((Lymphadenopathy))

- Elarged lymph nodes:
  - Painful = infection
  - Painless = chronic inflammation, metastatic carcinoma or lymphoma
    - In chronic inflammation, elargement of the lymph node is due to hyperplasia of lymph node regions:
      - Follicles: rheumatoid arthritis & early HIV
      - Paracortex: viral infection
      - Sinus histiocytes: lymph node draining tissue with cancer

* HIV: infects CD4+ cells
* Histology of lymph node
  1. Cortex: B-cells
  2. Paracortex: T-cells
  3. Medulla: sinus histiocytes

((Lymphoma))

- Lymphoma: it is a neoplastic proliferation of lymphoid cells that form a mass
  - Arising in: lymph nodes or extranodal tissues

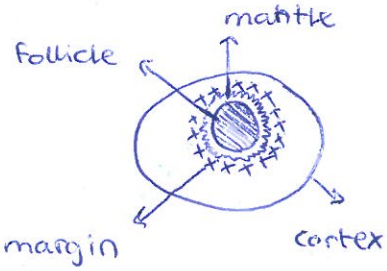
Lymphoma
- Non-Hodgkin lymphoma (60%)
- Hodgkin lymphoma (40%)

- NHL is further classified by:
  - Cell type: B-cells or T-cells
  - Cell size: small, intermediate or large
  - Pattern of growth: diffuse sheets or follicles
  - Expression of surface markers
  - Cytogenetic translocations

- NHL (especially of B-cells):

1. Follicular lymphoma:
   - Neoplastic small B-cells, CD20+, producing follicle-like nodules
   - Presenting in late adulthood with painless lymphadenopathy
   - Cause: t(14;18) → expression of BCL2 → inhibiting apoptosis
   - Patients are usually asymptomatic & live for a long time.
   - Treatment: for symptomatic patients
     - low-dose chemotherapy
     - Rituximab: anti-CD20 antibody

* Small neoplastic lymphocytes are well differentiated
* Remember that B-lymphocytes are present in the cortex of lymph nodes



((Lymphoma))

- NHL (especially of B-cells):
  - [1] Follicular lymphoma (continued):
    - Complications:
      - Progression to diffuse large B-cell lymphoma
        Presents as an enlarging lymph node
      - How to differentiate from follicular hypeplasia which is occurring in response to an infection?
        - In follicular lymphoma, there is disruption of normal architecture of the lymph node
        - No tingible body macrophages in follicular lymphoma
        - Expression of BCL-2 in follicular lymphoma
  - [2] Mantle cell lymphoma:
    - Neoplastic small B-cells, CD20+, expanding the mantle zone
    - Presenting in late adulthood with painless lymphadenopathy
    - Cause: t(11, 14) → expression of cyclin-D1 → causing the cell cycle to move from G_1 to S phase
  - [3] Marginal zone lymphoma:
    - Neoplastic small B-cells, CD20+, expanding the marginal zone
    - Cause: Hashimoto's thyroiditis, Sjögren's syndrome, H. pylori gastritis
      ↓
      gastric MALToma which may regress with treatment of H. pylori
  - [4] Burkitt lymphoma:
    - Neoplastic intermediate-sized, CD20+
    - Associated with: EBV
    - Presenting in children as extranodal mass
    - There are two types:
      - African: involving the jaw
      - Sporadic: involving the abdomen
    - Cause: t(8, 14) → expression of c-myc → promoting cell growth → ↑ mitotic activity → starry-sky appearance

((Lymphoma))

- NHL (especially of B-cells):

[5] DLBCL (Diffuse Large B Cell Lymphoma):

- → Neoplastic large B-cells, CD20+, growing diffusely in sheets
- → Most common form of NHL
- → Clinically aggressive: because large cells are not well differentiated
- → Arising:
  - → sporadically
  - → From transformation of follicular lymphoma
- → Presentation: late adulthood as enlarging lymph node or extranodal mass

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- Hodgkin Lymphoma
  - → Hallmark is Reed-sternberg cells ($CD15^+$, $CD30^+$) which will secrete cytokines resulting in:
    - → B-symptoms: fever, chills & nightsweats
    - → Attraction of lymphocytes, plasma cells, macrophages & eosinophils
    - → Fibrosis
  - → Subtypes of Hodgkin lymphoma:
    - → Nodular sclerosis (70% of cases):
      - → Elarged cervical or mediastinal lymph nodes
      - → Young female
      - → Biopsy: lymph node divided by large bands of fibrosis (generating nodules) + lacunar cells
    - → Lymphocytes-rich: best prognosis
    - → Lymphocytes-depleted: worst prognosis, seen in elderly & HIV (+) individuals
    - → Mixed cellularity: abundant eosinophils (IL-5).

* Reed-Sternberg cells are large B-cells with multilobed nuclei & prominant nucleoli (Owl's eye)

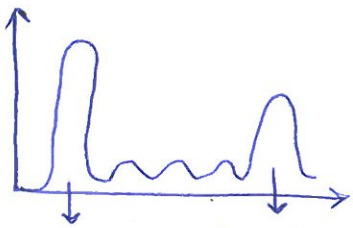
* Lacunar cells are special Reed-sternberg cells seen in nodular sclerosis

((Plasma Cell Disorders))

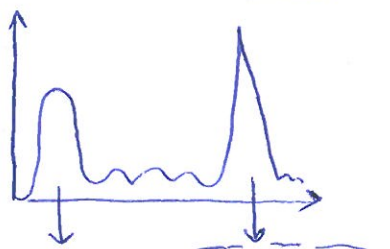
- **Multiple Myeloma:**
  - Malignant proliferation of plasma cells in bone marrow (most common primary malignancy of bone).
  - ↑ IL-6 (which is an important growth factor for plasma cells).
  - ✱ → Plasma cells producing → osteoclast activating factor → leading to punched-out lesions of bone seen on X-ray especially in:
    - Skull
    - Vertebra

    and this will result in ↑ risk of fractures & hypercalcemia
  - ✱ → These plasma cells will also produce immunoglobulins leading to → elevated serum protein ⟹ Detected by serum protein electrophoresis
    - Characterized by M-spike → which is usually monoclonal IgG or IgA
  - ✱ → There will be ↑ risk of infections with neoplastic plasma cells (why?) → because produced antibodies have no antigenic diversity
  - ✱ → Rouleaux formation on blood smear (due to ↓ charge between RBCs)
  - ✱ → Kidney:
    - Light chain excreted in urine as Bence-Jones proteins
    - Deposition of light chains in kidney tubules leading to renal failure (myeloma kidney)
  - → MGUS: only M-spike with no other features of multiple myeloma; seen in elderly; might develop into multiple myeloma.

normal:



multiple myeloma:



indicating monoclonal antibodies

*Rouleaux formation: RBCs are sticking to each other instead of being well distributed on the slide of blood smear