

HODGKINS LYMPHOMA TYPES

DR.V.SHANTHI

ASSOCIATE PROFESSOR, DEPARTMENT OF PATHOLOGY

SRI VENKATESWARA INSTITUTE OF MEDICAL SCIENCES

TIRUPATHI



HODGKINS LYMPHOMA

- Hodgkins lymphoma comprises 1% of all the denovo neoplasms occurring world wide every year
- Comprises 40% of adult lymphoma
- Less common than Non - Hodgkins lymphoma
- Males are usually more affected than females except in nodular sclerosis
- Bimodal age distribution
- Usually starts in cervical lymph nodes and spreads to extra nodal sites



CLASSIFICATION OF HODGKINS LYMPHOMA

Classic Hodgkins

more common

- Nodular sclerosis
- Mixed cellularity
- Lymphocyte rich
- Lymphocyte depletion

Nodular lymphocyte predominant Hodgkins



HODGKINS LYMPHOMA

Comprises of 1% of
all cancers

Nodular sclerosis
Comprises – 65% -
75%

**Nodular lymphocyte
predominant**
comprises 10%

Mixed cellularity
Comprises 20% - 25%

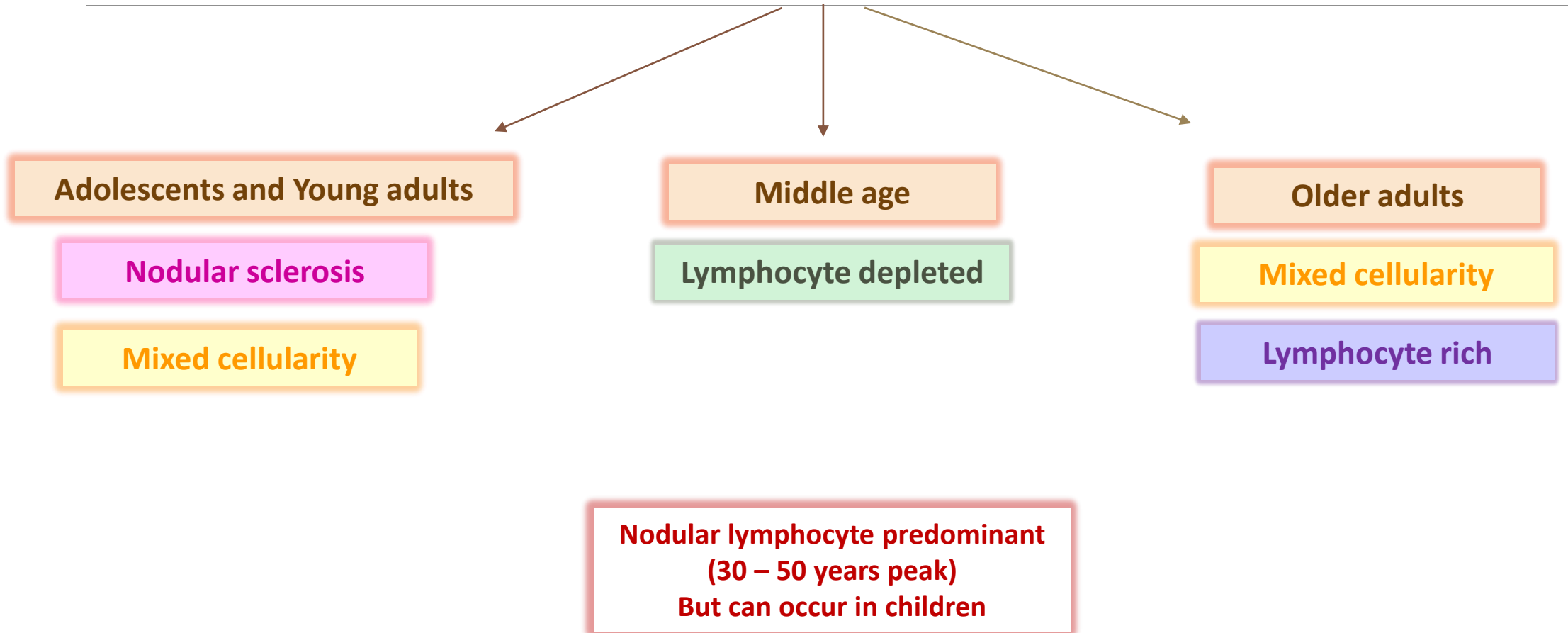
**Lymphocyte
depleted**
Comprises 1%

Lymphocyte rich
Comprises 5%



HODGKINS LYMPHOMA

AGE GROUP



HODGKINS LYMPHOMA

SEX



Male



Female

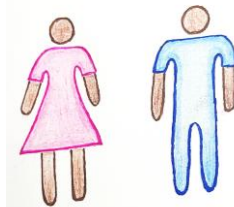
Mixed cellularity

Lymphocyte rich

Lymphocyte depleted

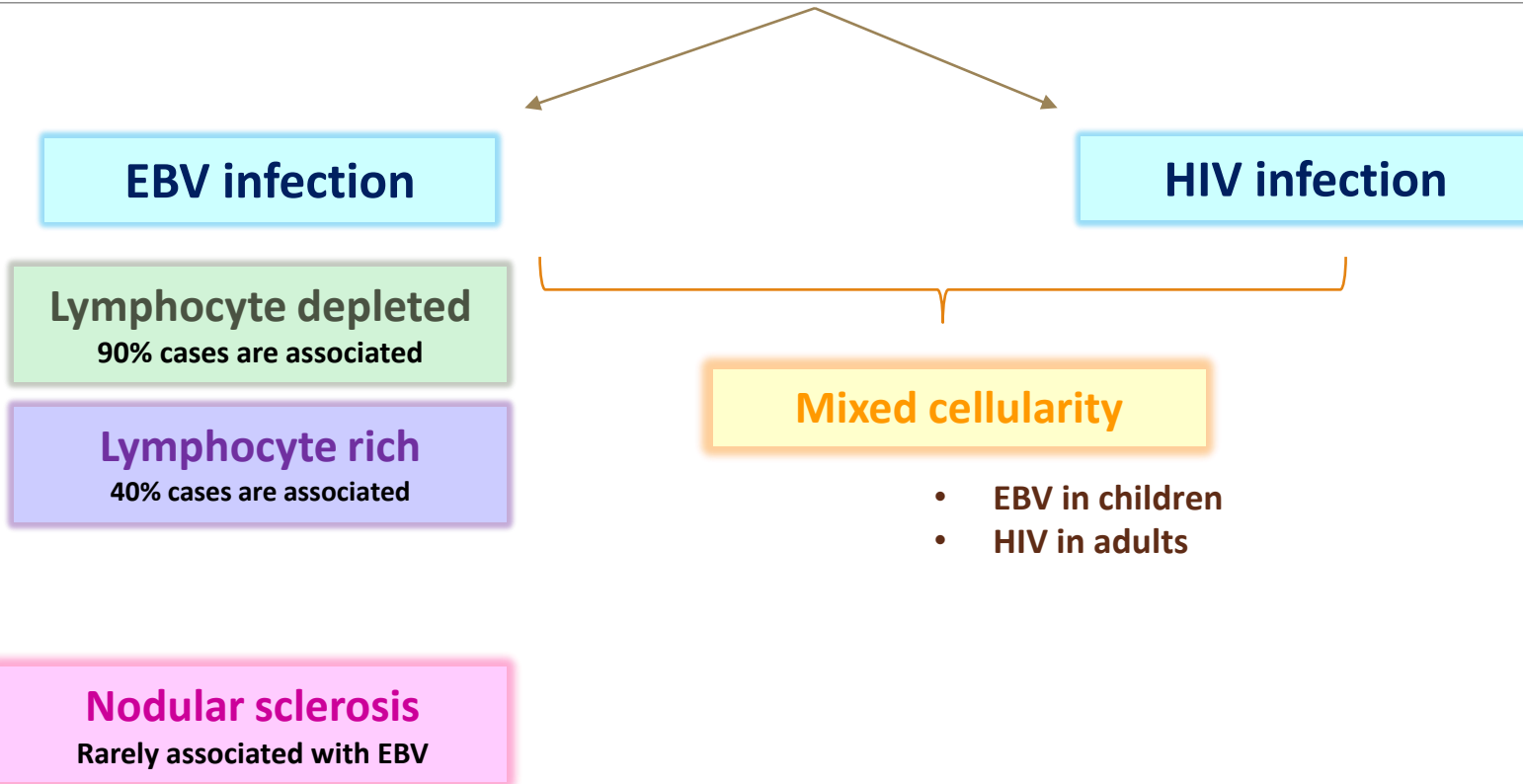
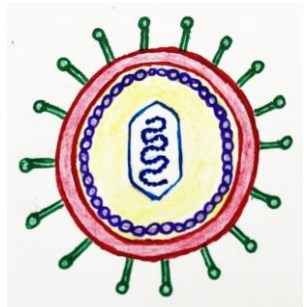
Nodular lymphocyte predominant

Nodular sclerosis



HODGKINS LYMPHOMA

ASSOCIATION WITH VIRAL INFECTION



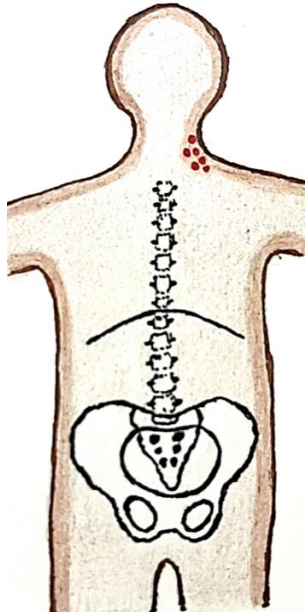
Nodular lymphocyte predominant type is not associated with EBV



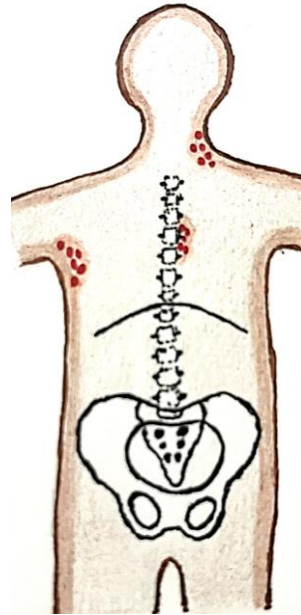
HODGKINS LYMPHOMA

ANN ARBOR STAGING SYSTEM FOR LYMPHOMA

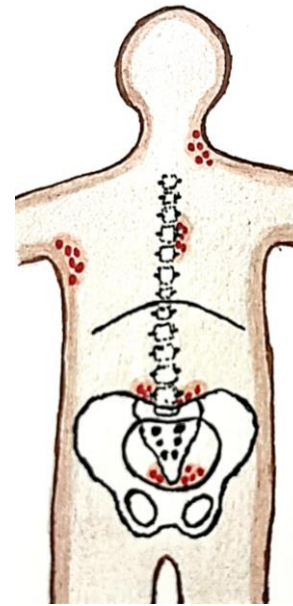
Stage I



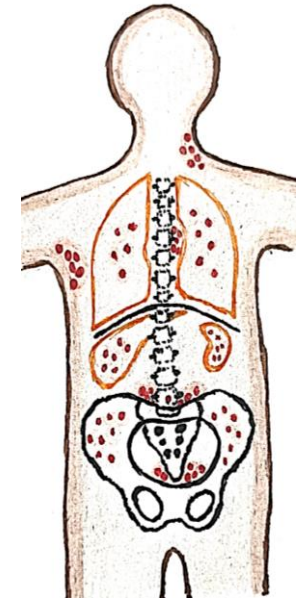
Stage II



Stage III



Stage VI



Involvement of single lymph node region with or without Involvement of single extra lymphatic organ or site

Involvement of two or more LN regions on the same side of the diaphragm with or without localized contiguous involvement of extra-nodal organ or site

Involvement of lymph node regions on both sides of diaphragm with or without localized contiguous involvement of an extra nodal organ or site

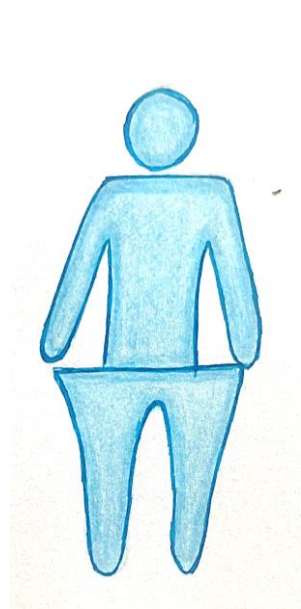
Diffuse involvement of one or more extra lymphatic organs or sites with or without lymph nodal involvement

All the stages are further divided on the basis of absence (A) or presence (B) of the B symptoms



HODGKINS LYMPHOMA

Clinical features - B symptoms



Unexplained weight loss of greater than 10% of normal body weight



Unexplained fever – presents as fever of unknown origin. Fever persists for days to weeks followed by afebrile period and then recurrence (Pel ebstein fever)



Drenching night sweats



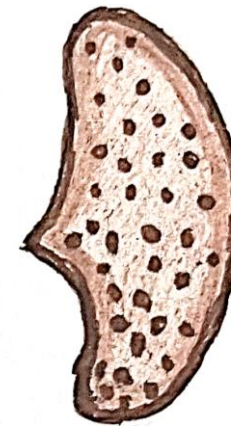
HODGKINS LYMPHOMA

Gross –

- Lymph nodes have **rubbery consistency**
- **Cut section** – bulging fish flesh like
- **Nodular sclerosis** – more nodularity due to fibrous bands
- **Splenic involvement** – scattered nodules in white pulp



Lymph node with nodular bulging surface



Spleen with scattered nodules

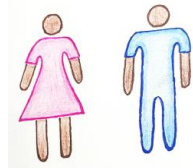


HODGKINS LYMPHOMA

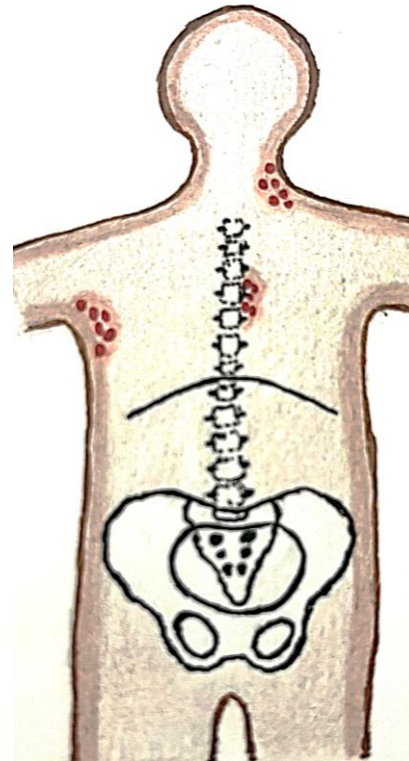
NODULAR SCLEROSIS

Most common subtype constituting 65% to 75% of cases

1. **Sex** – Equal incidence in both male and female



2. **common site** - mediastinal (70% of cases) or cervical lymphnodes showing predilection for contiguous spread



4. Patients usually present in stage II disease



3. **Age** – peaks in the range of 15 to 34 years

5. **B symptoms** are encountered in 40% of cases



HODGKINS LYMPHOMA

NODULAR SCLEROSIS

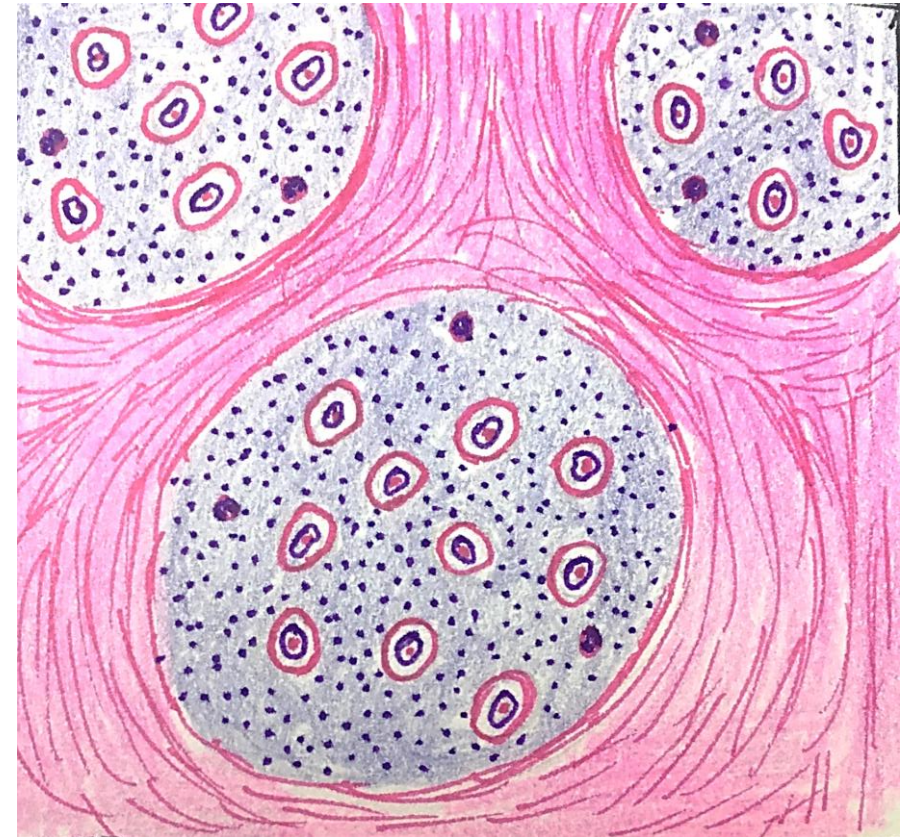
Macroscopy –

cut section of lymphnode shows nodular pattern separated by dense fibrosis

Microscopy

3 characteristic features are

- **Sclerosis** – fibrotic collagen bands from the thickened capsule, subdividing the lymphnode into nodules
- **Nodular pattern** - circumscribed nodules separated by deposition of collagen bands which are birefringent green color when viewed under polarized microscope (not seen in LD-HL)
- **Lacunar RS cells** – individually dispersed or as sheets resembling metastatic carcinoma



NODULAR SCLEROSIS



HODGKINS LYMPHOMA

NODULAR SCLEROSIS

Immunophenotyping of RS cell (Lacunar cell)

- CD15 – positive
- CD 30 – positive
- PAX 5 (a B cell transcription factor) – positive
- Negative for
- CD 45 and other B cell, T cell markers
- Prognosis – better than other types of Classic Hodgkin's Lymphoma
- Massive mediastinal disease is adverse prognostic marker

Lacunar cell



HODGKINS LYMPHOMA

MIXED CELLULARITY

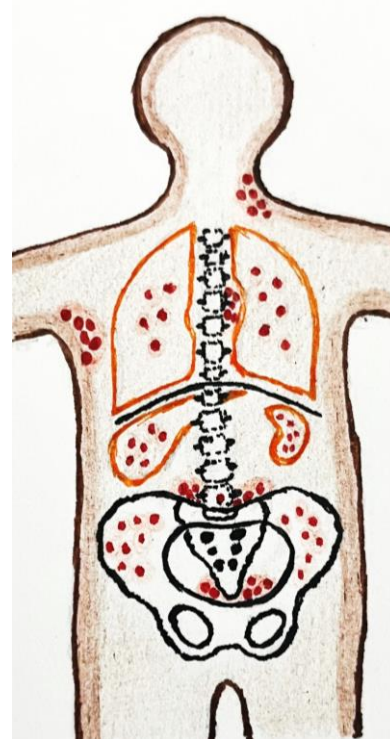
Constitutes 20% to 25% of cases

1. Sex: Male predominance

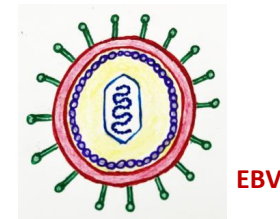


2. Site –

- peripheral lymphnodes are frequently involved (mediastinal involvement uncommon)
- Spleen, bone marrow, liver and other organs are involved in decreasing order of frequency



Virus associated



EBV



HIV

3. Age - Two peaks

- Children in developing countries (associated with EBV)
- Second peak in elderly age group (Associated with HIV infection)



4. B symptoms are frequent

5. Presentation - 50% of cases present in stage III and stage IV

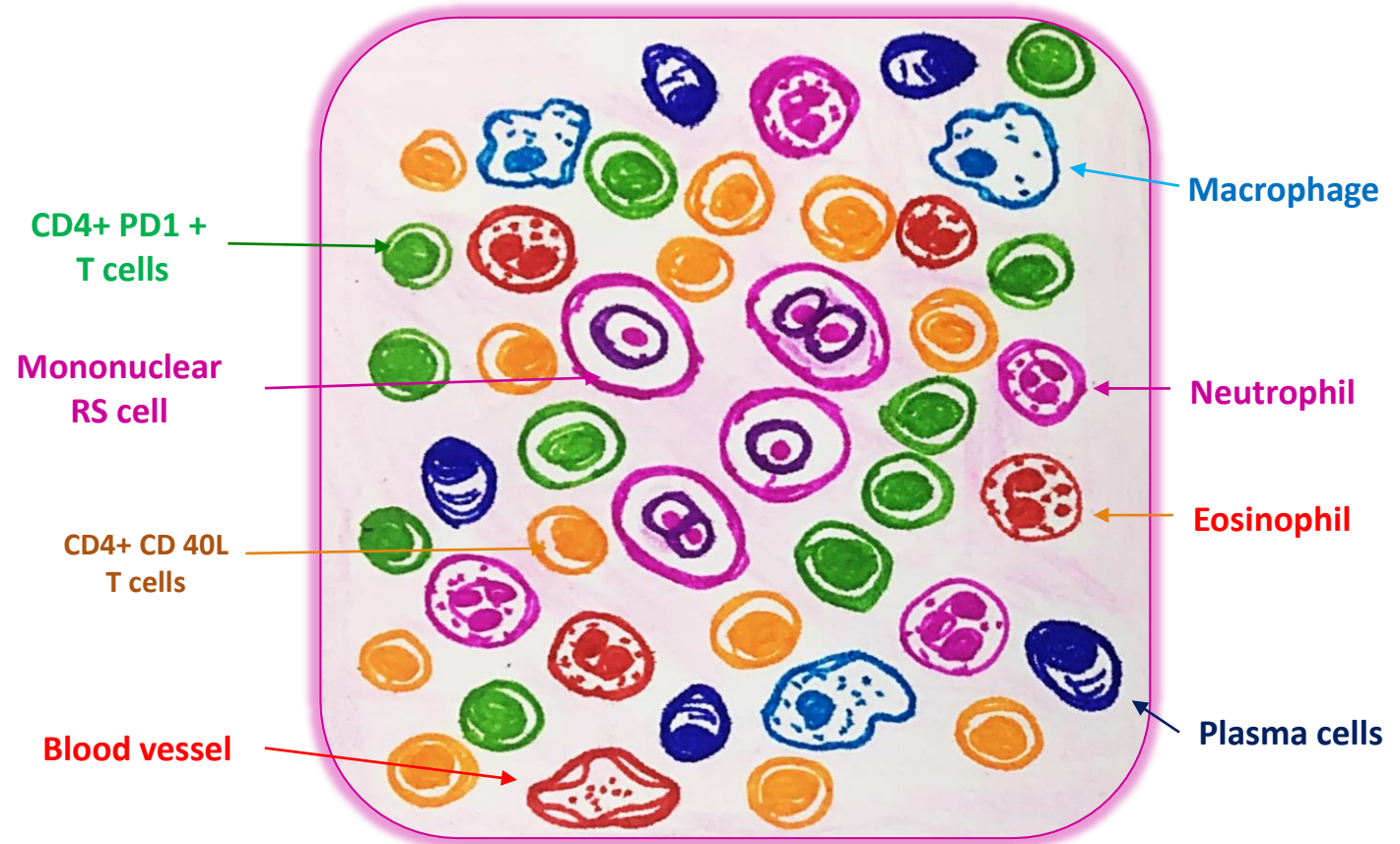


HODGKINS LYMPHOMA

MIXED CELLULARITY

Microscopic picture

- **Lymph node architecture** - diffusely effaced by heterogenous cellular infiltrate which contains T cells, plasma cells, eosinophils, and macrophages admixed with typical RS cells
- Histiocytes may have pronounced epithelioid features particularly in EBV associated cases
- **Type of RS cell** – mononuclear variant
- Immunophenotype of RS cell is similar to those of NS type
- **Prognosis** – good but worse than nodular sclerosis



HODGKINS LYMPHOMA

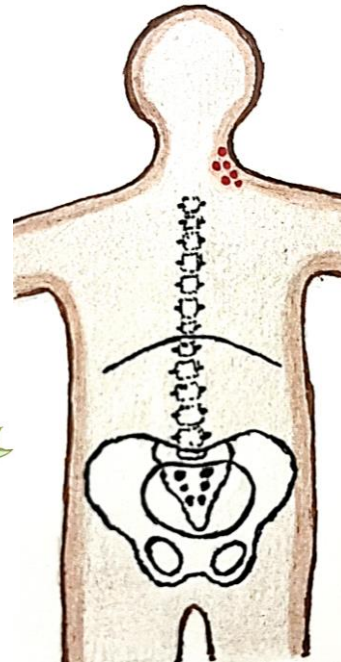
LYMPHOCYTE RICH TYPE

1. Uncommon form of HL (incidence is 5%)

2. Age/sex – elderly males

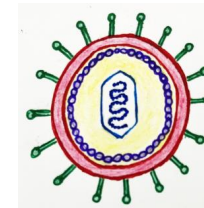


3. B symptoms are rare



4. Sites of involvement – peripheral lymph node and rarely mediastinal or extranodal involvement

5. Virus associated



Associated with EBV in 40% of cases

Presents in stage I and stage II

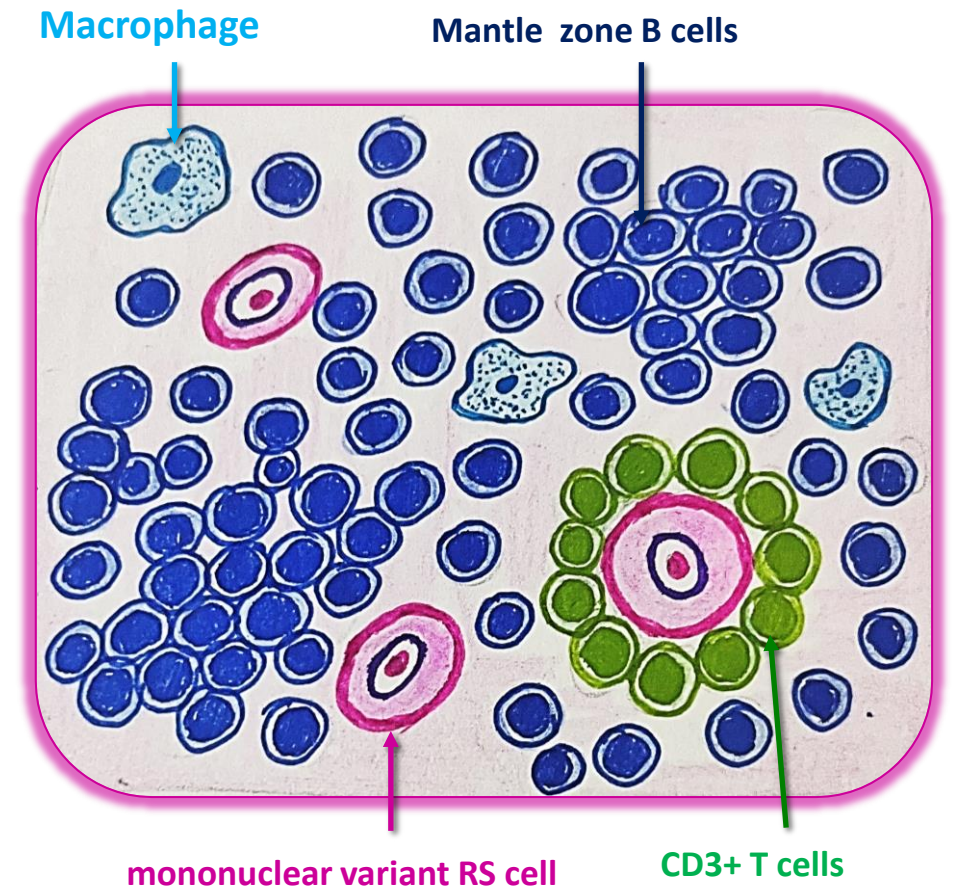


HODGKINS LYMPHOMA

LYMPHOCYTE RICH TYPE

Morphology

- **Lymph node architecture** – diffusely effaced or vague nodularity
- Cells are predominantly lymphocytes with few RS cells and few or absent eosinophils and neutrophils
- **Vague nodularity** can be due to presence of residual B – cell follicles
- **Reactive component** – abundant **mantle zone B cells** with surface IgD and IgM expression and variable amounts of **CD3+ T cells forming rosettes** around neoplastic elements
- **Diagnostic RS cell** - **mononuclear variant** with immunophenotypic profile of classic RS cell.
- **Prognosis** – Good to excellent



HODGKINS LYMPHOMA

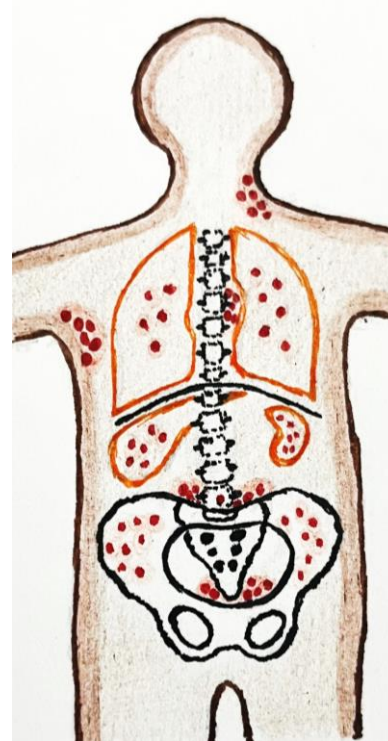
LYMPHOCYTE DEPLETION TYPE

Least common form accounting for 2% with Worst prognosis

1. Age/ sex - middle aged with male predominance



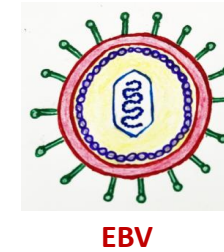
2. Site – predilection for retroperitoneal lymphnodes, abdominal organs and bone marrow. Peripheral lymphadenopathy may also be seen



3. Bone marrow involvement detected in 50% of cases

6. Presentation: Most cases present in stage III and stage IV

4. Virus associated



Associated with EBV infection in more than 90% of cases



5. B symptoms are present



HODGKINS LYMPHOMA

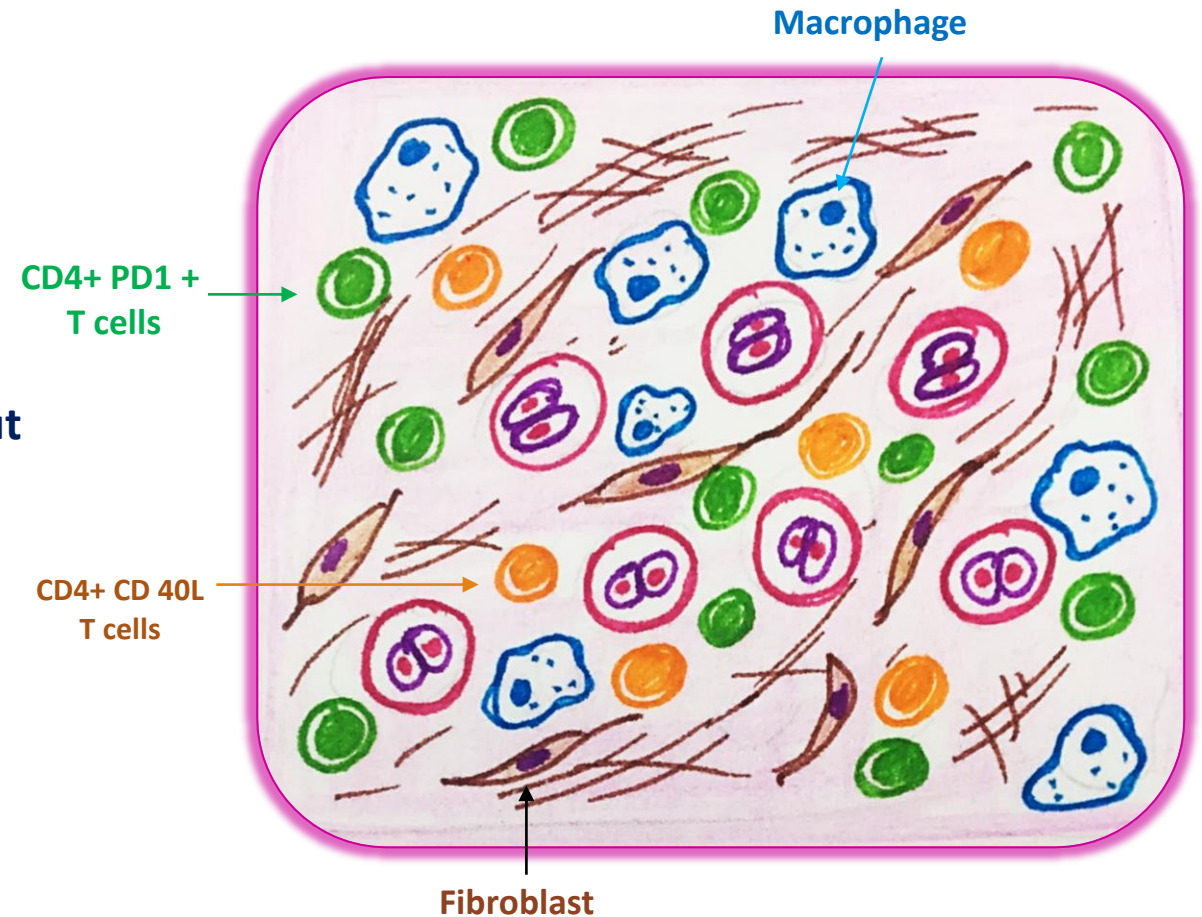
LYMPHOCYTE DEPLETION TYPE

Morphology

- characterized by **paucity of lymphocytes** and a relative abundance of RS cells or their pleomorphic variant

Two patterns are seen –

- **Diffuse fibrosis** – prominent fibroblastic proliferation is seen with numerous histiocytes and small lymphocytes but lack significant numbers of eosinophils and plasma cells
- **Reticular pattern** – rich in neoplastic cells showing pleomorphic and anaplastic features
- Immunophenotype of RS cell is similar to classic RS cell
- **Prognosis** is less favorable when compared to other subtypes



HODGKINS LYMPHOMA

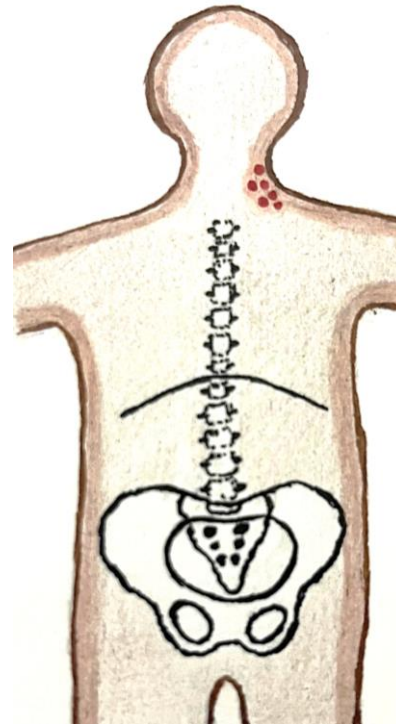
NODULAR LYMPHOCYTE PREDOMINANT TYPE

Accounts for 10% of all hodgkins lymphoma cases

1. **Age/sex** - male patients in the age group of 30-50 years (can occur in children also)

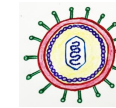


2. **Site** – cervical, axillary or inguinal LN (mediastinal and bone marrow involvement is rare)



3. **Virus associated**

Only 3 to 5% of cases are associated with EBV



4. 3% to 5% cases transform to diffuse large B cell lymphoma

5. **Prognosis** – excellent though this variant is likely to recur

Most cases present at stage I and II (20% present with advanced stage)

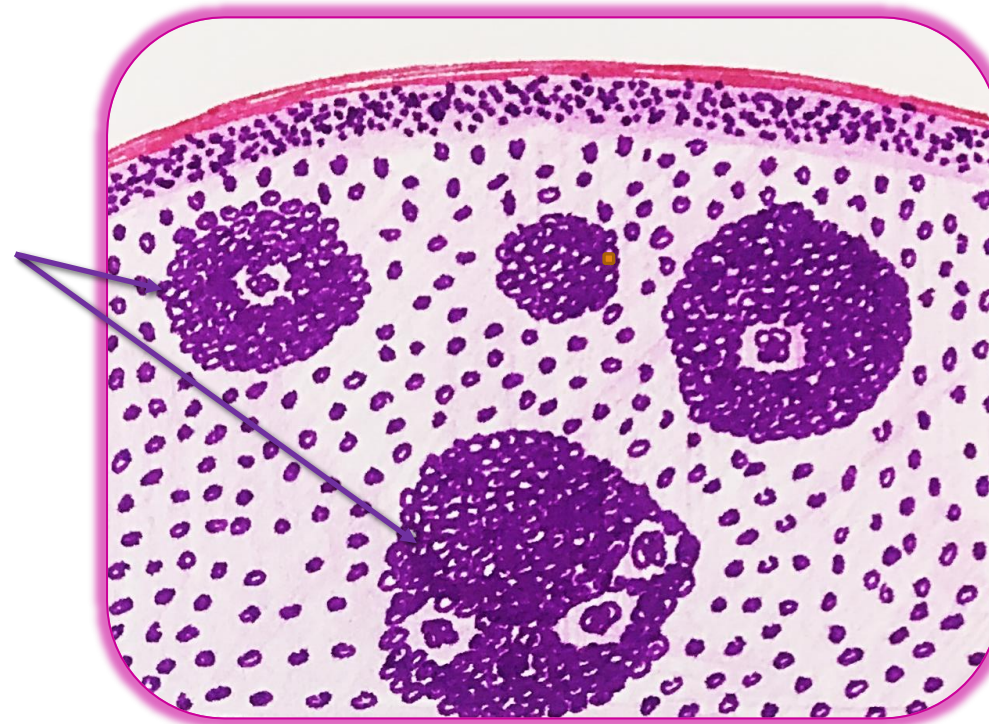


HODGKINS LYMPHOMA

NODULAR LYMPHOCYTE PREDOMINANT TYPE

Lymph node – effaced architecture with nodular infiltrate of small round lymphocytes admixed with variable number of epithelioid histiocytes which gives mottled appearance

Nodular pattern is due to the presence of expanded B cell follicles populated with RS cells (L & H variant), reactive B cells and follicular dendritic cells



Attenuated rim of residual normal node

Eosinophils and neutrophils are rare or absent

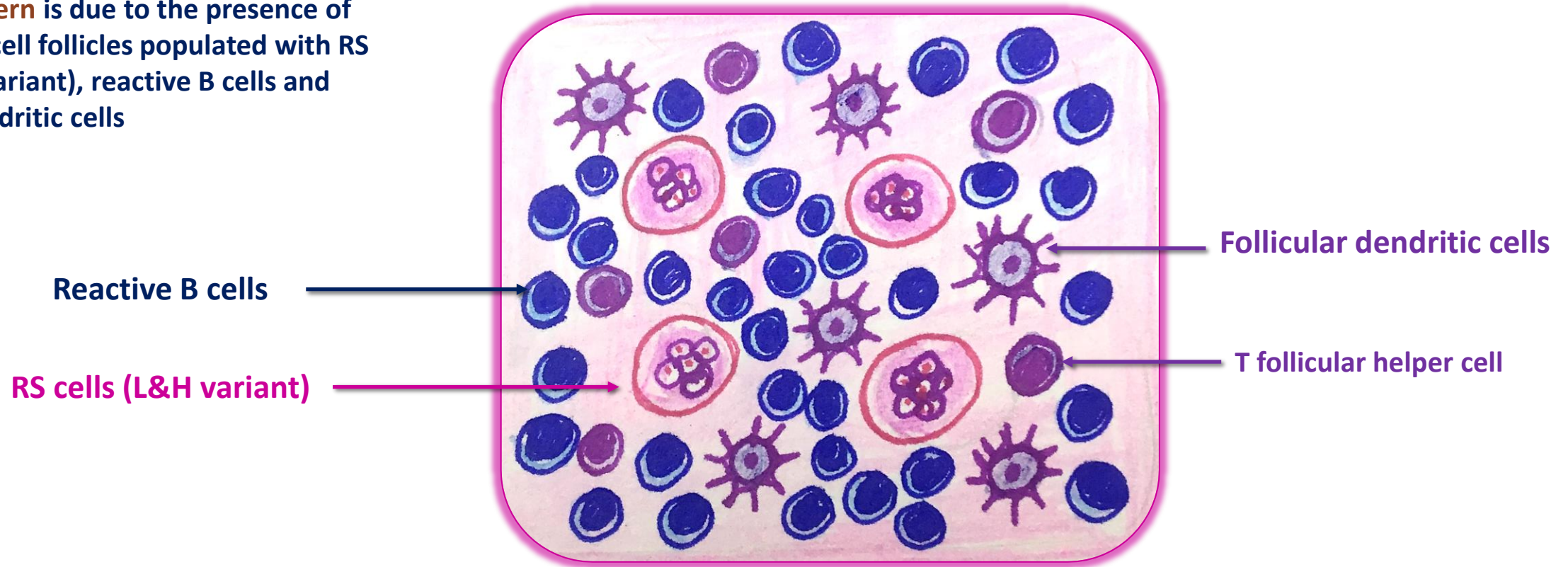
Histiocytes and some plasma cells may be found at the margin of the nodules containing LP cells



HODGKINS LYMPHOMA

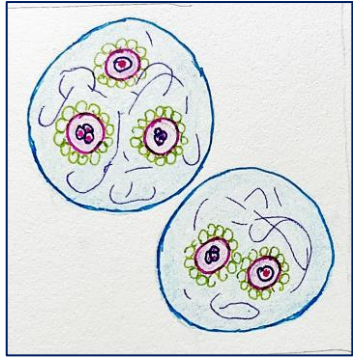
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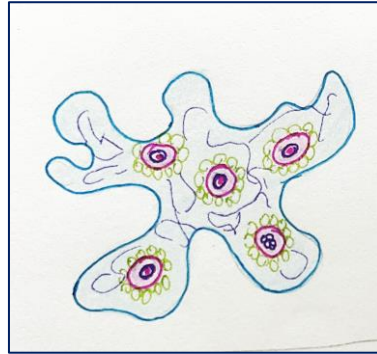


HODGKINS LYMPHOMA

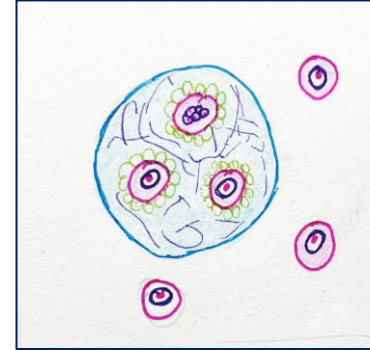
NODULAR LYMPHOCYTE PREDOMINANT TYPE



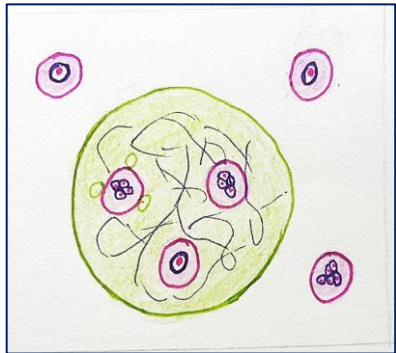
Pattern A
Typical B cell rich nodular



Pattern B
serpiginous nodular



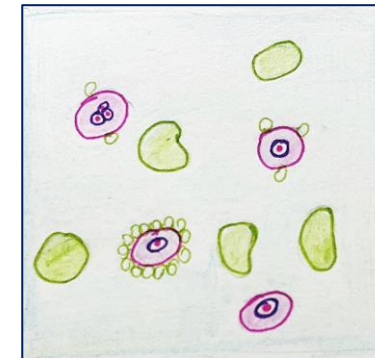
Pattern C
nodular with prominent extranodal LP cells



Pattern D
T cell rich nodular



Pattern E
T cell/histiocyte rich large B – cell lymphoma like



Pattern F
Diffuse moth eaten, B cell rich



B – cell rich



Follicular dendritic cell
meshwork



T cell rich



Reed Sternberg cell



T cell rosette

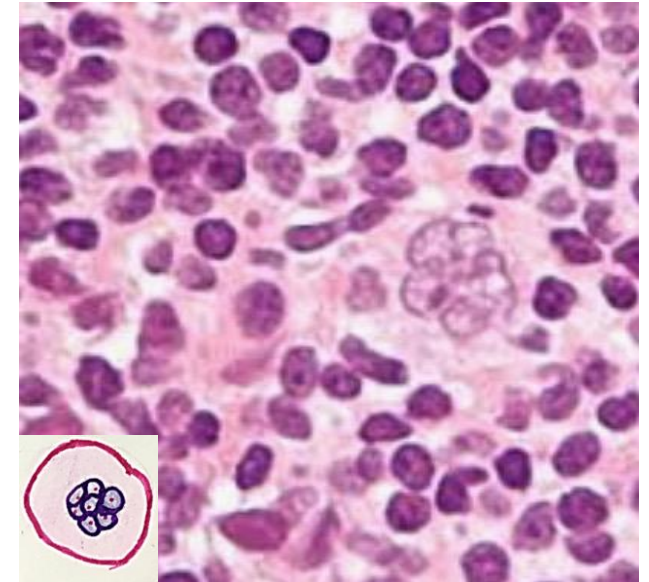


HODGKINS LYMPHOMA

NODULAR LYMPHOCYTE PREDOMINANT TYPE

L & H Reed Sternberg cells –

- Have multilobated nuclei resembling popcorn Kernel
- Express B cell markers typical of germinal center B cells
 - CD 20 – positive
 - CD 45 – positive
 - Bcl 6 – positive
 - CD 79a – positive
 - PAX 5 – positive
 - OCT 2 - positive
- Negative for CD 15 and CD 30 (which are positive in classical RS cell)



HODGKINS LYMPHOMA

PROGNOSTIC FACTOR

- **Age** – more than 50 years – poor prognostic factor
- **Clinical stage**
- **Extra nodal involvement** (especially if it is distant rather than direct spread) – bad prognostic factor
- **Degree of splenic involvement** – poor prognosis if more than 5 nodules
- **Microscopic type** – Lymphocyte predominant, Nodular sclerosis – best prognosis, mixed cellularity, lymphocyte depletion worse prognosis
- **Laboratory findings** – elevated LDH, raised ESR, decreased hematocrit, elevated serum levels of soluble CD25 and CD30 – poor prognosis
- **CD 15 negative expression** – poor prognosis



HODGKINS LYMPHOMA

Treatment and prognosis

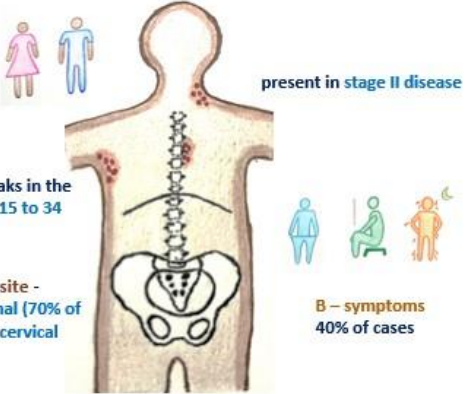
- **Cure rate is 90% - stage I and II**
- **Disease free 5 year survival rate for stage III and stage IV – 60% to & 70%**
- **Radiotherapy** is preferred treatment as chemotherapy leads to development of secondary tumors
- **Anti CD 30 antibodies – excellent result in patients with failed conventional therapy**



HODGKINS LYMPHOMA

NODULAR SCLEROSIS

constitutes 65% to 75% of cases



present in stage II disease

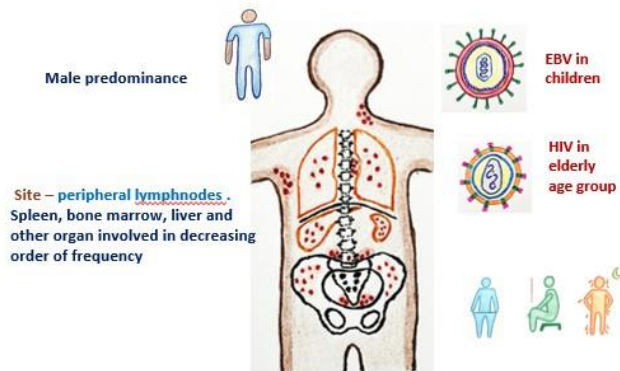
Age – peaks in the range of 15 to 34 years

common site - mediastinal (70% of cases) or cervical

B – symptoms
40% of cases

MIXED CELLULARITY

Constitutes 20% to 25% of cases



Male predominance

Site – peripheral lymph nodes. Spleen, bone marrow, liver and other organ involved in decreasing order of frequency

EBV in children

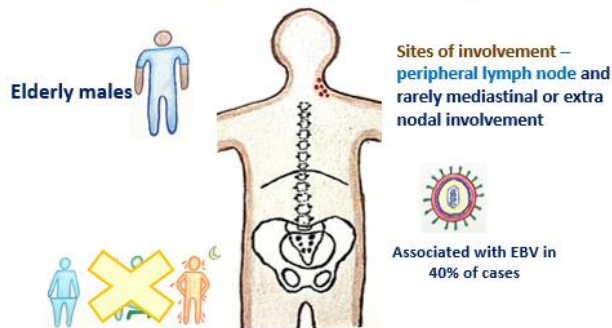
HIV in elderly age group

Presentation - stage III and stage IV

CLINICAL PRESENTATION

LYMPHOCYT RICH

Uncommon form of HL (incidence is 5%)



Elderly males

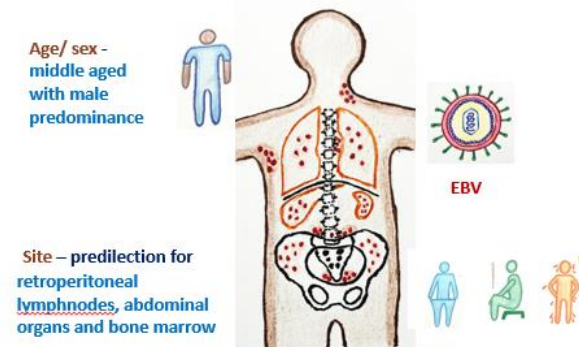
Sites of involvement – peripheral lymph node and rarely mediastinal or extra nodal involvement

Associated with EBV in 40% of cases

Presents in stage I and stage II

LYMPHOCYT DEPLETED

Least common form accounting for 2% with Worst prognosis



Age/ sex - middle aged with male predominance

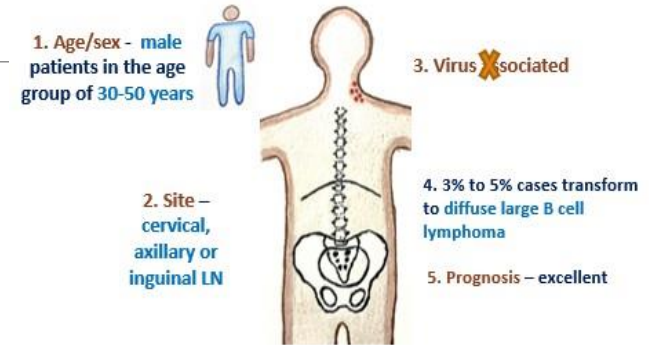
Site – predilection for retroperitoneal lymph nodes, abdominal organs and bone marrow

EBV

Presentation: present in stage III and stage IV

NLPHL

Accounts for 10% of Hodgkins lymphoma cases



1. Age/sex - male patients in the age group of 30-50 years

3. Virus X associated

2. Site – cervical, axillary or inguinal LN

4. 3% to 5% cases transform to diffuse large B cell lymphoma

5. Prognosis – excellent

present at stage I and II (20% present with advanced stage)

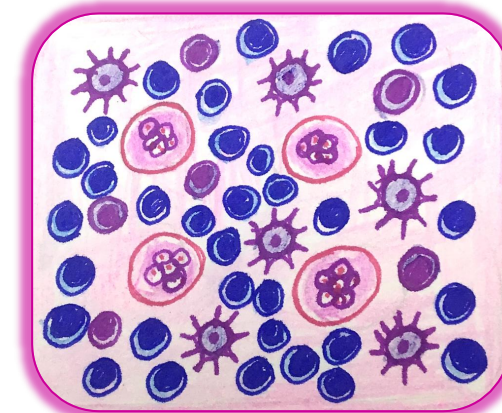


HODGKINS LYMPHOMA

NODULAR SCLEROSIS



NLPHL

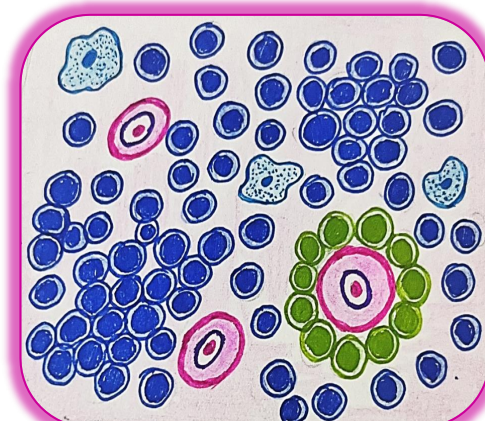


MICROSCOPY

MIXED CELLULARITY








LYMPHOCYTE RICH



LYMPHOCYTE DEPLETED



-  CD4+ PD1+ T cells
-  CD4+ CD 40L T cells
-  Reactive B cells
-  T follicular helper cell
-  Plasma cells
-  Fibroblast

-  Neutrophil
-  Follicular dendritic cell
-  Eosinophil
-  Macrophage
-  RS cell



Thank
You

