Hodgkin Disease (Lymphoma): Causes, Symptoms and Treatment

Hodgkin disease or Hodgkin's lymphoma is one of two common types of cancers of the lymphatic system. (specifically the white blood cells) The other type, non-Hodgkin's lymphoma, is far more common.

Hodgkin lymphoma is a **malignant neoplasm of B-cell origin** , characterized by the presence of **Reed-Sternberg (RS) cells** in a background of mixed inflammatory cells. It arises primarily in **lymph nodes** and spreads in a **contiguous, orderly fashion** .

- **Exact cause is unknown.**
- Strong association with **Epstein-Barr Virus (EBV)** infection—especially in mixed-cellularity and lymphocyte-depleted subtypes.
- Increased risk in **immunosuppressed patients** , particularly those with **HIV/AIDS** .

Epidemiology

- **Bimodal age distribution:**
  - Early peak: 15–34 years
  - Late peak: >55 years
- **More common in males** , especially in childhood (up to 85% of pediatric cases).
- Less common than non-Hodgkin lymphoma.

Pathophysiology

- Malignant transformation of **germinal center B-cells** into **Reed-Sternberg cells** .
- RS cells:
  - Large, binucleated or multinucleated ("owl’s eye" appearance).
  - Immunophenotype: **CD15+ and CD30+**
  - Rarely express B-cell markers **CD19/CD20** .
- EBV DNA is found in ~50% of cases, particularly **MCHD** (60–70%) and **LDHD** (up to 100% in HIV-positive).

Clinical Features

Typical Presentation:

- **Painless lymphadenopathy** (often cervical or supraclavicular; 80% above diaphragm)
- **B symptoms** (present in ~40% of patients):
  - Fever
  - Drenching night sweats
  - Unintentional weight loss (>10% in 6 months)
- **Pruritus**
- **Alcohol-induced pain** at lymph nodes (specific to HL)
- **Mediastinal mass** (causing chest pain, cough, SOB)

- Rare: **Pel-Ebstein fever** (cyclic fevers every 1–2 weeks)

Advanced Disease Signs:

- **Splenomegaly, hepatomegaly**
- **Superior vena cava syndrome**
- Paraneoplastic CNS syndromes (rare)

Histological Subtypes (WHO Classification)

Classical HL (95%) :

1. **Nodular Sclerosis HL (NSHL)** (60–80%)
    - Lacunar RS cells
    - Mediastinal involvement
    - Young adults; females
2. **Mixed Cellularity HL (MCHL)** (15–30%)
    - Classic RS cells
    - EBV common; associated with advanced disease
3. **Lymphocyte-Depleted HL (LDHL)** (<1%)
    - Elderly or HIV-positive
    - Poor prognosis; diffuse RS cells
4. **Lymphocyte-Rich Classical HL (LRCHL)** (5%)
    - Classic RS cells; good prognosis

Nodular Lymphocyte-Predominant HL (NLPHL) (5%)

- **Popcorn cells (L&H variant RS cells)**
- **CD20+** , **CD15-** , **CD30-**
- Indolent course; may transform to aggressive non-Hodgkin lymphoma

Diagnostic Workup

Laboratory Studies

- **CBC:** Anemia, lymphopenia, eosinophilia, neutrophilia, thrombocytopenia
- **ESR & CRP:** Often elevated (indicator of tumor burden)
- **LDH:** May be elevated (associated with high tumor burden)
- **LFTs:** Elevated ALP may suggest liver or bone involvement
- **Renal function & urinalysis:** Evaluate for paraneoplastic nephrotic syndrome

Imaging

- **Chest X-ray:** Mediastinal widening
- **CT neck, chest, abdomen, pelvis:** Assess nodal spread, organ involvement
- **PET-CT:** Preferred for staging and monitoring treatment response

Histopathology

- **Excisional lymph node biopsy** is gold standard
  - Shows RS cells in classical HL
  - Immunohistochemistry confirms subtype
- **Bone marrow biopsy:** Required in advanced-stage or systemic symptoms

Staging – Ann Arbor System

- **Stage I** : Single lymph node region or single extralymphatic site
- **Stage II** : ?2 lymph node regions on same side of diaphragm
- **Stage III** : Lymph node involvement on both sides of diaphragm
- **Stage IV** : Disseminated disease with extranodal involvement (e.g., bone marrow, liver)

Add "A" or "B" to indicate absence or presence of B symptoms

Prognostic Factors

- **Negative Predictors:**
  - B symptoms
  - Elevated LDH
  - Bulky disease
  - Advanced stage (III/IV)
  - Male gender
  - Age >45
  - Low albumin
- **Positive Predictors:**
  - Nodular sclerosis subtype
  - Absence of B symptoms
  - Early-stage disease

Treatment

1. Early-Stage (I–IIA):

- **ABVD chemotherapy** (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) ± involved-field radiation therapy (IFRT)

2. Advanced-Stage (IIB–IV):

- **ABVD or escalated BEACOPP** (Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone)

3. Relapsed/Refractory Disease:

- High-dose chemotherapy + **autologous stem cell transplant**
- **Brentuximab vedotin** (anti-CD30 antibody-drug conjugate)
- **PD-1 inhibitors** (nivolumab, pembrolizumab) in selected patients

Complications

- **Secondary malignancies** (e.g., leukemia, solid tumors)
- **Infertility** (chemotherapy-induced)
- **Cardiopulmonary toxicity** (from Adriamycin, Bleomycin)
- **Hypothyroidism** (post-neck irradiation)

Key NCLEX/USMLE High-Yield Points

- Presence of **Reed-Sternberg cells** = diagnostic hallmark
- Alcohol-induced pain in lymph nodes = **pathognomonic clue**
- **B symptoms** indicate worse prognosis and guide staging
- **PET-CT** is crucial for staging and treatment monitoring
- **CD15+ and CD30+** = classical HL; **CD20+** = NLPHL
- Always confirm diagnosis with **excisional biopsy** , not FNA