# Lymphoma

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# Introduction

- Malignant proliferation of lymphoreticular system
- 3rd most common malignancy in children and adolescents
  - 60% Non-Hodgkin lymphoma
  - 40% Hodgkin lymphoma
- Uncommon < 5 year, increases with age.



FIGHT
HODGKIN'S
LYMPHOMA

# Hodgkin Lymphoma

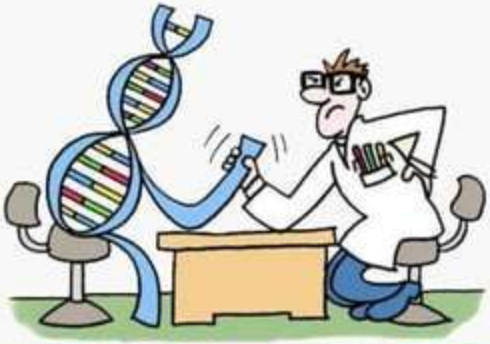
- B cell lineage lymphoreticular neoplasms
- 5-7/1,00, 000 population
- Uncommon< 5 years

- Three forms:
  - Childhood <14 years old 
  - Younger adult 15-44 years old
  - Older adults 55- 74 years old

- Male preponderence in < 7 years old 
- Almost equal sex distribution in > 12 years old

# Epidemiology

- Multifactorial etiology
  - Genetic
  - Viral illnesses (EBV)
  - Immune deficiency
  - Autoimmune conditions



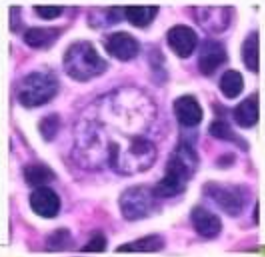
# Pathology

- Lymph nodes, liver,spleen, bone marrow, lung
- Excision biopsy,
- **1)WHO CLASSIFICATION :**

| HISTOLOGY | FREQUENCY | PROGNOSIS |
|---|---|---|
| **Nodular lymphocyte predominance (NLPHL)** | **10%** | **Excellent** |
| **Classical Hodgkin lymphoma** | | |
| Nodular sclerosis | 20-50% | Very good |
| Mixed cellularity | 20-40% | Good |
| Lymphocyte rich | <10% | Excellent |
| Lymphocyte depletion | 5-15% | Poor |

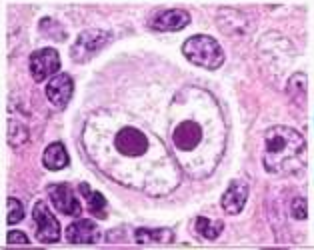
## NLPHL

- Popcorn cells (large cells with multilobed nuclei)
- Asymptomatic with localized non bulky disease
- Positive for CD15 and CD30, maybe for CD20




## Classic HL

- Reed –sternberg cell ( binucleated giant cell with two large nucleoli)
- Negative for CD15 and CD30
- Positive for CD20 and CD45



## 2)New WHO/ REAL classification

- Nodular lymphocyte predominance
- Classic HL
- Lymphocyte predominant
- Nodular sclerosing
- Mixed cellularity
- Lymphocyte depleted
- Anaplastic large-cell lymphomas (ALCL) Hodgkin like

# Clinical features

- Painless,firm, rubbery lymphadenopathy
  - Cervical, mediastinal ,axillary, inguinal lymph nodes
- Systemic 'B' symptoms (20-30%)
  - Unexplained weight loss >10%
  - Recurrent unexplained fever >38°C
  - Recurrent night sweats
- Bone marrow ( cytopenia)
- Paraneoplastic syndromes
- Uncommon sites of involvement:
  - GIT, skin, spleen

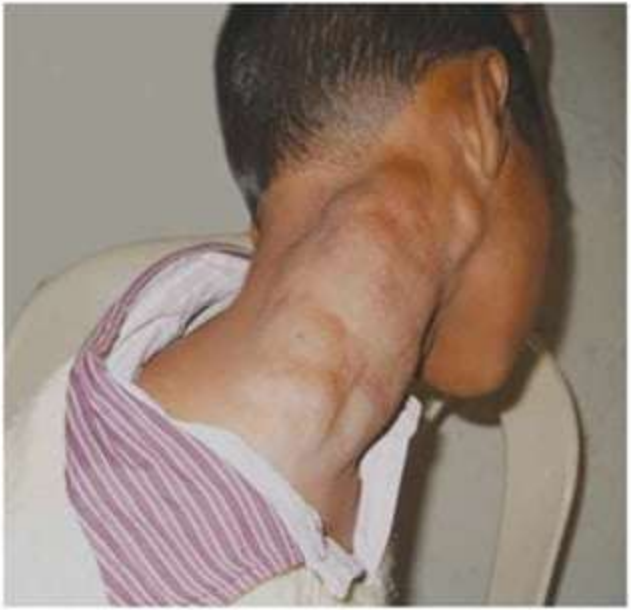


Fig. 20.5: A 12-yr-old boy presented with intermittent fever and significant bilateral cervical lymphadenopathy. Lymph node biopsy showed features of Hodgkin lymphoma

# Prognostic factors

- Presence of ‘B’ symptoms
- Stage of disease
- Histopathological subtype
- Bulky mediastinal disease
- Extensive splenic involvement
- > 5 nodal sites in stage III

# Diagnostic evaluation

- Physical examination with measurement of lymph nodes
- Complete hemogram with ESR, CRP
- Liver and renal function tests , ALP, LDH
- Chest X-ray
- CT scan of neck, chest, abdomen, brain
- Biopsy
  - Lymph node
  - Bone marrow (all children except stages IA/IIA)

- Bone scan (if bone pain or raised serum ALP)
- Cerebrospinal fluid examination (if indicated)
- PET-CT scan
- Surgical staging with lymph node sampling and lymphangiography (selected cases)

# Modified Ann-Arbor staging

| STAGE | INVOLVEMENT |
|---|---|
| **I** | Single lymph node region (I) **OR**<br>One extralymphatic site (IE) |
| **II** | Two or more lymph node regions on same side of diaphragm (II)<br>**OR** One or more lymph node regions on same side of diaphragm + local extralymphatic extension (IIE) |
| **III** | Lymph node regions on both sides of the diaphragm (III)<br>**+** local extralymphatic extension (IIIE) |
| **IV** | Diffuse involvement of one or more extralymphatic organ sites |
| **A** | No B symptoms |
| **B** | Presence of at least one B symptoms :<br>○ **Unexplained weight loss >10%**<br>○ Recurrent unexplained **fever >38°C**<br>○ Recurrent **night sweats** |
| **X** | Bulky tumor > 10cm **OR** mediastinal mass extending one-third of the max transverse intrathoracic diameter |

# Management

- Chemotherapy with/without radiotherapy (15-25 Gy)
- Chemotherapy
  - **ABVD** (adrimycin,bleomycin,vinblastine, dacarbazine)
    - Preferred front line regimen (superior results and no permanent gonadal toxicity)
    - Adverse effect: cardiomyopathy, pulmonary fibrosis
  - **COPP/ABVD** ( cyclophosphamide, oncovin, prednisolone, procarbazine)
  - **MOPP** (mechlorethamine, vincristine, prednisolone, procarbazine)
  - **BEACOPP** ( bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, prednisolone, procarbazine)

## Favourable features

- Localised disease (stage I, II,IIIA)
- No B symptoms
- No evidence of bulky tumor

## Unfavourable features

- Presence of B symptoms
- bulky mediastinal / peripheral lymphadenopathy
- Extranodal extension
- Advanced disease (stage III, IVB)

- Localised disease (stage I, II,IIIA) with favourable features
  - 2-4 cycles of chemotherapy (ABVD/others) and low dose radiation
- Localised disease (stage I, II,IIIA) with unfavourable features
  - Intermediate therapy intensity
- Localised disease / unfavourable features with B symptoms
  - 4-6 cycles of chemotherapy of ABVD with/without radiotherapy
- Relapse/ refractory patient
  - Hemopoietic stem cell transplantation

| Regimen | Drugs | Dose | Day |
|---|---|---|---|
| **ABVD** | i. Inj Doxorubicin or **Adriamycin** | 25mg/m² | IV day 1 and 15 |
| | ii. Inj **Bleomycin** | 10mg/m² | IV day 1 and 15 |
| | iii. Inj **Vinblastine** | 6mg/m² | IV day 1 and 15 |
| | iv. Inj **Dacarbazine** | 375mg/m² | IV day 1 and 15 |
| | v. Inj **Dexamethasone** | 0.15mg/m² | IV day 1 and 15 |
| **COPP** | i. Inj **Cyclophosphamide** | 600mg/m² | IV day 1 and 8 |
| | ii. Inj **Oncovin** (vincristine) | 1.5mg/m² | IV day 1 and 8 |
| | iii. Tab **Prednisonole** | 40mg/m² | PO day 1 and 14 |
| | iv. Cap **Procarbazine** | 100mg/m² | PO day 1 and 14 |
| **Keep off therapy from day 16-28. Repeat on day 28.** | | | |

support

# NON-HODGKINS LYMPHOMA

awareness

# Non-Hodgkin Lymphoma

- Heterogenous group of lymphoid neoplasms derived from cells of the immune system (B/T cells)
- Common in 20s , less in < 3 years of age
  - Adult : low grade
  - Children : high grade, diffuse, aggressive,
- Survival rate (80%) for at least 5 year

# Epidemiology

- Male preponderence (3:1) 
- **Age groups**
  - **5-15 years** : Burkitt, Burkitt-like lymphoma
  - **Older adolescents** : diffuse large B cell lymphoma
  - **All age groups** : lymphoblastic lymphoma
- **Geographical distribution**
  - **Africa** : Burkitt lymphoma
  - **US, Europe** : lymphoblastic, small and large cell lymphoma
  - **India** : lymphoblastic lymphoma

- **Risk factors:**
  - Previous chemotherapy for hodgkin disease
  - Immunodeficiency , AIDS, organ transplantation
  - DNA repair deficiency syndromes ( Wiskott-Aldrich syndrome, ataxia-telangiectasia)
  - Malaria, EB virus

# Pathology

## MAJOR PATHOLOGICAL SUBTYPES OF NHL

- Burkitt or Burkitt like lymphoma
- Lymphoblastic lymphoma
- Diffuse large B cell lymphoma
- Anaplastic large cell lymphoma

# Clinical presentation

- **Adults** : low / intermediate grade, dominantly nodal, variable growth fraction, poor long term outcome
- **Children** : high grade, extranodal (mediastinum, abdomen, head, neck), high growth fraction, good outcome
  - Intrathoracic →superior mediastinal syndrome
  - Pleural or pericardial effusion,
  - B cell disease:
    - Cervical adenopathy, abdominal pain, ascites, palpable abdominal mass, intestinal obstruction
  - Bone marrow involvement:
    - cranial nerve palsy, bone involvement, jaw swelling, cytopenias

# Diagnosic evaluation

- Histology
  - Lymph node biopsy
  - Percutaneous needle aspiration of accessible lymph node
- Immunophenotypic and cytogenetic studies
- Examination of body fluids or bone marrow

# St. Jude Staging System for childhood NHL

| STAGE | DEFINITION |
|---|---|
| **Localised ( low- risk)** | |
| I | ○ Single extranodal / nodal tumor excluding mediastinum and abdomen |
| II | ○ Single extranodal tumor with regional node involvement<br>○ Primary GI tumor (completely resected,w/wo mesenteric node involvement )<br>○ 2 or > tumors on one side of diaphragm |
| **Advanced ( high- risk)** | |
| III | ○ Primary intrathoracic tumor<br>○ Extensive primary intra-abdominal disease;<br>○ Paraspinal / epidural tumors<br>○ 2 or > tumors on both sides of diaphragm |
| IV | ○ Any of the above with central nervous system and/or bone marrow involvement |

# Management

- Chemotherapy
- Supportive care
- Surgery (diagnostic)
- Radiotherapy (emergency situations)

## Lymphoblastic lymphoma

- ALL treatment
- Cranial irradiation /prophylactic intrathecal chemotherapy (stage III and IV)
- 1-2 year duration of chemotherapy

## B cell lymphoma

- Short duration ( 6 months)
- Intensive alkylating high dose methotrexate, vincristine, anthracyclines, etoposide, cytarabine
- Intrathecal prophylaxis
- Anti-CD20 monoclonal antibodies (rituximab)

| FEATURES | HODGKIN'S LYMPHOMA | NON-HODGKIN'S LYMPHOMA |
|---|---|---|
| **Age** | <14 years old<br>15-44 years old<br>55- 74 years | All ages |
| **Sex** | M:F (10:1) <7, (1:1) >12 years | M:F (3:1) |
| **Predisposing factors** | Genetic<br>Autoimmunes,<br>Immunodeficiency<br>EB virus | Chemotherapy<br>Immunodeficiency<br>DNA deficiency syndromes<br>Organ transplant, Malaria, EBV |
| **Affected organs** | Lymph nodes, Liver, Spleen , Bone marrow, GIT, skin | Mediastinum, Abdomen, Head, Neck, CNS, Bone marrow |
| **Pathology** | Reed-Sternberg cell | T or B-cells |
| **Extra nodal involvement** | Less common | More common |
| **Prognosis** | Better | Bad |

# Reference


- Vinod K Paul, Arvind Bagga, **Ghai Essential Pediatrics**, 8th edition, 2014
- Kliegman, Stanton, St.Geme, Behrmann, **Nelson Textbook of Pediatrics**, 19th edition, 2011.