NOTES
LYMPHOMAS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Lymphocytic tumors
- *Nodal lymphomas:* develop in lymph nodes
- *Extranodal lymphomas:* develop in/spread to other organs/tissues
- Neoplastic B cells do not produce antibodies
- Attract non-neoplastic inflammatory cells (e.g. T cells) via chemokines
- Activate fibroblasts to make collagen, eosinophils

TYPES

Hodgkin's lymphomas

- Spread contiguously (to nearby lymph nodes; rarely extranodal)
  - *Prognosis better for Hodgkin's:* contiguous spread allows direct, targeted treatment
- Reed–Sternberg cells

Non-Hodgkin's lymphomas

- Spread non-contiguously
- No Reed–Sternberg cells

CAUSES

- Genetic mutation in lymphocytes → no apoptosis → cell divides → becomes neoplastic cell
- Possible link between viruses (e.g. HIV, EBV), lymphomas

COMPLICATIONS

- Metastasis to spinal cord → spinal cord compression → sensory/motor deficits
- Metastasis to bone marrow → crowds out normal marrow progenitor cells → decreases healthy erythrocytes/leukocytes/platelets

SIGNS & SYMPTOMS

- *B (systemic) symptoms:* fever, night sweats, weight loss, fatigue, loss of appetite, chills

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, positron emission tomography (PET) scan

- Stage of lymphoma

LAB RESULTS

Lymph node biopsy

- Confirmation, type

TREATMENT

- Depends on extent, stage, category; age, health of individual; coexisting diseases

MEDICATIONS

- Chemotherapy

SURGERY

- Stem cell transplant

OTHER INTERVENTIONS

- Radiation therapy

HODGKIN'S VS. NON-HODGKIN'S

	HODGKIN'S LYMPHOMA	NON-HODGKIN'S LYMPHOMA
OCCURRENCE	Bimodal: young adulthood; > 55y	Children and adults; risk increases with age
CELLULAR CHARACTERISTICS	B cells, Reed-Sternberg cells	B cells, T cells, natural killer (NK) cells
NODE INVOLVEMENT	Contiguous spread	Non-contiguous spread; extranodal
TYPES	Classic (nodular sclerosis, mixed cellularity, lymphocyte-depleted, lymphocyte-rich) Nodular lymphocyte predominant (has popcorn cells & no Reed-Sternberg cells)	Small lymphocytic, lymphoplasmacytic, extranodal marginal zone (MALT), follicular, mantle cell, diffuse large B-cell, Burkitt, precursor T-lymphoblastic, peripheral T-cell
PRESENTATION	Painless localized lymphadenopathy "B" symptoms	Painless localized lymphadenopathy; "B" symptoms and/or symptoms of extranodal spread
RISK FACTORS	Associated with EBV	Associated acquired or congenital immunodeficiency Endemic Burkitt lymphoma closely associated with EBV

HODGKIN'S LYMPHOMA

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PATHOLOGY & CAUSES

- *B-cell tumors; Reed–Sternberg cells:* large mononuclear, neoplastic cells; two cells fused, two nuclei (resemble owl eyes)

TYPES

Classical Hodgkin's lymphoma (CHL)

- More common
- Reed–Sternberg cells express CD45/CD20; not CD15/CD30
- *Histological subtypes:* background inflammatory cells, fibrosis

Histological CHL subtypes

- Nodular sclerosis Hodgkin's lymphoma
  - Most common; esp. in young adults
  - Neoplastic, inflammatory cells surrounded by collagen from fibroblasts forming nodules
  - Lacunar cells (Reed–Sternberg cells with shrunken cytoplasm, nucleus appears as if in middle of lacuna/lake)
  - Good prognosis
- Mixed cellularity
  - Second most common; more common in older adults
  - Prevalent in HIV-positive individuals
  - Mixed inflammatory background

composed of eosinophils, neutrophils, plasma cells, histiocytes surrounding Reed–Sternberg cells

- Lymphocyte-rich
  - Reed-Sternberg cells surrounded by lymphocytes
  - Best prognosis, caught early
- Lymphocyte-depleted
  - *Rarest; median age:* 30–37 years
  - No reactive lymphocytes, abundance of Reed–Sternberg cells
  - Prevalent in HIV-positive individuals
  - Worst prognosis, advanced stage diagnosis

Nodular lymphocyte predominant Hodgkin's lymphoma

- More common in individuals who are biologically male
- Abnormal B cells express CD20/CD45; not CD15/CD30
- Lymphocyte-predominant cells; no Reed–Sternberg cells
  - Large groups of lymphocytes form nodules around lobulate-nucleated "popcorn" cells (variant of Reed–Sternberg cells)
- Slow-growing, highly curable
- Small risk of transformation to aggressive non-Hodgkin's lymphoma

STAGING

- *Stage 1:* limited to one lymph node group/group of adjacent lymph nodes
- *Stage 2:* ≥ two lymph node regions on same side as diaphragm
- *Stage 3:* lymph nodes on both sides (superior, inferior) of diaphragm
- *Stage 4:* lymph nodes superior, inferior to diaphragm; liver/spleen/lungs/bone marrow
- Subdivisions
  - *Category A:* no symptoms
  - *Category B:* B symptoms present
  - *Category E:* organs/tissues beyond lymph system

SIGNS & SYMPTOMS

- Painless cervical lymphadenopathy
  - *Mediastinal lymphadenopathy:* nodular sclerosis subtype
- *Cytokine release:* fever, drenching night sweats, weight loss
  - Rarely present with nodular lymphocyte predominant Hodgkin's lymphoma
- B symptoms
  - *Nodular sclerosis:* about 50%
  - *Mixed cellularity:* common
  - *Lymphocyte-rich:* rare
  - *Lymphocyte-depleted:* common

DIAGNOSIS

DIAGNOSTIC IMAGING

- CT scan, PET scan

LAB RESULTS

- Lymph node biopsy

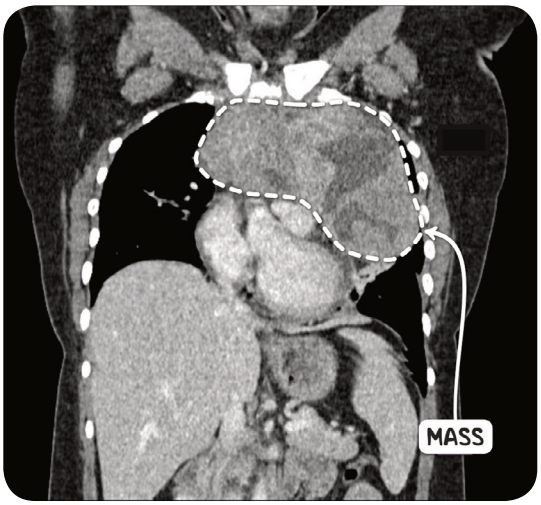

Figure 49.1 A CT scan of the chest in the coronal plane demonstrating a large mediastinal mass. The mass is a focus of Hodgkin's lymphoma.

TREATMENT

MEDICATIONS

Rituximab

- For nodular lymphocyte predominant Hodgkin's lymphoma
- Monoclonal antibody, binds CD20, induces complement-mediated lysis → apoptosis

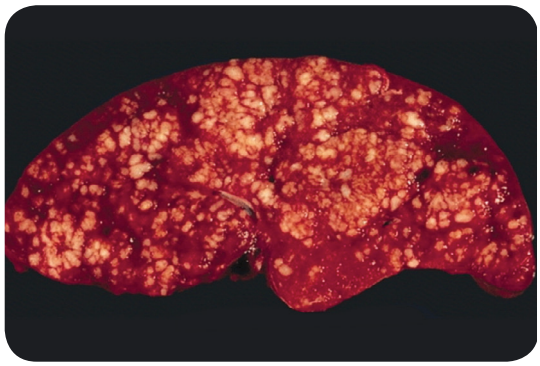

Figure 49.3 The gross pathology of a spleen that has been infiltrated by Hodgkin's lymphoma.

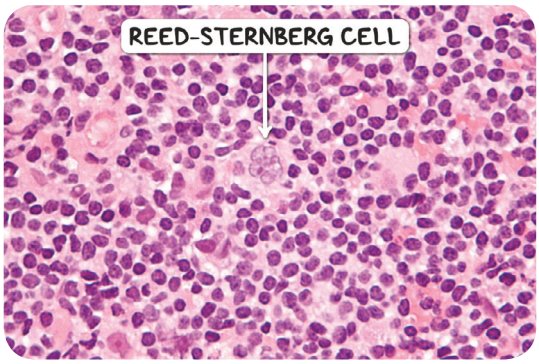

Figure 49.2 The histological appearance of Hodgkin's lymphoma. Reed–Sternberg cells are pathognomonic of this disease.

NON-HODGKIN'S LYMPHOMA

osms.it/non-hodgkin

PATHOLOGY & CAUSES

- B/T cell tumors, no Reed–Sternberg cells

TYPES

B cell lymphomas

- More common
- *Neoplastic B cells:* CD20 on surface
- *Rate of growth:* slow/aggressive/highly aggressive

B cell lymphoma subtypes

- Diffuse large B cell lymphoma
  - Aggressive
  - Most common
- Follicular lymphoma
  - Slow growing
  - *Chromosomal translocation:* t(14,18) → *BCL2* gene placed after Ig heavy chain promoter → overexpression of BCL2 → inhibition of apoptosis → cell proliferation
  - BCL2 promotes cell viability, blocks apoptosis
- Burkitt lymphoma
  - Highly aggressive
  - "Starry sky" appearance under microscope
  - *Stars:* tingible bodies (macrophages) with phagocytosed dead neoplastic cells
  - *Sky:* dark neoplastic lymphocytes
  - *Chromosomal translocation:* t(8,14) → Myc gene moved adjacent to IgH

promoter sequence → upregulation of *Myc* gene → Myc gene stimulates cell growth, metabolism → increased cell division
    - *Variant in individuals of African descent:* extranodal involvement of jaw, associated with EBV infection
    - *Variant in individuals of non-African descent:* extranodal involvement of abdomen (e.g. at ileocecal junction), less frequently associated with EBV infection
- Mantle cell lymphoma
    - Aggressive
    - *Chromosomal translocation:* t (11,14) → *BCL1* gene moved to Ig promoter → upregulation of *BCL1* gene → stimulation of cell growth
- Marginal zone lymphoma
    - Indolent
    - Most common type
    - Associated with mucosa-associated lymphoid tissue (extranodal) in cases of chronic inflammation of stomach lining (e.g. chronic H. pylori infection)
    - May occur in lymph nodes (nodal marginal zone lymphoma)/spleen (splenic marginal zone lymphoma)
- Lymphoplasmacytic lymphoma
    - Indolent
    - Bone marrow, lymph nodes, spleen
    - *Waldenstrom macroglobulinemia:* neoplastic cells produce M proteins (IgM) in high levels → IgM released into

TYPES OF NON-HODGKIN'S LYMPHOMAS

	OCCURRENCE	CHARACTERISTICS
BURKITT (VERY AGGRESSIVE)	Adolescents, young adults	Arises from germinal center B cell; Clinical forms: endemic, sporadic, immunodeficiency-associated; "Starry sky" appearance
DIFFUSE LARGE B CELL (AGGRESSIVE)	Mostly adults (Most common type)	Arises from germinal center or post-germinal center B cell; Diffuse extranodal involvement, often present in GI tract; Variant arises from thymic (medullary) B cells
EXTRANODAL MARGINAL ZONE (MALT) (SLOW GROWTH)	Mostly adults (Risk ↑ with age)	Arises from B cells of the mucosa-associated lymphoid tissue (MALT) Often present in GI tract; Gastric MALT lymphoma linked with H. pylori Forms lymphoepithelial lesions
FOLLICULAR (SLOW GROWTH)	Adults	Arises from germinal center B cells (centrocytes and centroblasts); Painless, relapsing/remitting pattern of lymphadenopathy; Microscopic and gross nodular appearance May transform into more aggressive NHL
LYMPHOPLASMACYTIC	Adults (Risk ↑ with age)	Arises from peripheral B lymphocytes; Manifests from Waldenström macroglobulinemia; Malignant cells resemble plasma cells with large amounts of basophilic cytoplasm; Nucleus contains "spoke wheel -like" chromatin
MANTEL CELL (MODERATELY AGGRESSIVE)	Adults (Risk ↑ with age)	Arises from pre-germinal center B cells of the mantle zone; Results from deregulation of cyclin D1; Diffuse growth pattern; Cells have "notched" nuclei

blood → increases blood viscosity

T cell lymphomas

- Adult T cell lymphoma
  - *AKA leukemia:* abnormal leukocytes in bloodstream
  - *Possibly cause:* human T-lymphotropic virus (HTLV)
  - HTLV infects T cells → becomes incorporated into T cell DNA → genetic mutation → adult T cell lymphoma
- Mycosis fungoides
  - T cell lymphoma of of skin, resembles fungal infection
  - *Neoplastic cells:* CD4+ helper T cells circulate in blood → Sezary syndrome (erythroderma)

SIGNS & SYMPTOMS

- Painless lymphadenopathy
- *B symptoms:* release of cytokines
- *Extranodal involvement of GI tract:* bowel obstruction
- *Extranodal involvement of bone marrow:* fatigue, easy bruising, recurrent infections
- *Extranodal involvement of spinal cord:* motor/sensory deficits (esp. legs)

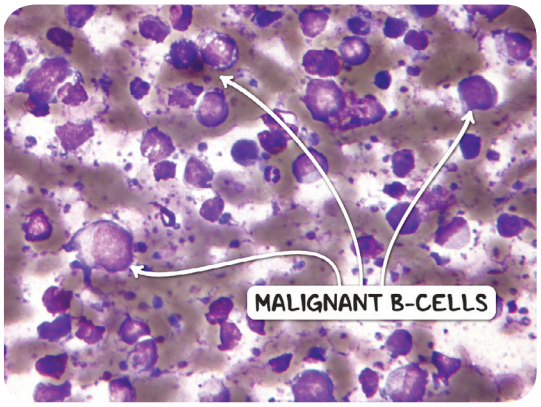

Figure 49.5 A diffuse large B-cell lymphoma in a cytology specimen.

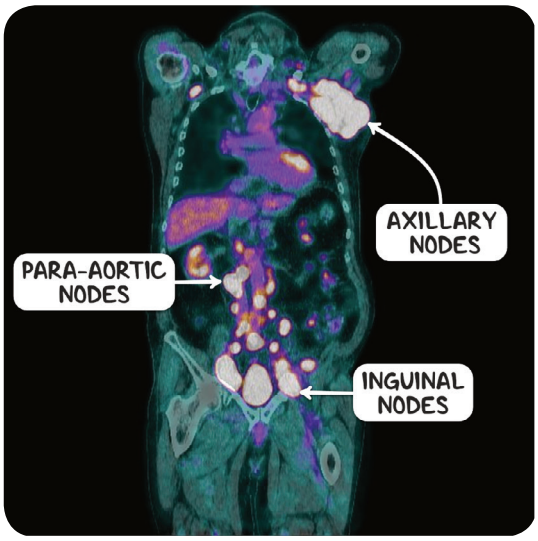

Figure 49.4 A PET scan in the coronal plane demonstrating gross lymphadenopathy in the axillary, para-aortic and inguinal chains. The underlying cause is a Non-Hodgkin lymphoma.

DIAGNOSIS

DIAGNOSTIC IMAGING

- CT scan, PET scan

LAB RESULTS

- Lymph node biopsy

TREATMENT

MEDICATIONS

Rituximab

- CD20-positive B cell non-Hodgkin lymphomas

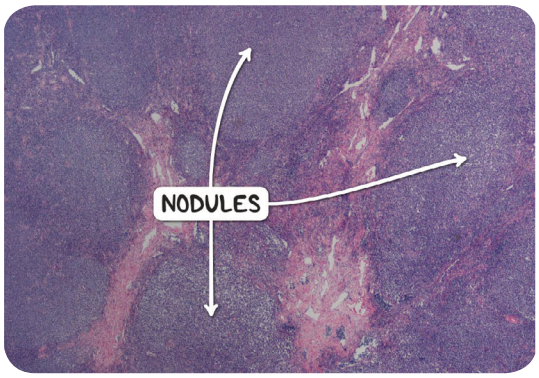

Figure 49.6 The histological appearance of mantle cell lymphoma at low power. This lymph node has been infiltrated by the malignant lymphocytes which have a vaguely nodular architecture.

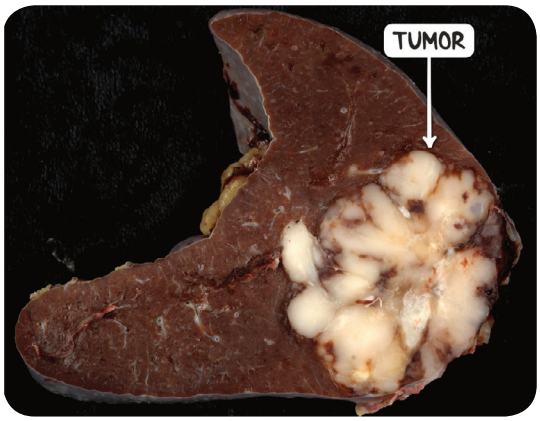

Figure 49.7 A diffuse large B-cell lymphoma in a cytology specimen.