

# **The "CHOPS" and "Bends" of Lymphoma: Breakdown of Lymphoma and the Current Therapeutic Approaches**

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# Presenter Disclosure

- **Faculty:** Roopesh Kansara
- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
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  - **Consulting Fees:** None
  - **Other:** None

# Mitigating potential bias

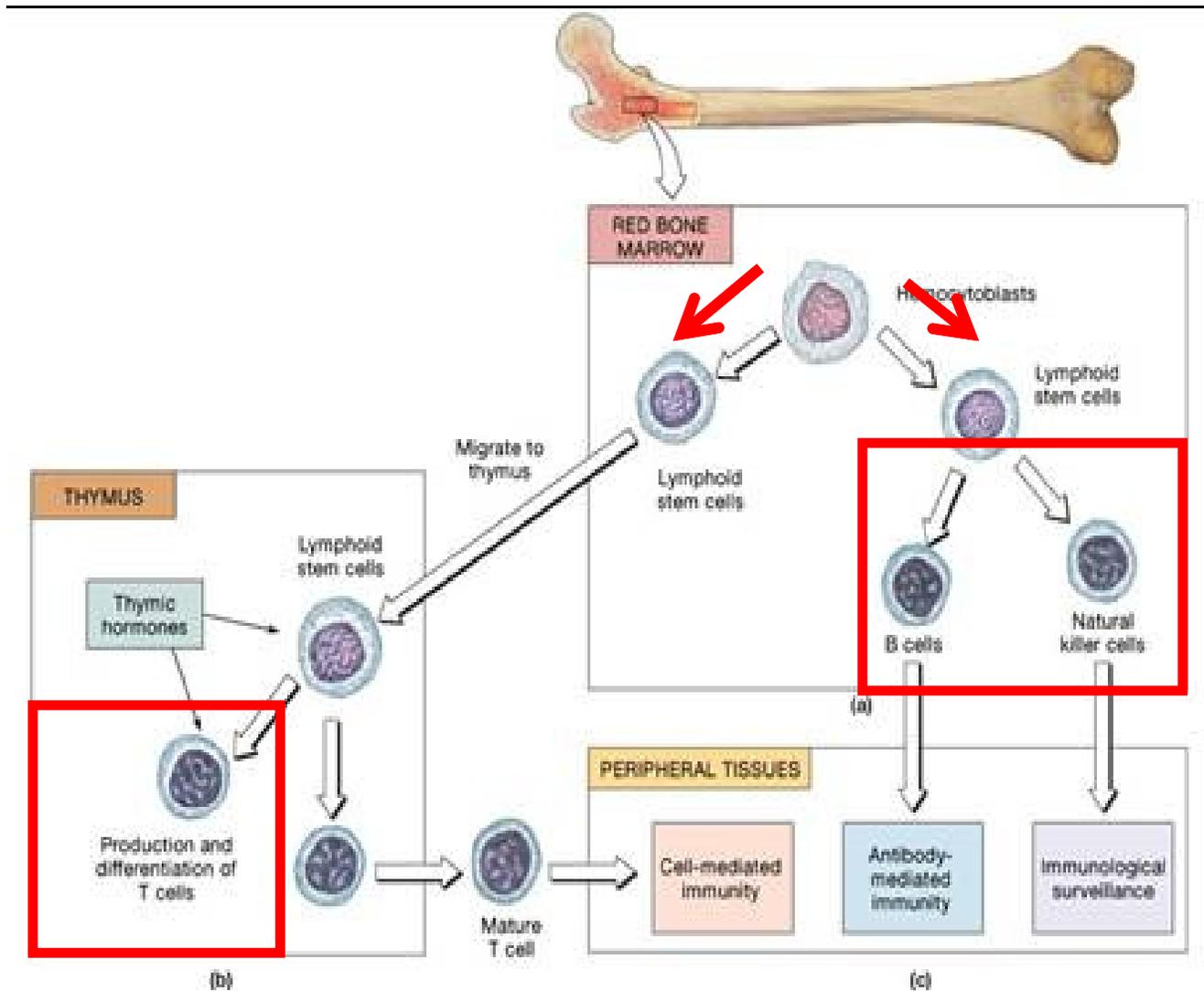
- No bias as this is an overview

# Learning Objectives

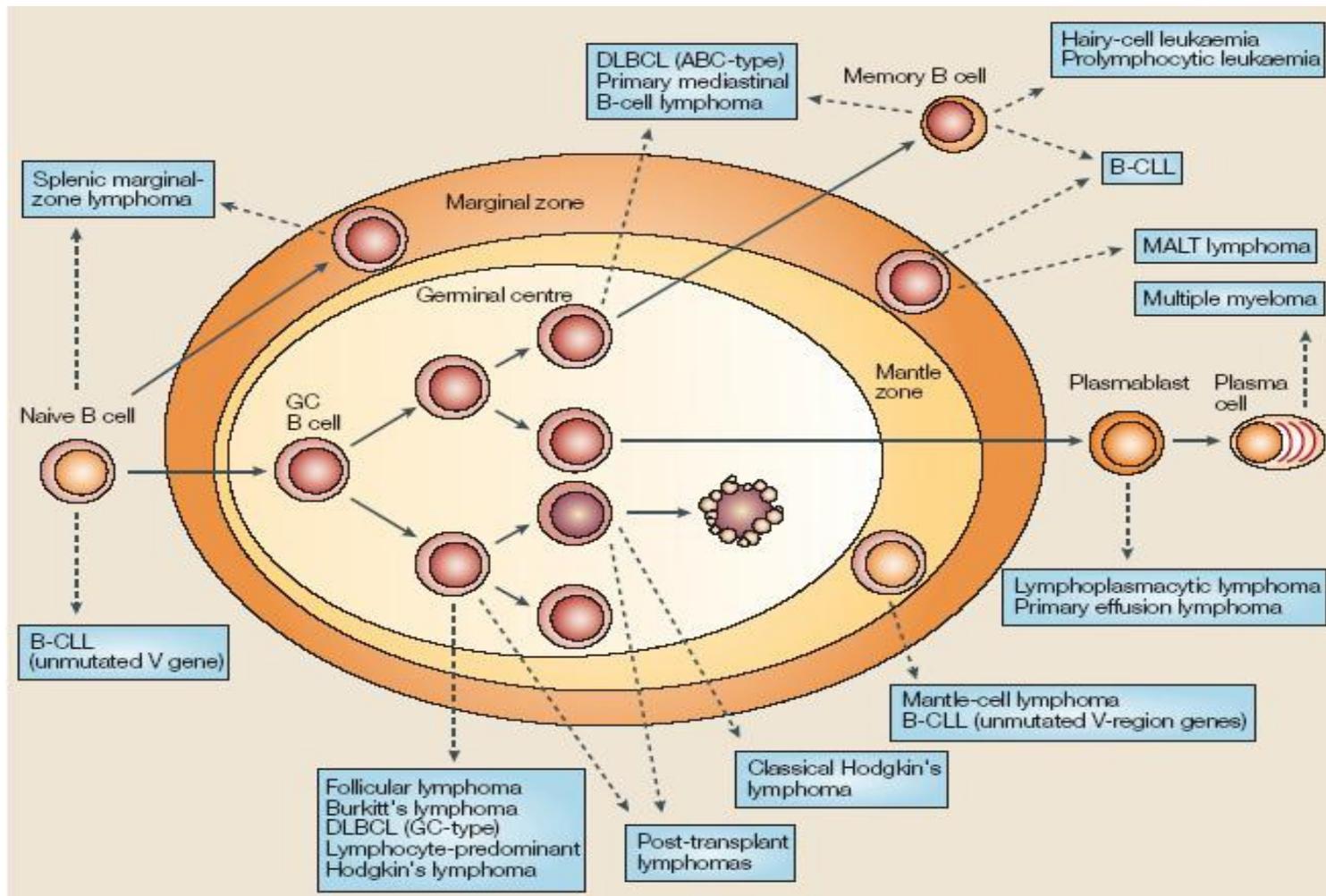
- At the end of this session, participants will be able to:
  - ✓ Classify lymphomas
  - ✓ Outline the prognosis and explain the curative/non-curative distinction
  - ✓ Describe-current therapeutic approaches and the associated side effects
  - ✓ List emerging trends in the management of lymphoma



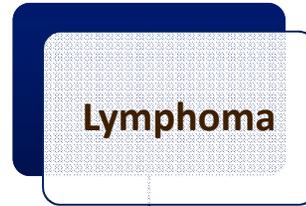
# Lymphopoiesis



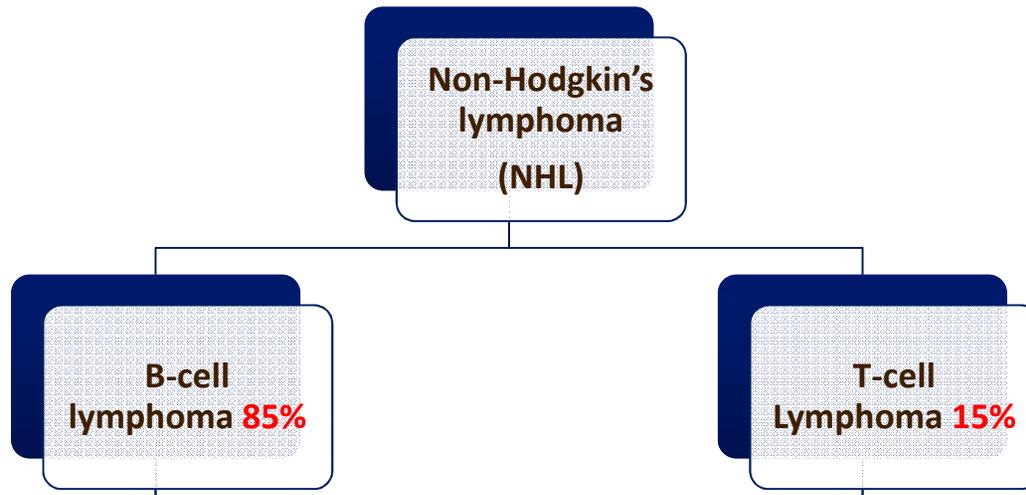
# Lymphopoiesis



# Classification of Lymphoma



# Classification of Lymphoma



# Prognosis

- Dependent on sub-type of lymphoma
- **Potentially curable:**
  - Aggressive lymphoma (Hodgkin's, Burkitt's, DLBCL, PTCL)
  - Limited Stage Indolent lymphoma (Follicular, Marginal zone)
- **Potentially controllable but not curable:**
  - Most advanced stage indolent lymphoma
  - Multiply refractory aggressive lymphoma

# Prognostic Scores

- Hodgkin's lymphoma:
  - International Prognostic Scoring system (IPSS)
- Diffuse Large B-Cell Lymphoma (DLBCL)
  - International prognostic index (IPI)
  - Cell of origin
- Follicular lymphoma:
  - Follicular lymphoma international prognostic index (FLIPI)
- Mantle cell lymphoma:
  - Mantle cell international prognostic index (MIPI)

# Therapeutic approaches



# Treatment

- Dependent on:
  - 1) Type of lymphoma (indolent versus aggressive)
  - 2) Stage of lymphoma (limited versus advance)
  - 3) Prognosis
    - Molecular testing (MYC and BCL2 gene rearrangement)
    - Central nervous system involvement
  - 4) Performance status/age

# Diffuse large B-cell lymphoma (DLBCL)

- Treatment: **R-CHOP (improves outcome)**
- **R-CHOP:**
  - **Rituximab:** Allergic reactions, pulmonary hypersensitivity
  - **Cyclophosphamide:** Nausea, Hemorrhagic cystitis, pulmonary hypersensitivity
  - **H(ydroxy) doxorubicin:** Cardiotoxicity, Hairloss, nail discoloration, cytopenia, Infection
  - **Oncovin (Vincristine):** Neuropathy, constipation, hoarseness
  - **Prednisone:** Insomnia, mood changes, diabetes, Hypertension, water retention

# **Diffuse large B-cell lymphoma (DLBCL)**

- Each cycle is 21 days (3 weeks)
- **Limited stage (Stage I/II):**
  - R-CHOP x 3 cycles + Radiation
  - R-CHOP x 4 cycle, if PET negative after cycle 3
- **Advanced stage (Stage III/IV), (Stage I/II with constitutional symptoms, mass > 10cm)**
  - R-CHOP x 6 cycles
  - NO additional benefit to 8 cycles
  - NO additional benefit giving every 14days

# More aggressive B-cell lymphoma

- Gray zone lymphoma: features intermediate between DLBCL and Burkitt's lymphoma
- Double HIT lymphoma: DLBCL with gene rearrangements in C-MYC and BCL2
- Triple HIT lymphoma: DLBCL with gene rearrangements in C-MYC, BCL2 and BCL6
- **R-CHOP is insufficient for the above patients**

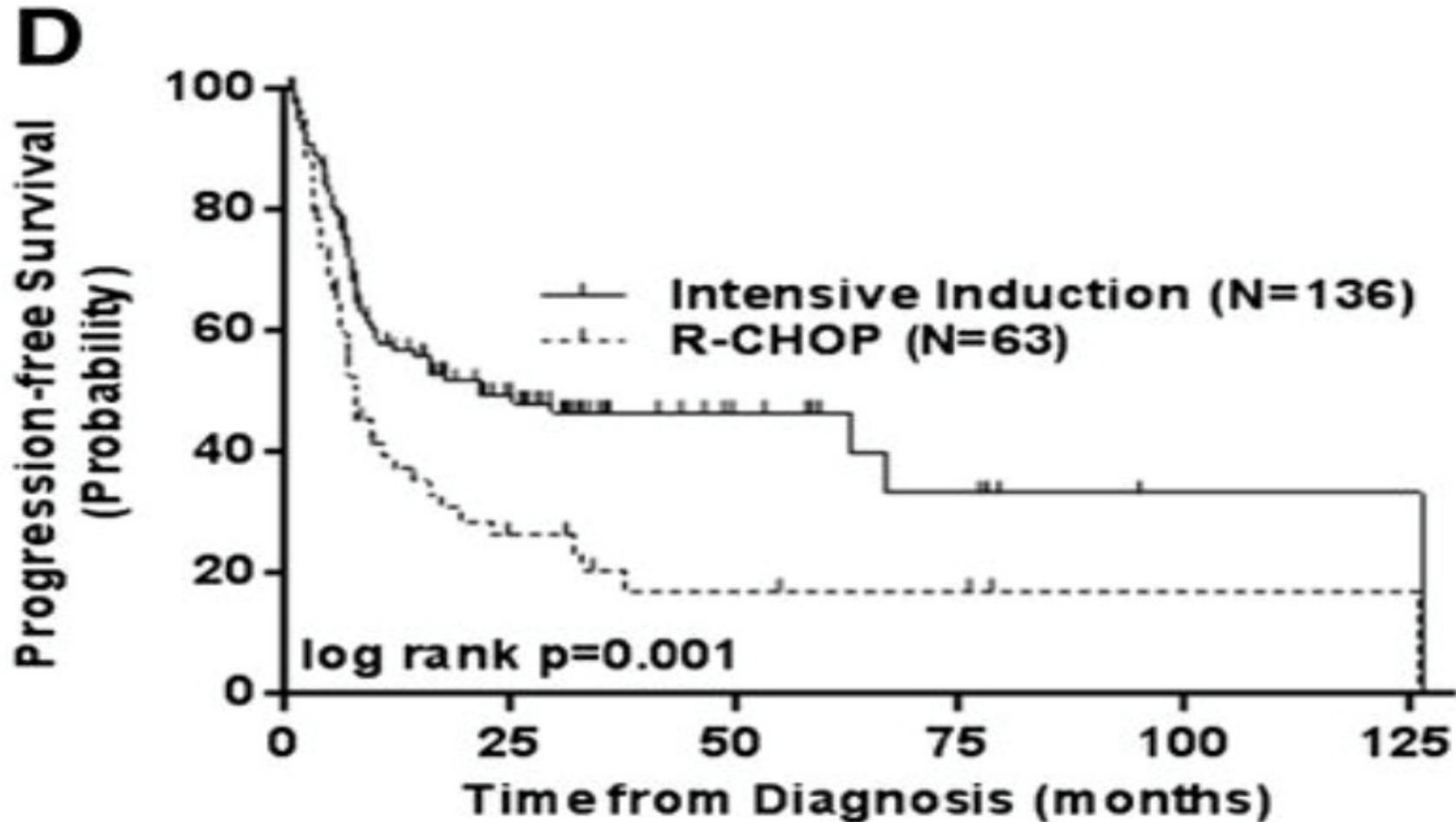
# More aggressive B-cell lymphoma

- Dose adjusted EPOCH-R

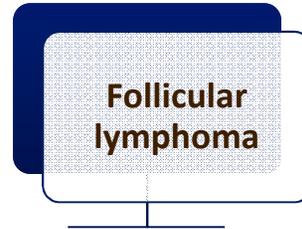
R-CHOP	EPOCH-R	Route
<b>Rituximab</b> 375mg/m <sup>2</sup> Day 1	<b>Rituximab</b> 375 mg/m <sup>2</sup> Day 1	IV
<b>Cyclophosphamide</b> 750 mg/m <sup>2</sup> Day 1	<b>Cyclophosphamide</b> 750 mg/m <sup>2</sup> Day 5	IV
<b>Doxorubicin</b> 50 mg/m <sup>2</sup> Day 1	<b>Doxorubicin *</b> 10 mg/m <sup>2</sup> /day Days 1 to 4	IV
<b>Vincristine</b> 1.4 mg/m <sup>2</sup> Day 1	<b>Vincristine *</b> 0.4 mg/m <sup>2</sup> /day Days 1 to 4	IV
<b>Prednisone</b> 100mg/day Days 1 to 5	<b>Prednisone</b> 60 mg/m <sup>2</sup> /day Days 1 to 5	Oral
	<b>Etoposide *</b> 50 mg/m <sup>2</sup> /day Days 1 to 4	IV

# Dose adjusted EPOCH-R

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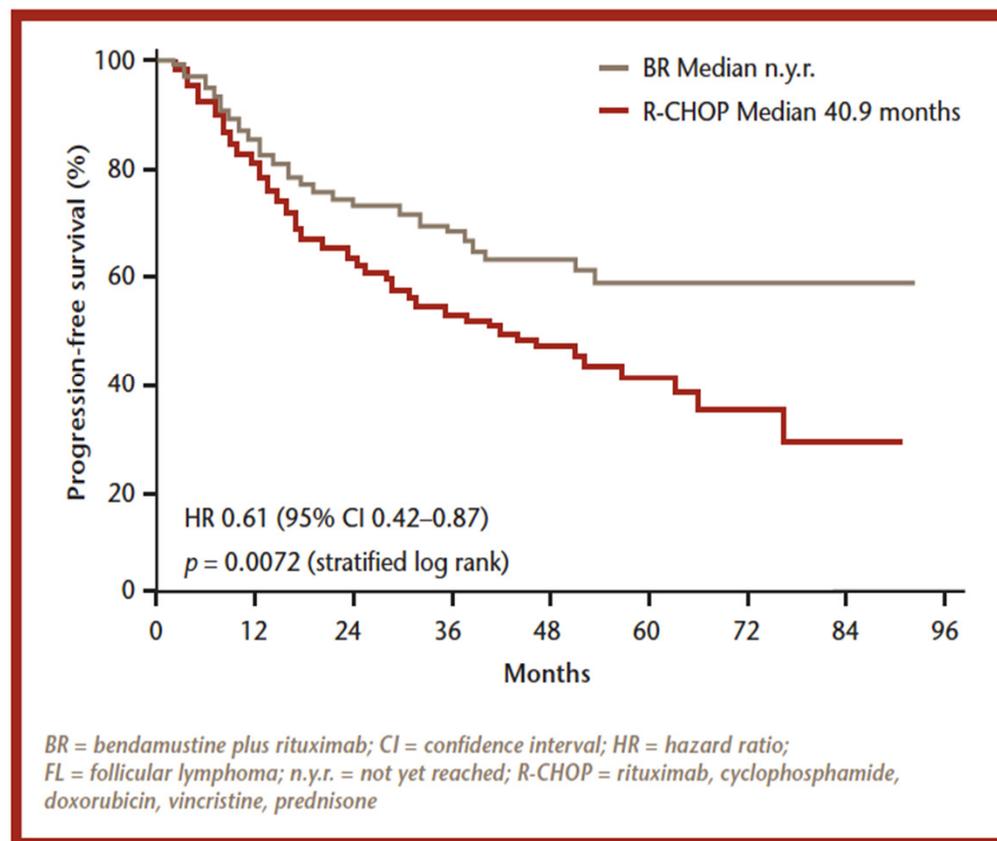
# Indolent B-cell lymphoma: Follicular lymphoma



# Follicular lymphoma

- Chemotherapy: **BR**
- **BR:**
  - **Bendamustine**
    - Rash, neutropenia
  - **Rituximab**
    - Allergic reaction
- Given every 28 day
- Total 6 cycles

Figure 2. Progression-free survival in patients with follicular lymphoma after treatment with BR or R-CHOP



# Other indolent B-cell lymphomas

- Extrapolated results from management of follicular lymphoma
- If symptomatic, all given BR x 6 cycles
- Some variation:
  - Splenic marginal zone: Splenectomy
  - Gastric H.Pylori MALT: Triple therapy
- **TRANSFORMED LYMPHOMA: 2-3% of indolent lymphoma transform to aggressive; these patients warrant R-CHOP**

# Maintenance rituximab

- **PRIMA trial:**
  - Maintenance rituximab improved time to relapse in patients with follicular lymphoma
  - Only enrolled those who attain complete (CR)/partial response (PR)
- **Indications for Maintenance rituximab**
  - Follicular lymphoma, in CR/PR after induction
  - Other indolent lymphoma in CR/PR after induction
  - Mantle cell lymphoma after induction/transplant
  - NO role of maintenance rituximab in DLBCL

# T-cell NHL

- Prognosis is poor compared to DLBCL; 5-yr OS ~ 20%
- Treatment evolving
- CHOP (no rituximab) not effective
- CHOEP improves outcome
- Autologous stem cell transplant in 1<sup>st</sup> CR maybe beneficial

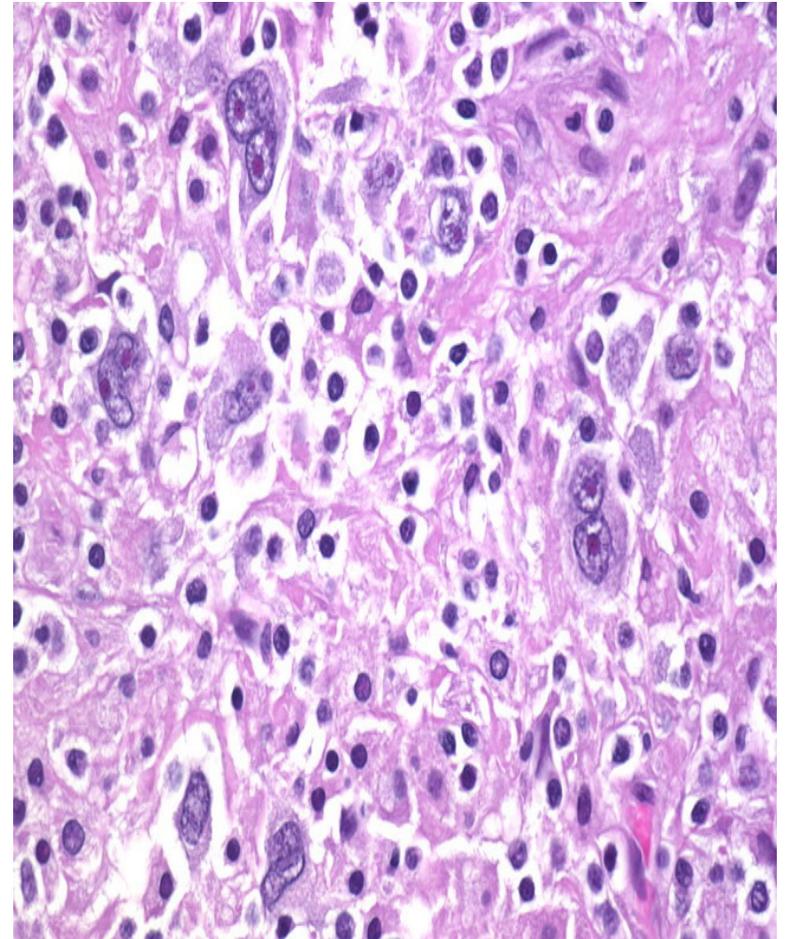
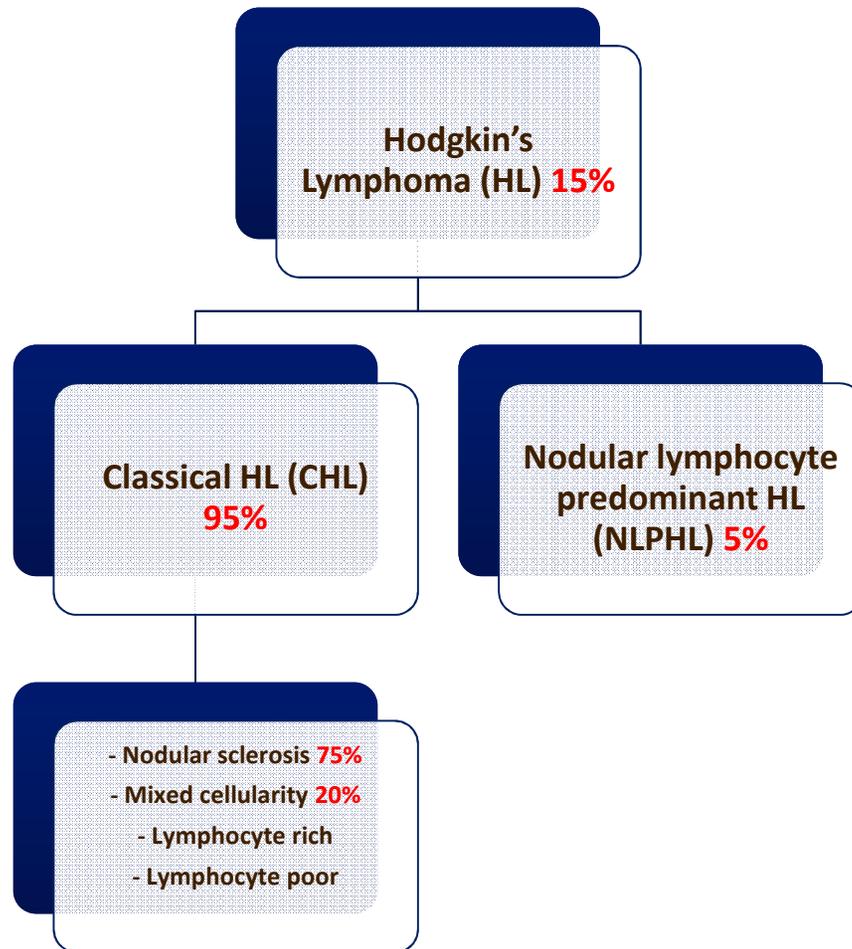
# Back to square one



# Relapsed B-cell NHL

- **DLBCL:**
  - Most receive salvage
  - Potentially curable if candidate for transplant
  - GDP(R), ICE(R), single agents
- **Follicular/Indolent:**
  - Not curable
  - Treatment depend on previous therapies
  - R-CHOP, R-CVP, Fludarabine, Chlorambucil, Gemcitabine, Ifosphamide and Etoposide

# Hodgkin's Lymphoma



# Treatment of Hodgkin's lymphoma

- Treatment: **ABVD**
- **ABVD:**
  - **A**driamycin (**D**oxorubicin): Cardiotoxicity, nail discoloration, hair loss, cytopenia, infection
  - **B**leomycin: Pulmonary toxicity (10 to 50%, but fatal only 4 to 5%)
  - **V**inblastine: Peripheral neuropathy, constipation
  - **D**acarbazine: Nausea

# Treatment of Hodgkin's lymphoma

- **Limited stage:**
  - ABVD x 2 then RT
  - ABVD x 4 then RT
  - ABVD x 4 (if PET negative after 2 cycle)
  - ABVD x 3 (if PET negative after 3 cycles)
- **Advanced stage:**
  - ABVD x 6
  - ABVD x 2, then AVD (if PET negative after 2)

# **Relapsed Hodgkin's lymphoma.**

- Salvage then transplant if candidate
- Brentuximab (anti-CD30)
- Nivolumab (PD1 inhibitors)

# Crossing over to new generation



# Novel agents:

- Ibrutinib (oral): CLL, Mantle cell, DLBCL
- Idelalisib (oral): CLL, Indolent lymphoma
- Venetoclax (ABT-199) (oral): CLL
- Brentuximab (IV): Hodgkin's
- Nivolumab (IV): Hodgkin's

# Take home message

- Various type of lymphoma
- Treatment depends on type, stage and prognosis
- Combination chemotherapies; each with it's own subset of side effects.
- Treatment given as either induction, maintenance, salvage/relapsed setting