd remission

2) Immunotherapy → CarT: if not chemosensitive

DLBCL

Relapsed/Refractory Chemo Regimens

2nd line regimens referred to as ”platinum-based”
1st line regimens referred to as “anthracycline-based”

R-ICE

ICE = ifosfamide, carboplatin, etoposide

R-DHAP

DHAP = dexamethasone, high-dose cytarabine, cisplatin

R-GDP

GDP = gemcitabine, dexamethasone, cisplatin

R-GemOx

GemOx = gemcitabine, oxaliplatin

DLBCL

Immunotherapy

Polatuzumab (R-Pola-Benda)
Anti-CD79b

Tafasitamab (Tafasitamib-Venetoclax)
Anti-CD19

Brentuximab
Anti-CD30

Blinatumomab
BiTE = bispecific T cell engager CD3/CD19

CAR-T
Chimeric antigen receptor T cell

Common Regimens:

1. R- Polatuzumab-Bendamustine

2. Tafastiamib-Venetoclax

Primary Mediastinal B-Cell Lymphoma

Pathology

- From thymic (medullary) B cells

Flow Cytometry

CD20+
CD10+/-
CD30+/-

Cytogenetics

CIITA t(16;X)

Presentation

- Rapidly enlarging, symptomatic mass
- Can have airway compromise or SVC syndrome

Primary Mediastinal B-Cell Lymphoma

R-EPOCH x 6-8 Cycles	
R	Rituximab
E	Etoposide
P	Prednisone
O	Vincristine
C	Cyclophosphamide
H	Doxorubicin

RCHOP x 6 cycles + RT	
R	Rituximab
C	Cyclophosphamide
H	Doxorubicin
O	Vincristine
P	Prednisone

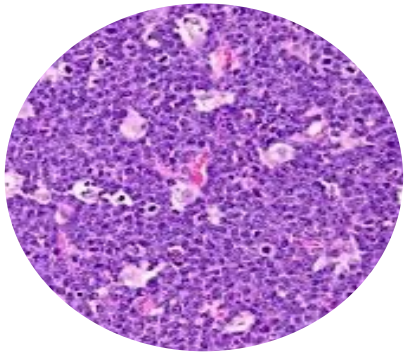
Burkitt Lymphoma

* Endemic Burkitt Lymphoma occurs in young boys classically. t(**8**;14) is **young.**
* **"Myc"-y** mouse is **young**.

Flow Cytometry — **CD10+/CD20+**

Cytogenetics — **C-MYC = t(8;14),** t(2;8), t(8;22)

Histology — **"starry sky"**



Sky = monotonous lymphoid cells
Stars = macrophages w/ apoptotic tumor cells

Burkitt Lymphoma

Types

- Endemic (associated w/ EBV)
  common sites: jaw, bone, kidney, breast, ovaries, cecum
  peak incidence 4-7 yo; male > female
- Sporadic
  common sites: ileocecal
  median age 30 yo
- Immunodeficiency Associated (HIV, post-transplant)

Clinical Features

- TLS
- 70% BM involvement
- 40% leptomeningeal disease

Burkitt Lymphoma

Prognosis

- 5 Year OS 90%

R-HyperCVAD	
R	Rituximab
C	Cyclophosphamide
V	Vincristine
A	Doxorubicin
D	Dexamethasone
IT MTX/ARAC alternating	

Mantle Cell Lymphoma

Flow Cytometry	**CD5+/CD23-, Cyclin+**
Cytogenetics	**Cyclin = t(11;14)**

*C**LL** = Two “L”s = CD5**+** and CD23**+.** Mant**L**e = One “L” = just CD5**+**
** A Mantle has two pillars = like t(**11**;**14**)

Mantle Cell Lymphoma

Stage I-II → **Chemo + RT**

Stage IIB-IV → **Chemo + AutoSCT**
+ maintenance rituximab

Chemotherapy Options
R-HyperCVAD
R-HyperCHOP
R-Bendamustine * Better if older/poor ECOG

Relapsed/Refractory
BTK Inhibitor Ibrutinib, Acalabrutinib
Lenalidomide
CAR-T

Post Transplant Lymphoproliferative Disorder = PTLD

Definition

- Occurs post-transplant
- Especially in solid-organ transplants (heart, lung)
- Associated w/ EBV+
- Can be any type of lymphoma

Treatment

- **HL PTLD =**
  Treat as Hodgkin's Lymphoma (ABVD/RT)
- **NHL PTLD =**
  1st line = Reduce immunosuppression
  2nd line = Rituximab
  3rd line = R + chemotherapy

INDOLENT LYMPHOMAS

Aggressive NH Lymphomas

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Aggressive NH Lymphomas

GENERAL TREATMENT PRINCIPLES

- All stages need aggressive chemotherapy, ex:

  R-CHOP
  R-HyperCVAD
  R-EPOCH
  R-Bendamustine (*old/poor ECOG)

Indolent NH Lymphomas

GENERAL TREATMENT PRINCIPLES

- Early stages (I-II), low-grade or slow growing can:

  Observe if asymptomatic
  RT Monotherapy
  Rituximab

- Advanced Stages (III-IV) often require chemo

Follicular Lymphoma

Flow Cytometry	**CD10+/CD20+**
Cytogenetics	**BCL2 = t(14;18)**

* **Follicular** is like **Four** = t(**14**,18) = **Fourteen** (and 4x2 = 8 → 18)

Follicular Lymphoma

FLIPI = FL International Prognostic Index

Age > 60	**Low = 0-1** **Intermediate = 2** **High = 3-5**
Node Sites > 4	
Elevated LDH	
Hb < 12	
Ann Arbor III-IV	

Histological Grade

Grade 1-2 **LOW GRADE**	**< 15 centroblasts/hpf**
Grade 3 **HIGH GRADE**	**> 15 centroblasts/hpf**

Follicular Lymphoma

Treat If:

- Curative
- B symptoms
- Organ dysfunction
- Cytopenias
- Bulky Disease
- POD

Limited Stage I-II
Low Grade

→

Observation
Rituximab Monotherapy
RT curative in stage I or contiguous stage II

Advanced Stage III-IV
Low Grade

→

Observation
Rituximab Monotherapy
R-CHOP
R-Bendamustine
R-Lenalidomide
R-CVP

High Grade

→

Treat like DLBCL: R-CHOP

* Maintenance therapy w/ rituximab x2 years improves PFS not OS

Marginal Zone Lymphoma

Flow Cytometry — **CD20+, MUM1+**

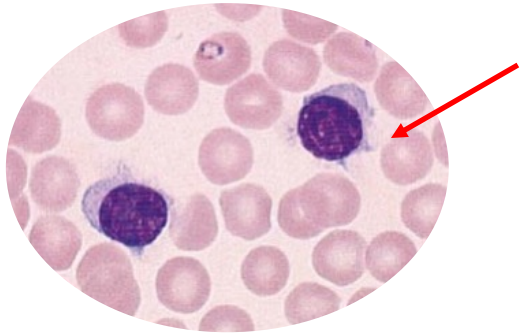
Cytogenetics — **t(11;18)**

ID Associations

Gastric MALT	**H.pylori**
Splenic MZL	**HCV**
Cutaneous MZL	Borrelia burgdorferi
Body cavity MZL	HHV8
Orbital MZL	Chlamydia psittacosis
Intestinal MZL	Campylobacter

Pathology

- **"Marginal Zone"** = lymphoma that grows at edge or margin of lymphoid tissue
- Can involve any organ
- Associated with autoimmune conditions
- Associated with infections
- Marginal Zones = near blood stream → circulating Lymphocytes w/ villous cytoplasmic projections



villous cytoplasmic projections

https://www.nejm.org/doi/full/10.1056/nejmoa013376

Marginal Zone Lymphoma

"MALT" = Mucosa Associated Lymphoid Tissue
= Type of MZL

Gastric MALT

Stage I-II **+ H.pylori**	Treat H.pylori
Stage I-II **- H.pylori**	RT Rituximab
Stage III-IV	RT Rituximab Systemic Chemo

Splenic Marginal Zone Lymphoma

Stage I-II **+ HCV**	Treat HCV
Stage I-II **- HCV**	Splenectomy Rituximab
Stage III-IV	RT Rituximab Systemic Chemo

Lymphoplasmacytic Lymphoma/Waldenstrom's Macroglobulinemia

Pathology

- **Lymphoplasmacytic precursors**
  (unlike MM, where plasma cell is precursor)
- **Produces IgM**

Flow Cytometry

CD20+
CD25+/-
CD38+/-

Cytogenetics

PAX5 = t(9;14)

Complications

- **Hyperviscosity Syndrome**
- **Cryoglobulinemia**
- **Cold agglutinin**

Lymphoplasmacytic Lymphoma/Waldenstrom's Macroglobulinemia

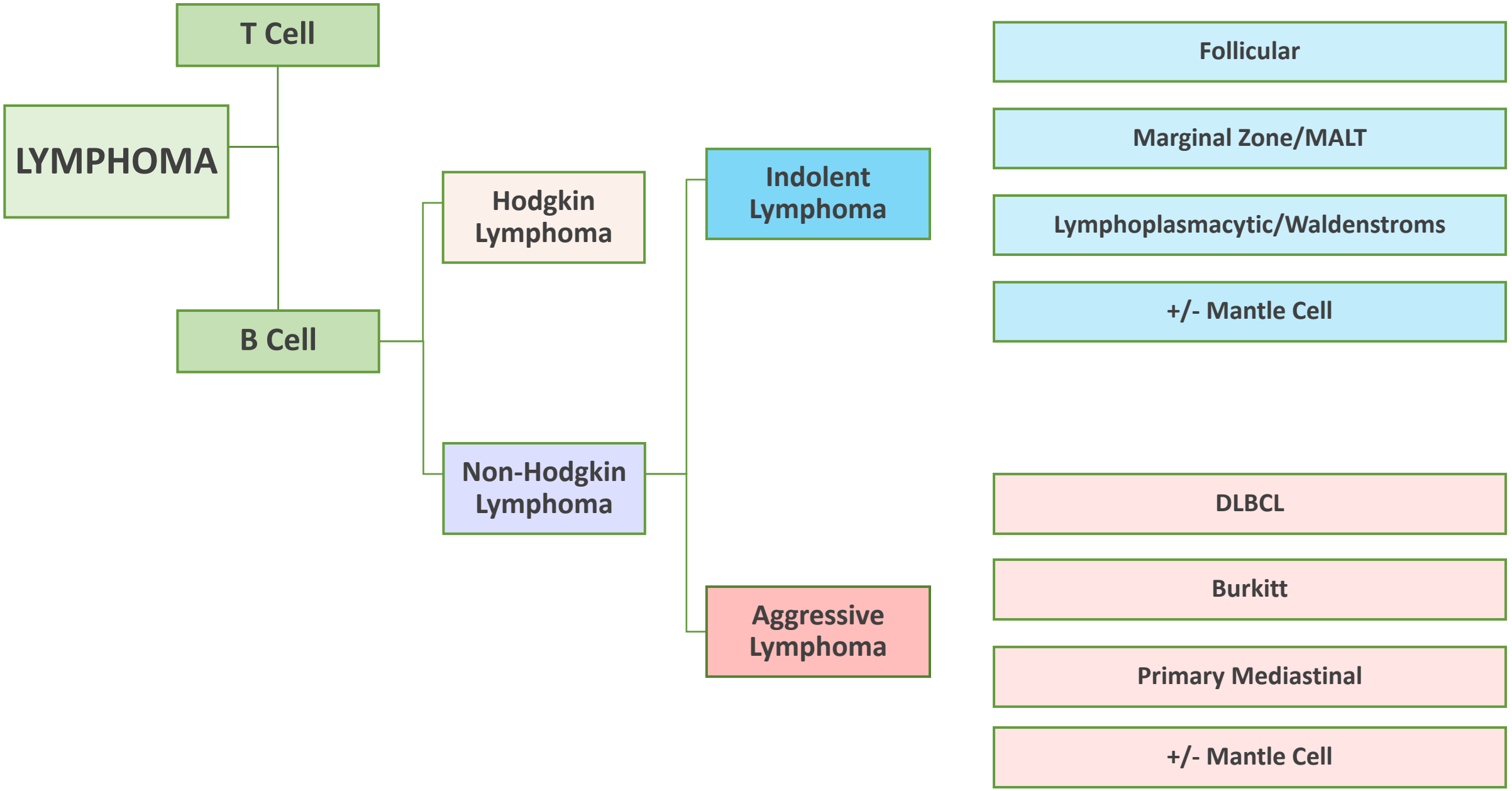
Proteasome Based
Bortezomib/Rituximab
Bortezomib/Dexamethasone
Bortezomib/Dexamethasone/Rituximab
Carfilzomib/Rituximab/Dexamethasone

Chemo-Immunotherapy/Immunotherapy
R-CHOP
R-Bendamustine

Other
Ibrutinib

* Avoid single-agent rituximab as this can cause an IgM flair

B CELL LYMPHOMA Reference Handout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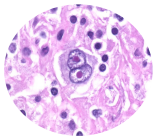
HL Pathology & Histology

Hodgkin's Lymphoma

Presence of Reed-Sternberg Cells



Non-Hodgkin's Lymphoma (NHL)

Absence of Reed-Sternberg Cells

Classical HL = 95%	Non-Classical HL = 5%
Nodular Sclerosis	Nodular Lymphocytic Predominant HL
Mixed	
Lymphocyte Rich	
Lymphocyte Poor	

HL Risk

Risk Factors
Age (Bi-modal: 20's, 60s)
Immunosuppression
Autoimmune Disease
Infections (HIV, EBV)

HL Diagnosis

#1 Excisional LN Biopsy → DIAGNOSIS

- Histology → Reed Sternberg Cells
- Flow Cytometry → CD15+/CD30+
  ** NLPHL sub-type is CD20+

#2 PET Scan → STAGING

Deauville Score	
Score 1	No uptake
Score 2	Uptake < Liver
Score 3	Uptake similar to Liver
Score 4	Update moderately > Liver
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HL/NHL staging

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Stage I	1 LN
Stage II	2+ LN same side diaphragm
Stage III	2+ LN both sides diaphragm
Stage IV	Extra-Nodal Organ
A/B	A = No B symptoms B = Yes B symptoms
X	Bulky Disease: 1. Mediastinal mass > 1/3 diameter thorax 2. Mass > 10 cm

HL Chemotherapy

ABVD	side effects
A Doxorubicin	* cardiac toxicity
B Bleomycin	* pulmonary toxicity
V Vinblastine	* neuropathy
D Dacarbazine	

General Side Effects:
myelosuppression, infertility, secondary malignancy

BEACOPP

Stanford V

MOPP

HL Treatment Paradigm

Classic HL Treatment Stage I- IIA

2-4 Cycles ABVD + RT

* 4 cycles if unfavorable
(bulky disease, B symptoms, 3+ LN)

Classic HL Treatment Stage IIB-IV

6 Cycles ABVD +/- RT

* RT if bulky disease

TREATMENT RESPONSE MONITORING

- Usually get re-staging PET after cycle 2 to assess response (goal Deauville <3)

PULMONARY CONSIDERATIONS

** Can omit bleomycin in cycle 3-6
** Can replace bleomycin with brentuximab if bad lung disease

HL Prognosis

Prognosis

Cure > 80% Patients

Early Stage >90% 5 yr OS

Late Stage > 75% 5 yr OS

Poor Prognostic Factors

Age >45

Male

Stage IV

WBC > 15 or lymphopenia

Hemoglobin < 10.5

Albumin < 4

* Positive PET after 2 cycles chemotherapy

Aggressive NHL

DLBCL

- Most common NHL (25%)
- Primary or Secondary disease

Flow Cytometry

CD10+, CD20+

Cytogenetics

BCL2 = t(14;18), t(3;14)
BCL6 = t(3;V)
C-MYC = t(2;8), t(8;14), t(8,22)

RCHOP	
R	Rituximab
C	Cyclophosphamide
H	Doxorubicin
O	Vincristine
P	Prednisone

DOUBLE HIT DLBCL = mutations in **MYC** and **BCL2 +/- BCL6**

Aggressive NHL

Burkitt Lymphoma

Flow Cytometry

CD10+/CD20+

Cytogenetics

C-MYC= t(2;8), t(8;14), t(8,22)

Histology

"starry sky"

R-HyperCVAD	
R	Rituximab
C	Cyclophosphamide
V	Vincristine
A	Doxorubicin
D	Dexamethasone
IT MTX/ARAC alternating	

1) Endemic (EBV)
2) Sporadic
2) Immunodeficiency Associated (HIV, post-transplant)

Aggressive NHL

Primary Mediastinal B-Cell Lymphoma

Flow Cytometry

CD20+, CD10 +/-, CD30 +/-

Cytogenetics

CIITA t(16;X)

- From thymic (medullary) B cells
- Rapidly enlarging, symptomatic mass: can have airway compromise or SVC syndrome

R-EPOCH	
R	Rituximab
E	Etoposide
P	Prednisone
O	Vincristine
C	Cyclophosphamide
H	Doxorubicin

+/- Aggressive NHL

Mantle Cell Lymphoma

Flow Cytometry

CD5+/CD23-, Cyclin+

Cytogenetics

Cyclin = t(11;14)

Stage I-II → **Chemo + RT**

Stage IIB-IV → **Chemo + AutoSCT**

Chemotherapy Options
RCHOP
R-HyperCVAD
R-Bendamustine * Better if older/poor ECOG

Relapsed/Refractory
BTK Inhibitor: Ibrutinib, Acalabrutinib
Lenalidomide
CAR-T

Indolent NHL — Follicular Lymphoma

Flow Cytometry

CD10+/CD20+

Cytogenetics

BCL2 = t(14;18)

FLIPI

Age > 60	**Low = 0-1** **Intermediate = 2** **High = 3-5**
Node Sites > 4	
Elevated LDH	
Hb < 12	
Ann Arbor III-IV	

Histology

Grade 1-2 = LOW GRADE	**< 15 centroblasts/hpf**
Grade 3 = HIGH GRADE	**> 15 centroblasts/hpf**

Limited Stage I-II
Low Grade → **Observation**
RT (curative)
Rituximab

Advanced Stage III-IV
Low Grade → **Observation**
Rituximab
R-CHOP
R-Bendamustine
R- Lenalidomide
R- CVP

High Grade → **Treat like DLBCL: R-CHOP**

* Maintenance therapy w/ rituximab x2Y improves PFS

Indolent NHL — Marginal Zone Lymphoma/MALT Lymphoma

Flow Cytometry

CD20+, MUM1+

Cytogenetics

t(11;18)

- **"Marginal Zone"** = lymphoma that grows at edge or margin of lymphoid tissue
- Can involve any organ
- MALT = mucosal associated lymphoid tissue = type of MZL
- Associated with autoimmune conditions, infections

Gastric MALT

Stage I-II **+ H.pylori**	Treat H.pylori
Stage I-II **- H.pylori**	RT Rituximab
Stage III-IV	RT Rituximab Systemic Chemo

Splenic Marginal Zone Lymphoma

Stage I-II **+ HCV**	Treat HCV
Stage I-II **- HCV**	Splenectomy Rituximab
Stage III-IV	RT Rituximab Systemic Chemo

Indolent NHL — Lymphoplasmacytic Lymphoma/ Waldenstroms Macroglobulinemia

Flow Cytometry

CD20+
CD25+/-, CD38+/-

Cytogenetics

PAX5 = t(9;14)

- **Lymphoplasmacytic precursors**
- **Produces IgM**
- **Complications:**
  - hyperviscosity
  - cryoglobulinemia
  - cold agglutinin

Proteasome-Based:
Bortezomib, Rituximab, Dexamethasone

Chemo-Based:
R-CHOP, R-Bendamustine

TKI: Ibrutinib