



Pathology of the head and neck region and lymphomas

The topics today...

I. Differential diagnosis of a neck mass

II. Neck cysts

III. Diseases of the lymphnodes

Metastasis

Hodgkin and non-Hodgkin lymphoma

IV. Diseases of the esophagus

Developmental diseases

Diverticuli

Esophagitis

Esophageal carcinoma

Topics covered for the exam

Cervical and orofacial cysts
Esophageal diverticles. Tracheo-esophageal fistules
Oesophagitis forms
Esophageal cancer
Principles of the lymphoma classification
Chronic lymphocytic leukemia. Follicular lymphoma
Diffuse large B-cell lymphoma. Burkitt lymphoma
Hodgkin-lymphoma
Cervical lymph node metastases
Orofacial manifestations of haematological diseases

Differential diagnosis of a mass in the neck

Congenital/Iatrogen:

Cystic lesions of the neck
Torticollis
Hygroma colli
Skin emphysema

Inflammatory/Idiopathic:

Lymphadenitis
Lymphadenopathy
Phlegmone of the neck
Cysts
Fistula

Tumor:

Malignant Lymphoma
Glomus tumor
Lipoma
Fibroma
Hemangioma
Lymphangioma
Tumors of the salivary glands

Neurologic:

Neurofibromatosis

Systemic:

Lymphoedema
Venous congestion of neck

Endocrine:

Goiter

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Torticollis is a dystonic condition defined by an abnormal, asymmetrical head or neck position, which may be due to a variety of causes.

- **Congenital muscular torticollis**
- **Acquired torticollis**
- Noncongenital muscular torticollis may result from scarring or disease of cervical vertebrae, adenitis, tonsillitis, rheumatism, enlarged cervical glands, retropharyngeal abscess, or cerebellar tumors.
- Tumors of the skull base (**posterior fossa** tumors)
- Infections in the posterior **pharynx** (irritate the nerves supplying the neck muscles and cause torticollis).
- Ear infections
- The use of certain drugs, (**antipsychotics**, Antiemetics)



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Subcutaneous emphysema after tooth extraction
(a rare complication)
Air accumulates subcutaneously
-- Crepitation

Airway damage
Trauma
PTX, etc.



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Systemic:

Lymphoedema

Venous congestion of neck

Endocrine:

e.g. Goiter

Lateral branchiogenic cysts – Fistulas

They are remnants of the embryological branchial cleft or cervical sinus

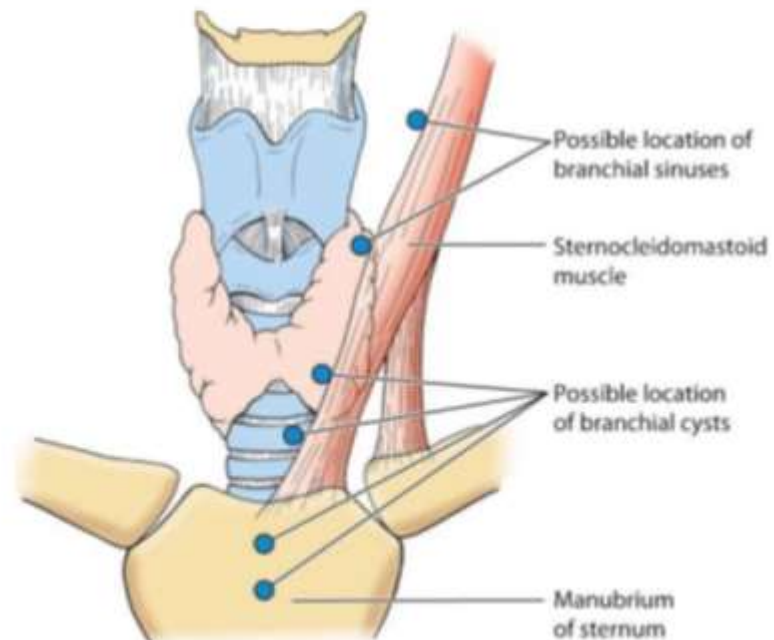
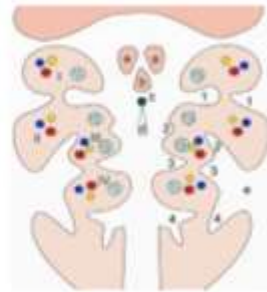
- Second branchial cleft cysts (most common type)

They are usually located just inferior to the angle of the mandible and anterior to the sternocleidomastoid muscle.

- First branchial cleft cysts (< 1%) (typically appear on the face near the auricle)
- Third branchial cleft cysts (rare) (located anterior to the sternocleidomastoid muscle but are typically lower than a second branchial cleft cyst)

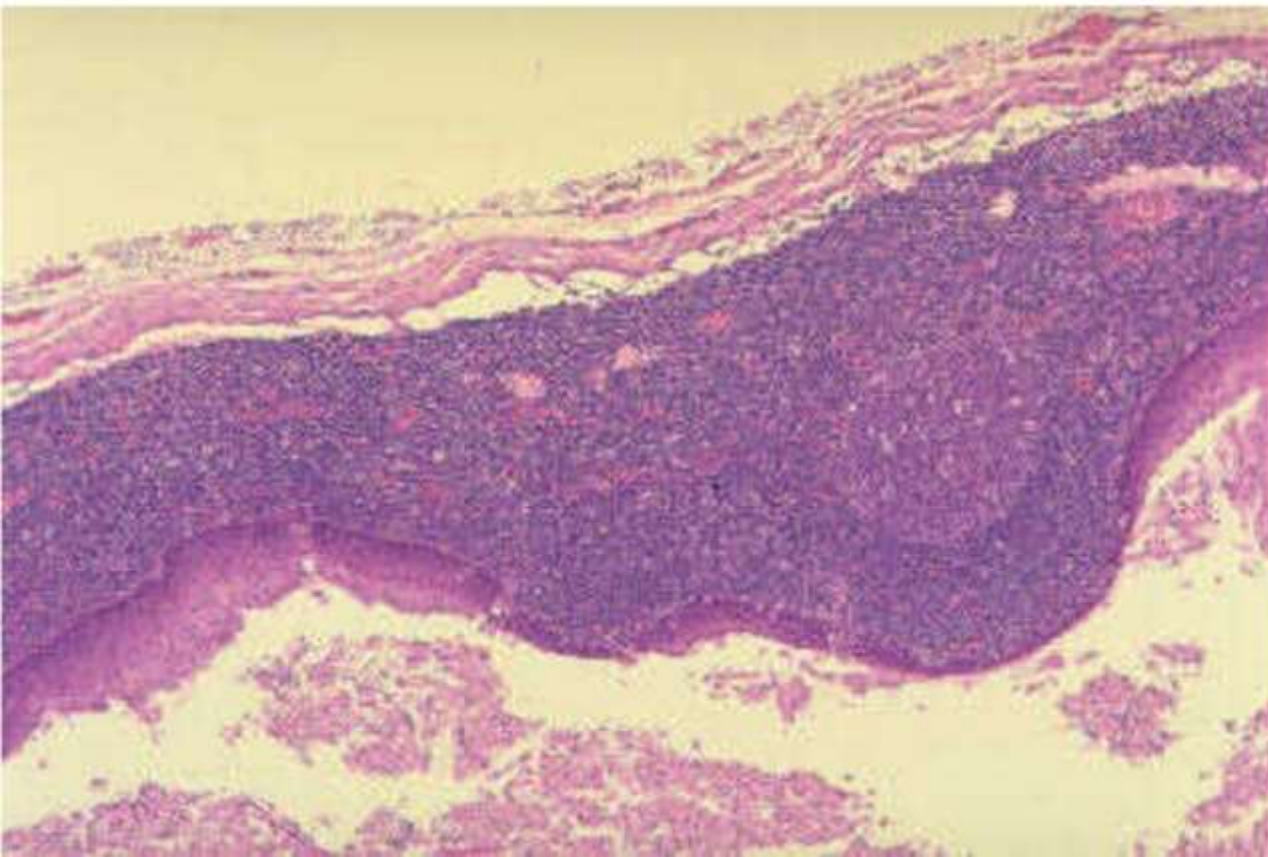
Complications:

- Recurrent infections
- Acute severe infections of third or fourth branchial cleft cysts can cause pharyngeal edema and airway and swallowing problems.



Branchyogenic cyst –

Epithelial lining surrounded with lymphoid tissue

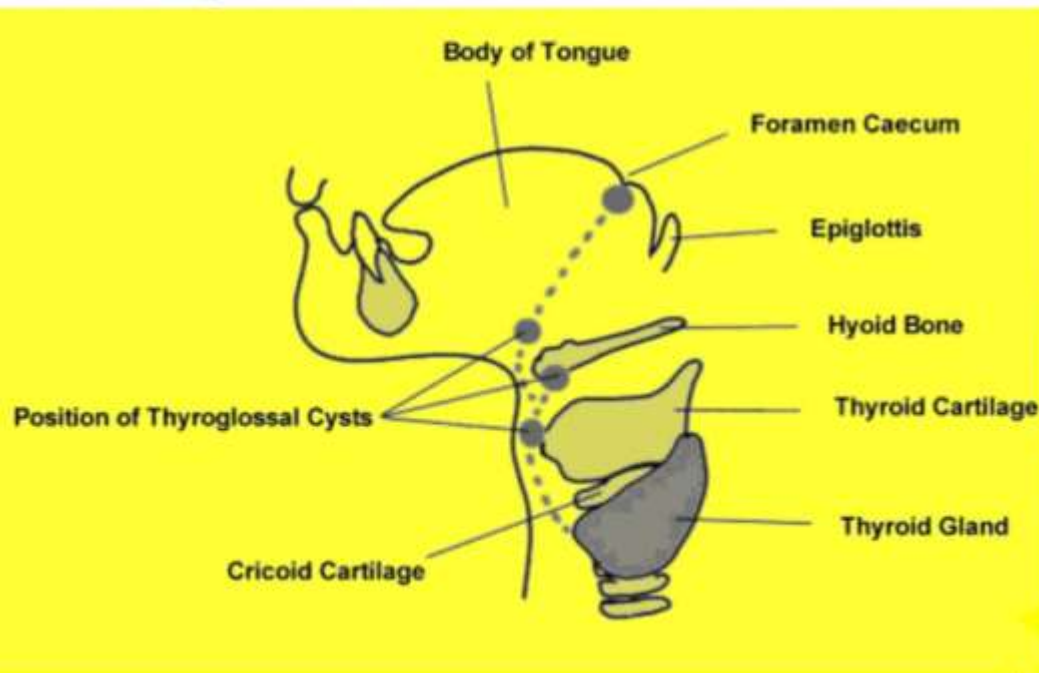


Thyroglossal duct cyst —

In contrast to branchial cleft cysts, thyroglossal duct cysts present as a midline mass in the anterior neck.

They are often asymptomatic until they become infected in the setting of an upper respiratory tract infection.

- Surgical treatment is the standard in the management of thyroglossal duct cysts.
- Since thyroid carcinoma can be present in a small percentage (1 to 2 percent) of thyroglossal duct cysts, all thyroglossal duct cysts and tracts should undergo a careful histologic examination.



A lymphnode enlargement in the neck region must be counted as a metastasis or lymphoma until proven otherwise.

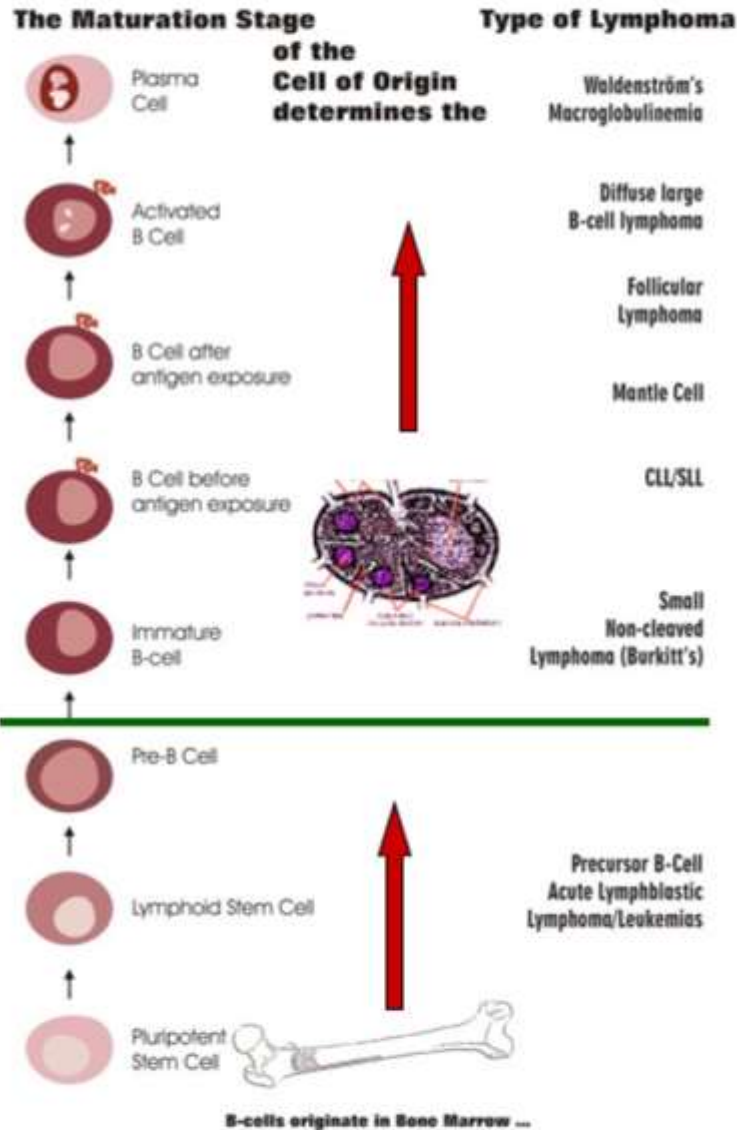


Abb. 86: Palpation des Halses

- | | |
|-------------------|---------------------------|
| 1. präauriculär | 5. prä- und paralaryngeal |
| 2. retroauriculär | 6. jugulär |
| 3. submandibulär | 7. nuchal |
| 4. submental | 8. supraclaviculär |

| Lymph node group | Anatomic areas drained |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Occipital | Posterior scalp |
| Postauricular | Temporal and parietal scalp |
| Preauricular | Anterior and temporal scalp, midface, nose, anterior ear canal and pinna, lateral conjunctivae |
| Parotid | Forehead and temporal scalp, midface, nose, external ear canal, middle ear, gums, parotid gland |
| Submandibular (submaxillary) | Cheek, nose, lips, anterior tongue, submandibular gland, buccal mucosa |
| Submental | Central lower lip, floor of mouth, tongue |
| Superficial cervical | Skin, lower larynx, lower ear canal, parotid |
| Superior deep cervical | Tonsil, adenoid, posterior scalp and neck, tongue, larynx, hypopharynx, thyroid, palate, nose, esophagus, paranasal sinuses, nasopharynx, other cervicofacial nodes |
| Inferior deep cervical | Dorsal scalp and neck, nasopharynx, superficial pectoral region of the arm, superior deep cervical |

II. Diseases of the lymphoid system

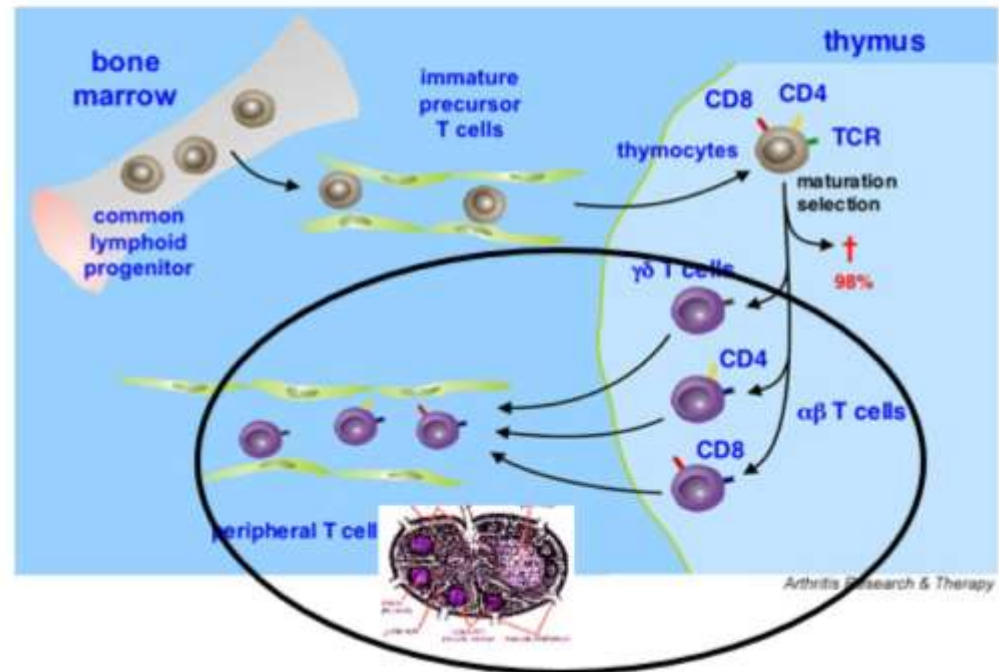


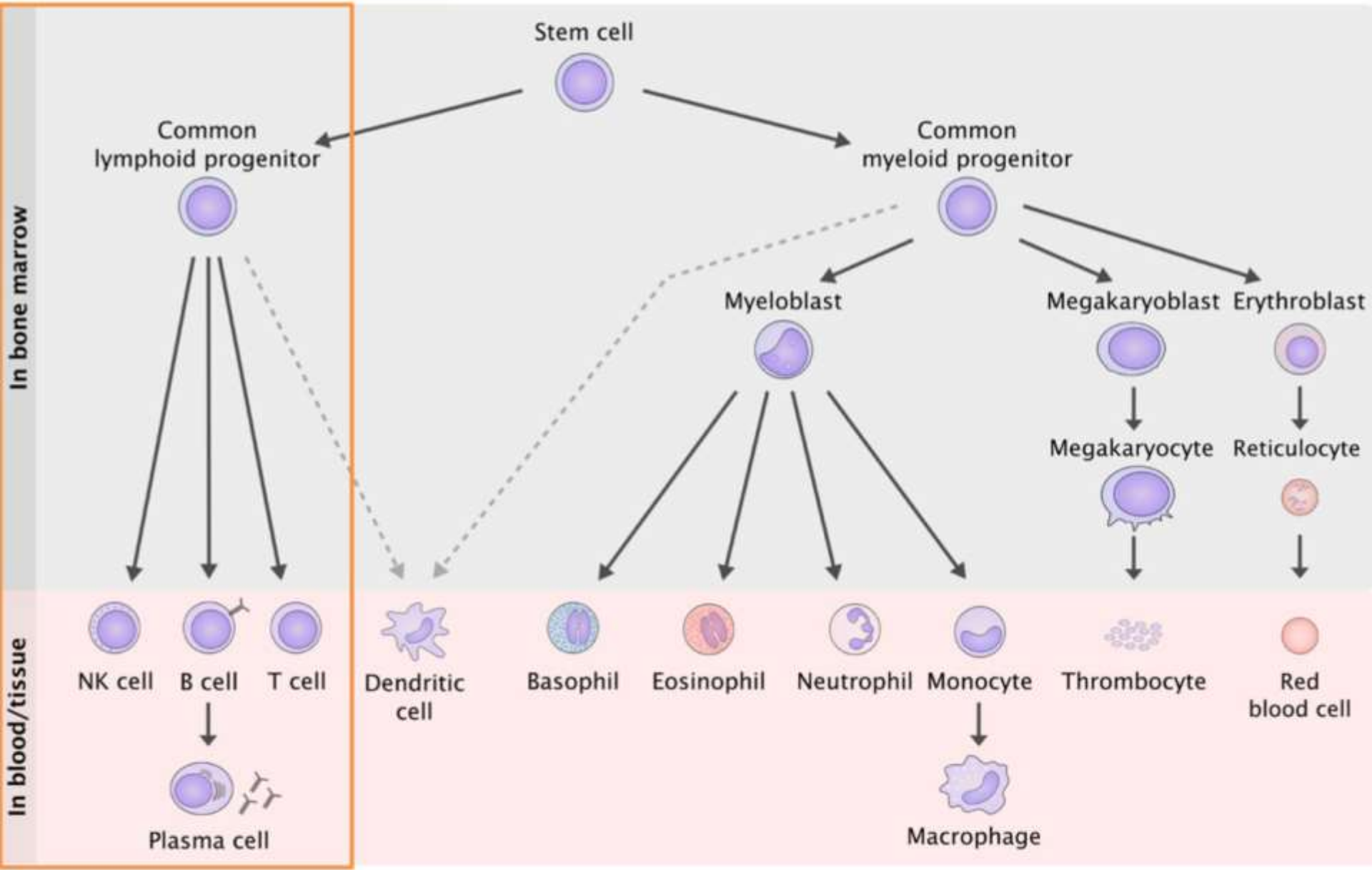
Stem cells – Bone marrow (BM)

Progenitors: T-cell – thymus

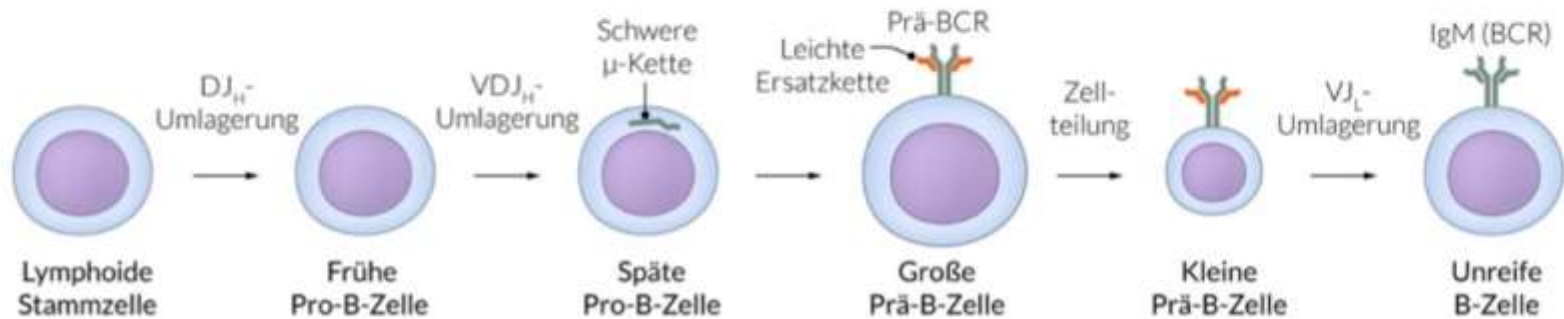
B-cell – BM

Mature T + B cells: lymph nodes, spleen, extranodal lymphoid tissues

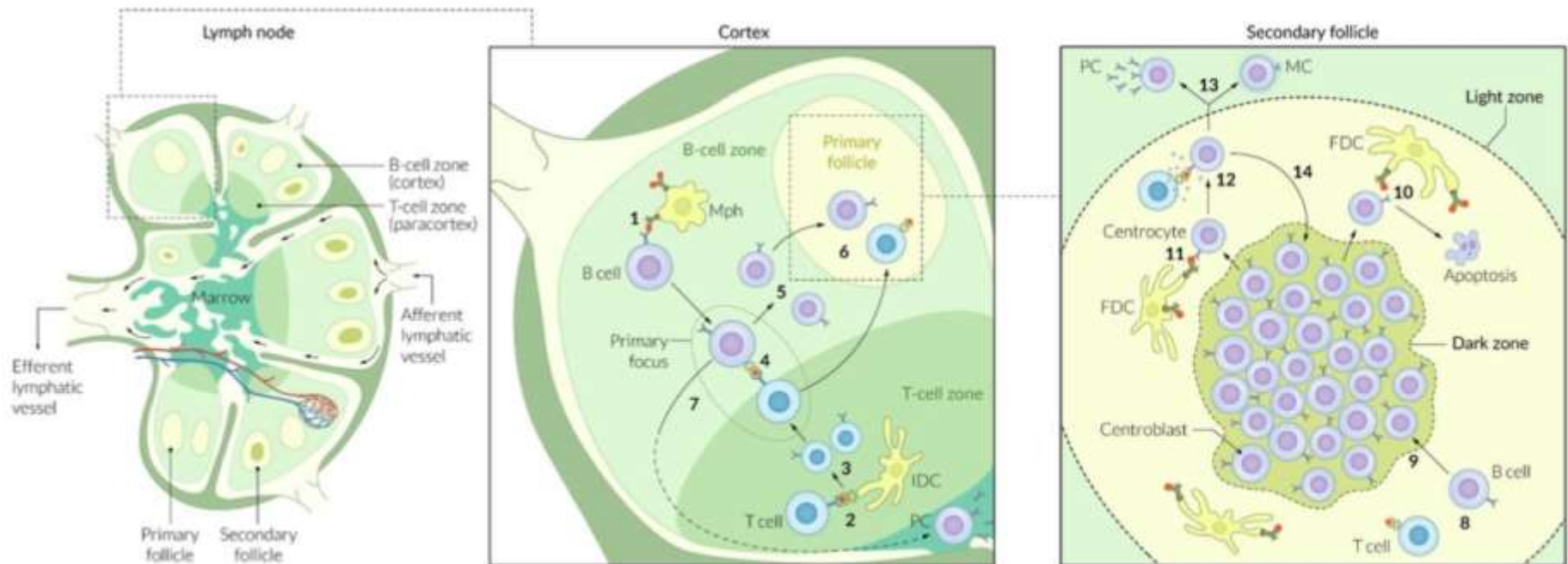




B-sejt érés folyamata a csontvelőben (Antigen independens)



B-sejt érés folyamata a nyirokcsomóban (Ag dependens)



Function

- Filtration of lymph
- As secondary lymphoid organ: Activation of the immunsystem

Location

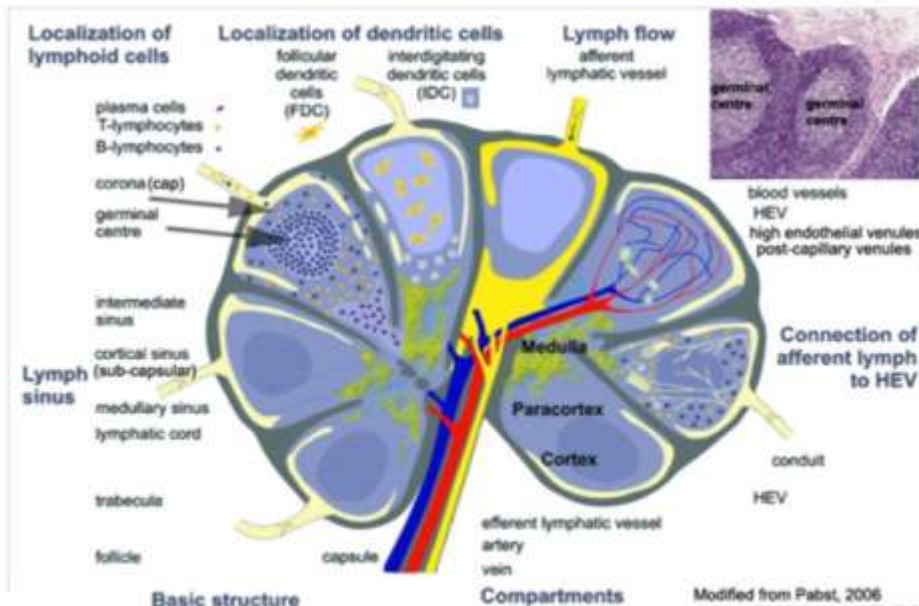
- Forming regions throughout the body (mainly close to organs, perivascular)

Form

- Bean shaped organ

Size

- Few mm – 1,5 cm

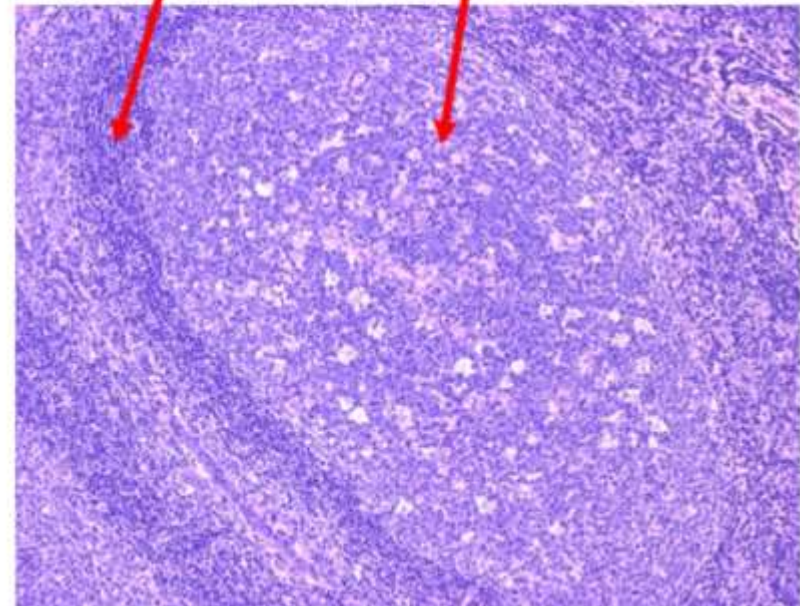


Modified from Pabst, 2006
J. Anat. (2006) 209, pp585–595

Secondary follicle

Mantle zone

Germinal center





Enlarged lymph node

Reactive

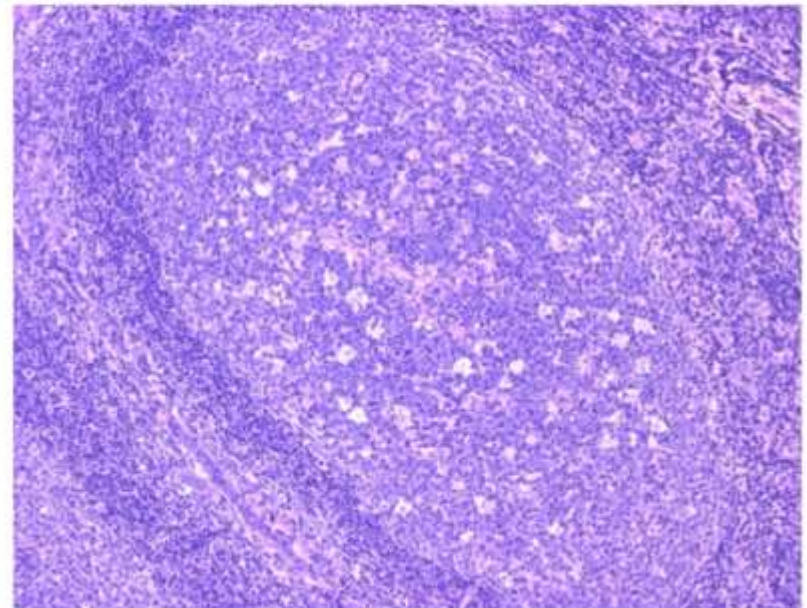
- Follicular hyperplasia
- Paracortical hyperplasia
- Sinus histiocytosis



- Infectious diseases
specific lesions
- Systemic diseases
often with lymph
node involvement

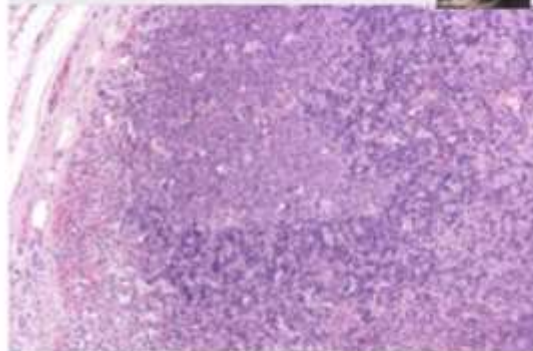
Neoplastic

- Lymphoma
- Metastasis

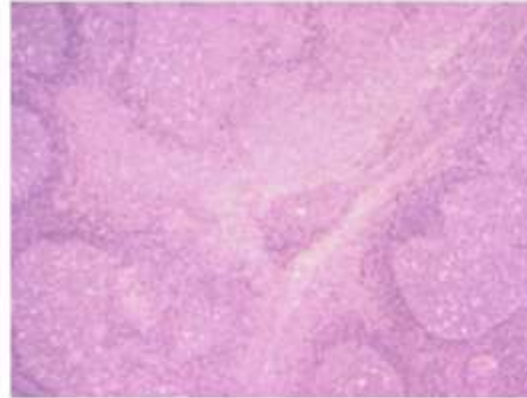




Infectious mononucleosis (EBV)
Paracortical activation



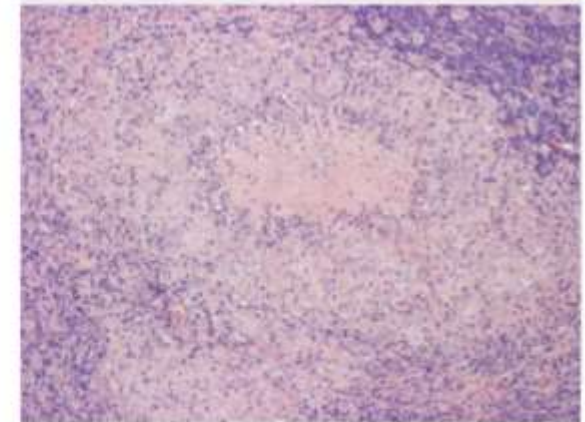
Toxoplasmosis
Piringer-Kuchinka



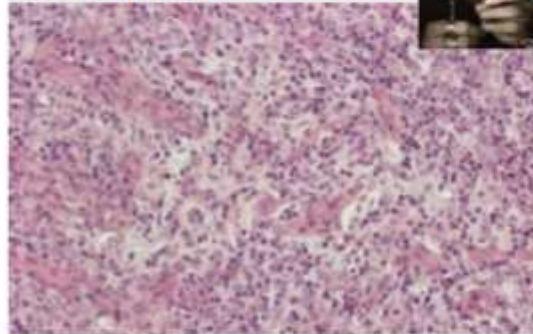
Cat-scratch disease
Lymphogranuloma venereum
Tularemia



Granulomatous with accumulation neutrophils



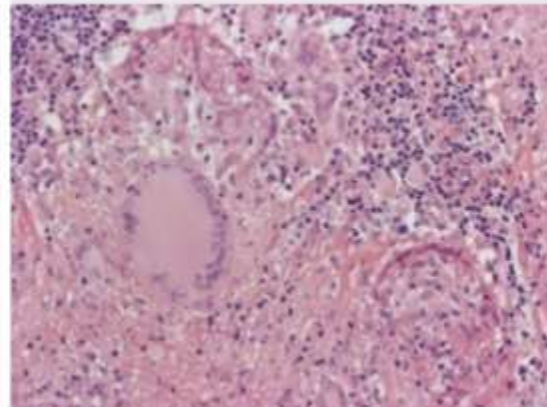
AIDS (HIV)



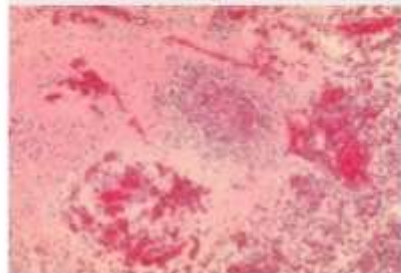
Mycobacteriosis



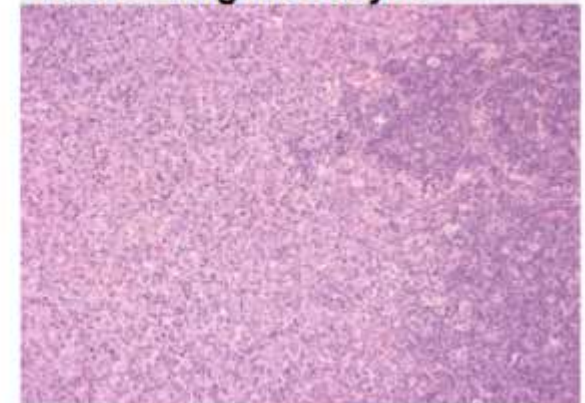
Caseating granulomatous



Plague (Y. pestis)
Hemorrhagic necrotizing



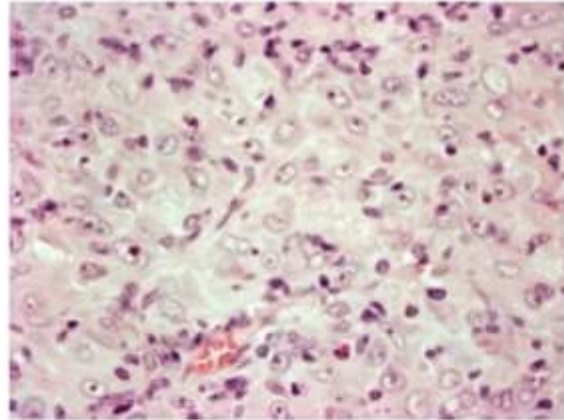
Kikuchi's disease
necrotizing histiocytic





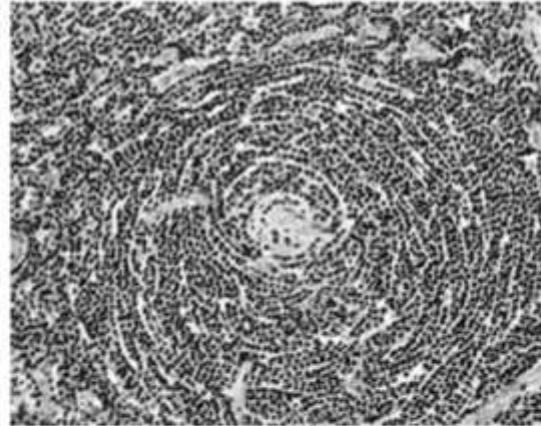
Rosai – Dorfman

Sinus histiocytosis
with massive
lymphadenopathy

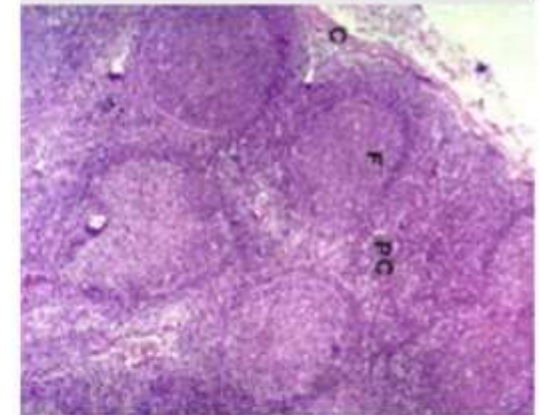


Castleman disease

Hyalin vascular,
plasmacytic,
multicentric



Rheumatoid arthritis follicular hyperplasia

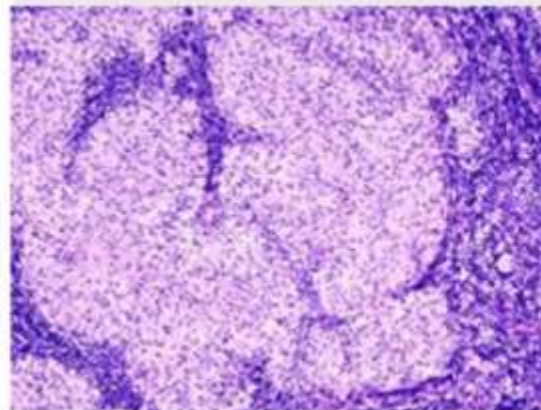


Dermatopathic lymphadenitis Langerhans cell proliferation



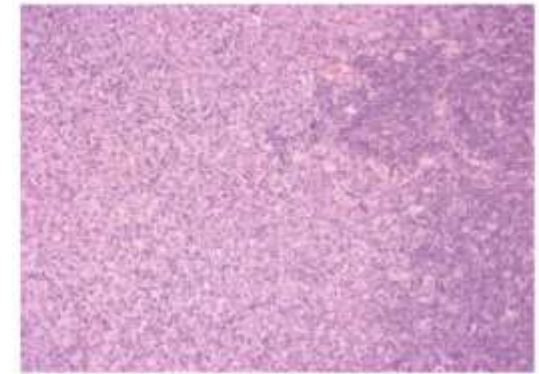
Boeck sarcoidosis

Non caseous
granulomatous



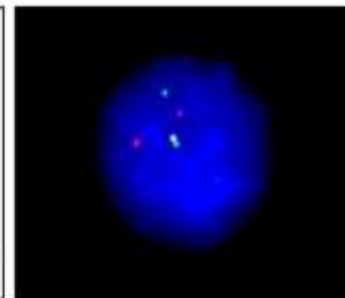
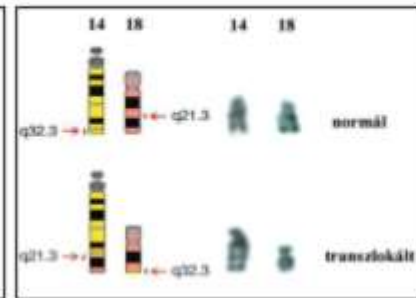
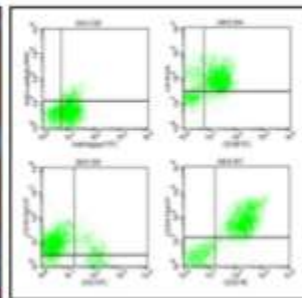
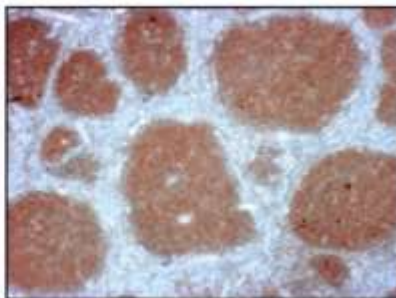
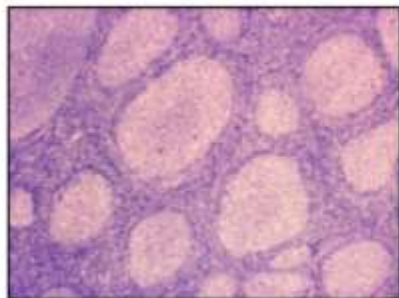
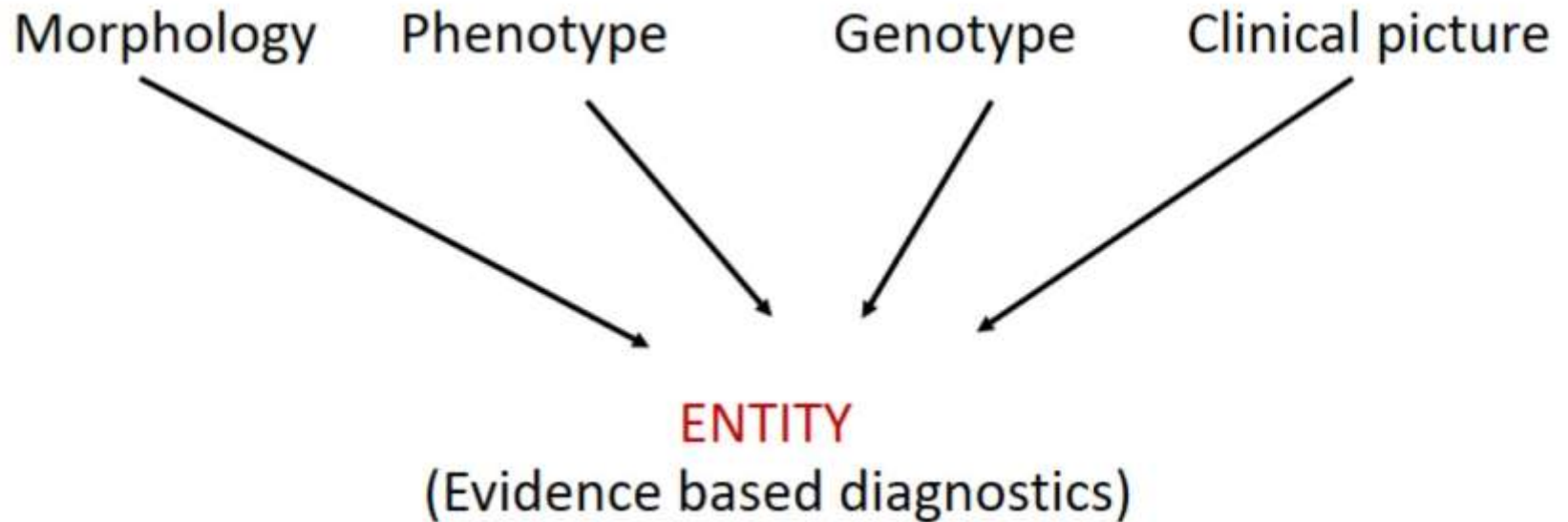
SLE

Necrotizing
histiocytic
lymphadenitis



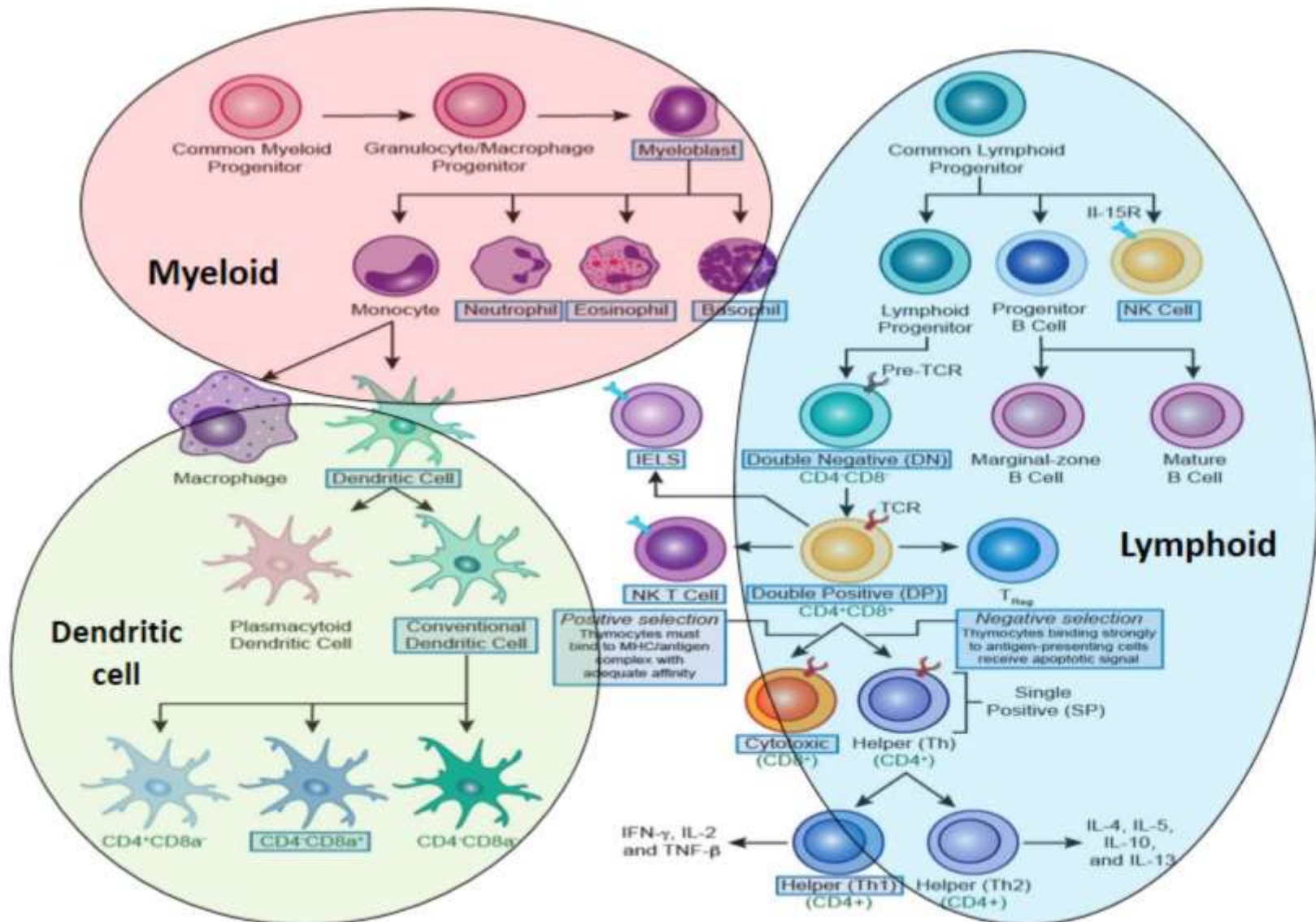
Classification of hematological malignancies

Entity based classification



Classification of hematopoietic neoplasias

(Grouping based on normal lineage counterpart)



Classification of hematopoietic neoplasias

(Grouping based on normal lineage counterpart)

Myeloid neoplasias

- Myeloproliferative neoplasia (MPN)
- Myelodysplastic syndrome (MDS)
- Myelodysplastic/myeloproliferative neoplasia
- Acute myeloid leukaemia (AML)

Lymphoid neoplasias

- Precursor lymphoid neoplasias
- Mature B-cell neoplasias
- Mature T- / NK-cell neoplasias
- Hodgkin lymphoma

Histiocytic, dendritic cell neoplasias

B-cell lymphomas

WHO classification (2016)

Precursor B-cell neoplasms

- B-lymphoblastic leukemia/lymphoma

Matured (peripheral) B-cell neoplasms

- B-cell chronic lymphocytic leukemia, small lymphocytic lymphoma
- B-cell prolymphocytic leukemia
- Lymphoplasmocytic lymphoma
- Hairy cell leukemia
- Plasma cell myeloma/plasmacytoma
- Extranodal marginal zone B-cell lymphoma MALT type
- Nodal marginal zone B-cell lymphoma (+/- monocytoid B-cells)
- Splenic marginal zone lymphoma (+/- villous lymphocytes)
- Follicular lymphoma
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
 - Mediastinal large B-cell lymphoma
 - Intravascular large B-cell lymphoma
 - Primer effusional lymphoma
- Burkitt's lymphoma

T/NK -cell lymphomas

WHO classification (2016)

Precursor T-cell tumors

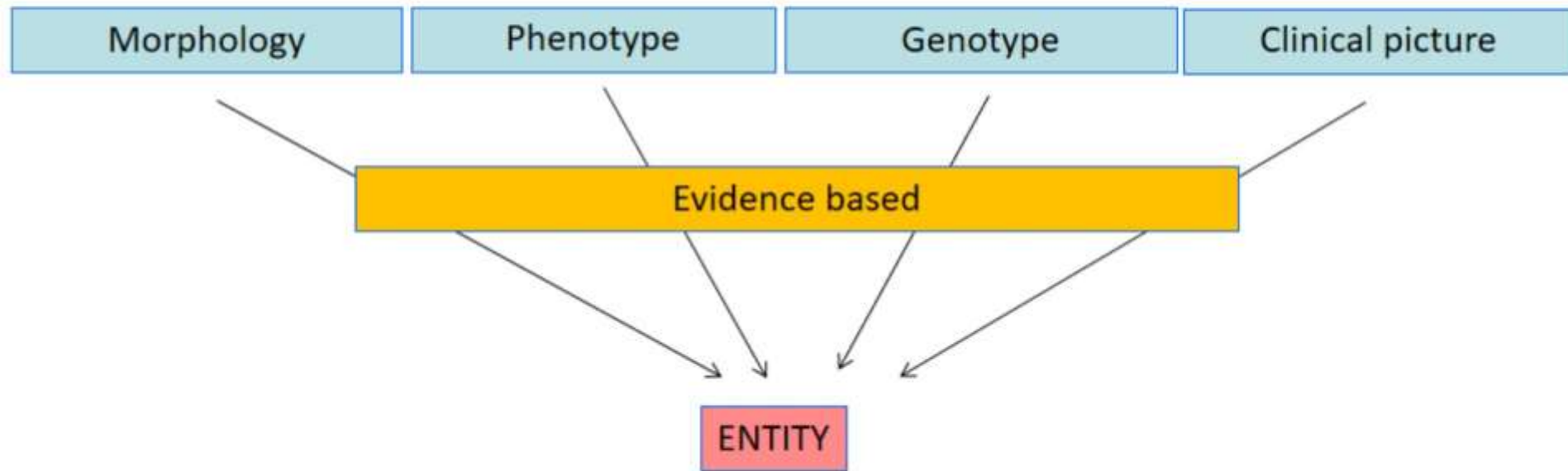
- T-lymphoblastic lymphoma/leukemia

Matured (peripheral) T-cell tumors

- T-cell prolymphocytic leukemia
- T-cell large granular lymphocyte leukemia
- Aggressive NK-cell leukemia
- Adult T-cell lymphoma/leukemia (HTLV1+)
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-type T-cell lymphoma
- Hepatosplenic $\gamma\delta$ T-cell lymphoma
- Subcutan panniculitis-like T-cell lymphoma
- Mycosis fungoides/Sezary syndrome
- Anaplastic large cell lymphoma
- Peripheral T-cell lymphoma (not otherwise specified)
- Angioimmunoblastic T-cell lymphoma

B and T/NK-cell lymphomas

WHO classification (2016)



| | Precursor cell | Mature cell |
|---------------------|----------------|-------------|
| B-cell lymphomas | | |
| T/NK-cell lymphomas | | |
| | (Leukemias) | |



(Malignant) Lymphoma

Definition: Malignant, clonal proliferation of lymphoid cells

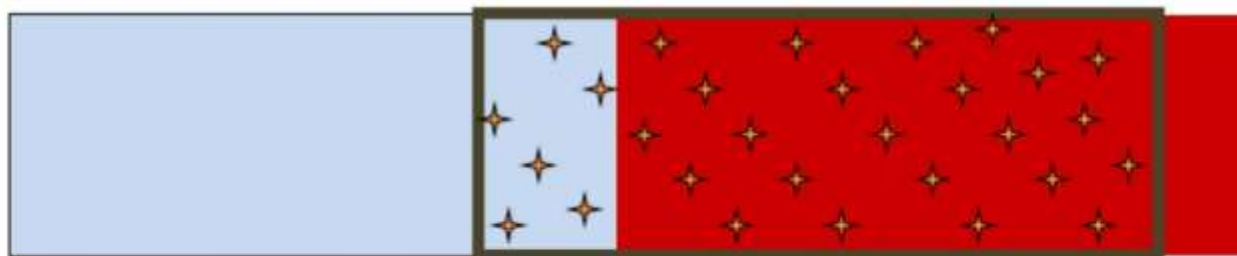
Lymphoid: has a common-leukocyte antigen, B- /T/ or NK cell marker

Clonal: originates from one cell

Pathogenesis: cells are arrested in a certain stage of differentiation.

They resemble to the “normal” counterpart

Leukemia: ✦ ✦ ✦



Lymphoid malignancies

Myeloid neoplasm



LYMPHOMA

● Non-Hodgkin lymphoma



B-cell

- Precursor cell (ALL)

- Mature cell



T-cells

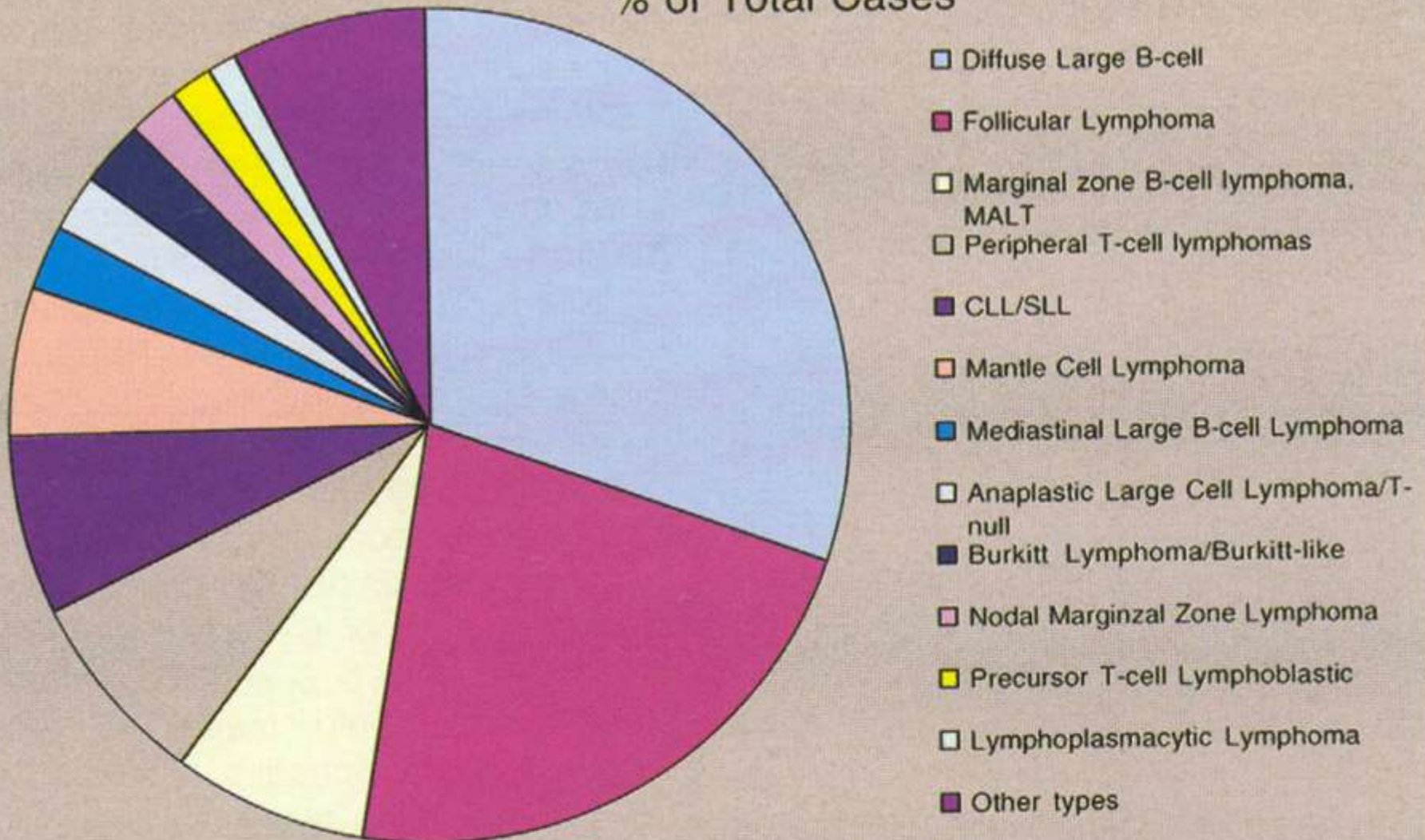
- Precursor (ALL)

- mature

● Hodgkin lymphoma

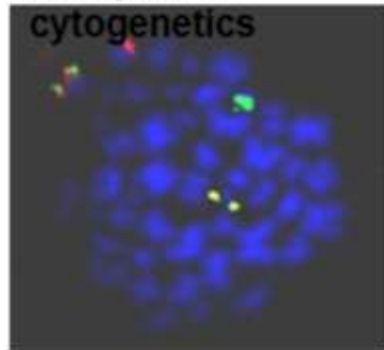


% of Total Cases

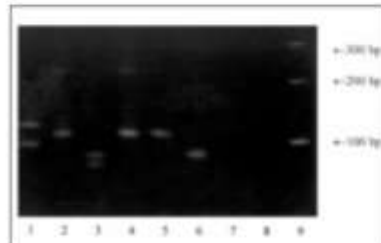




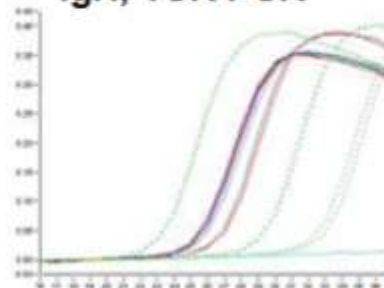
Metaphase
cytogenetics



FISH



IgH, TCR PCR



MLL, bcr/abl QR-PCR

Hyperacute onset

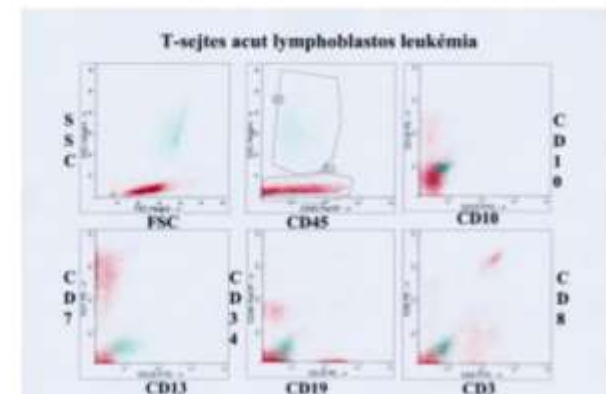
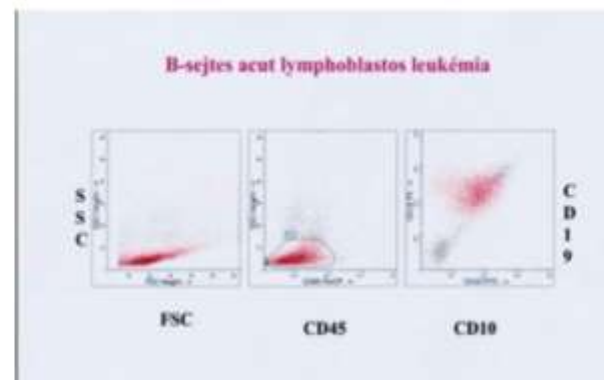
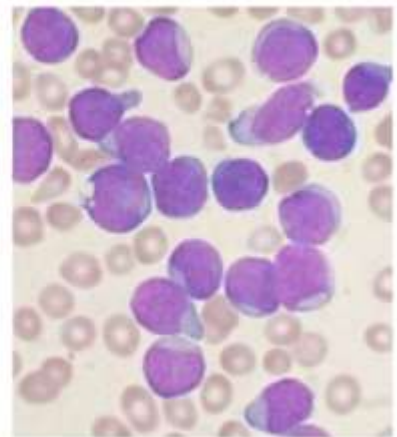
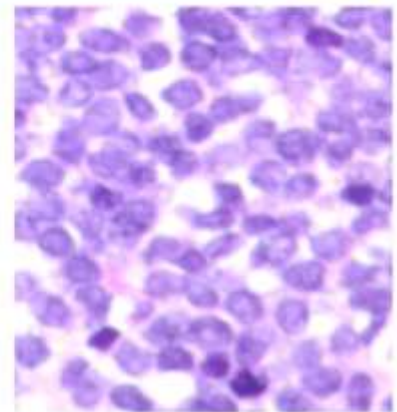
Bleeding, fever, sepsis, high LDH

**80% B-cell, mainly leukemic,
75% children 1- 6 years-old**

**20 % T-cell, mediastinal tumor
(thymus) + leukemic blood picture**

**Prognosis: blast percent, AL type,
cytogenetic aberration, blast
reduction by induction therapy**

75 % curable





Diffuse large B-cell lymphoma

Most frequent type of lymphoma

Large category with many special subtypes

Nodal and extranodal forms exist

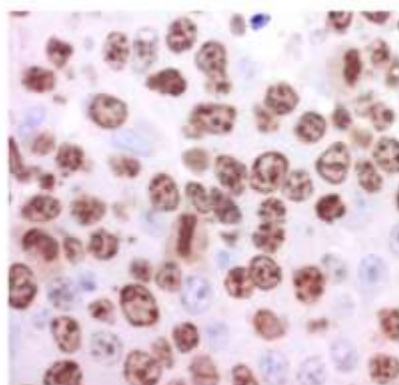
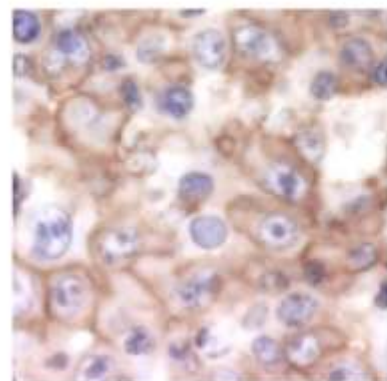
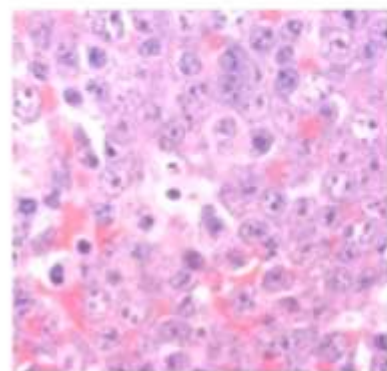
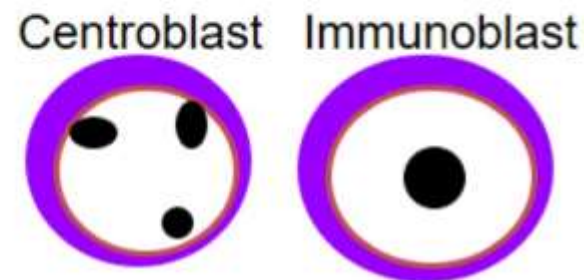
Also exists as a GIT, CNS, primary cutan lymphoma

Evolves as “de novo” or transforms from low grade B-cell lymphoma

High grade lymphoma

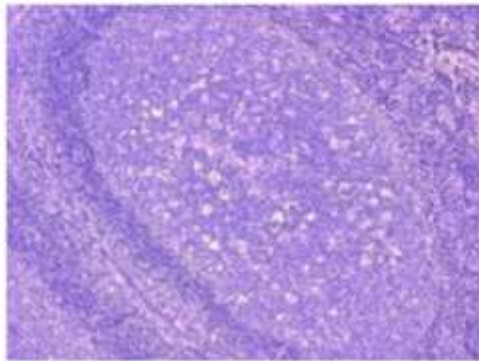
LCA+ , CD 20+, CD79a+, CD 19+

Immuno (anti CD 20) and chemotherapy → 60 % in remission

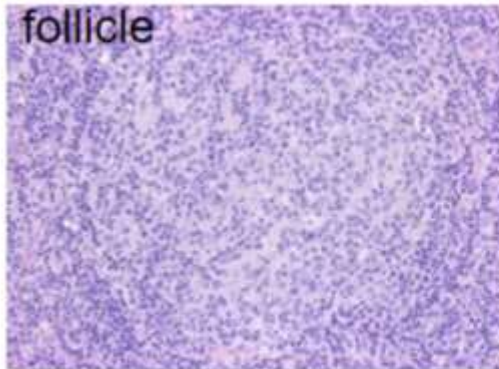




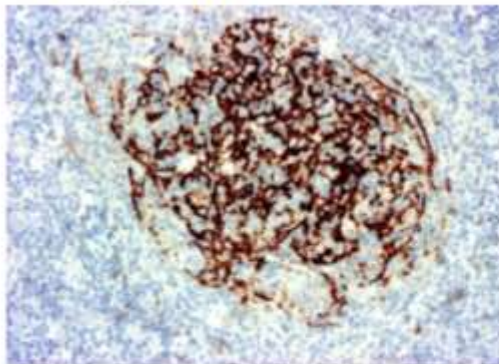
Follicular lymphoma



Reactive secondary follicle

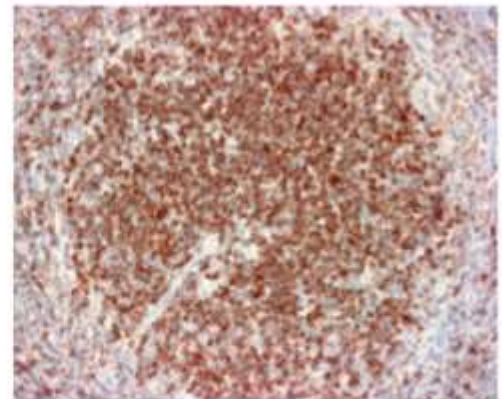
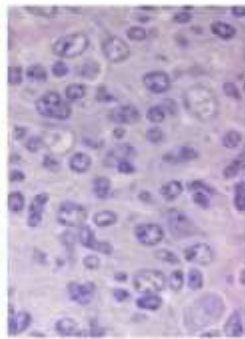
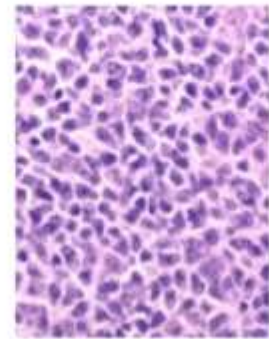


Neoplastic follicle

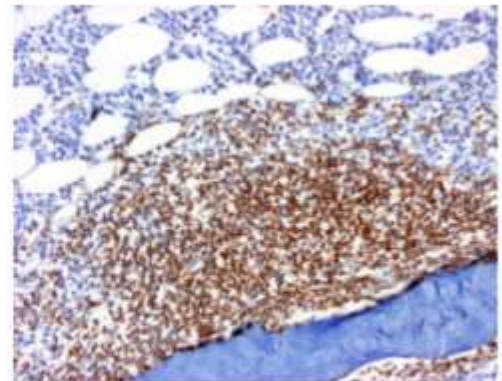


Dendritic reticular cell

- The most frequent type of lymphoma in adults in the Western World
- Germinal center origin
- CD20, CD10, bcl6, bcl 2 +
- t (14;18) IgH – bcl2 apoptosis inhibition
- recapitulate follicular structures
- Indolent
- Bone marrow is often involved
- Immuno + chemotherapy



bcl 2



CD 20



Burkitt lymphoma

Most frequent lymphoma of childhood

Fastest growing tumor

Endemic, sporadic, immunodeficiency associated

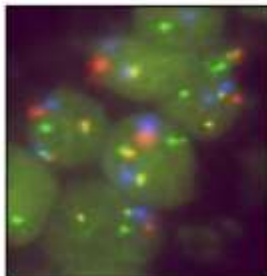
EBV- related

Frequently extranodal presentation: jaw, gonads, coecum

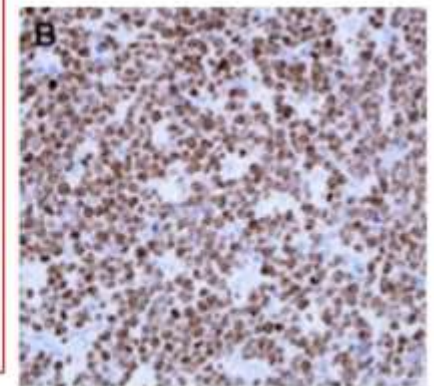
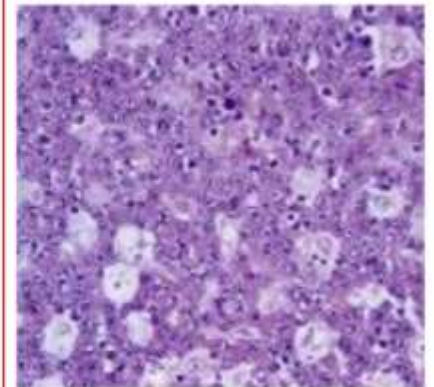
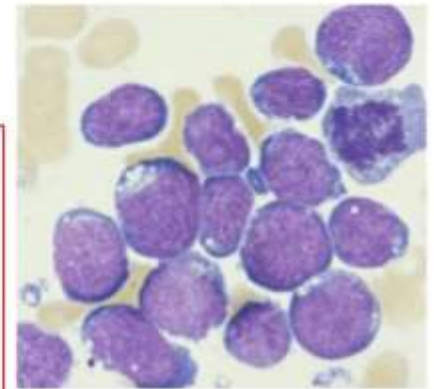
C-myc $t(8;14)$ $t(8;22)$ $t(2;8)$
IgH Igκ/λ

Diffuse, medium sized cells, basophilic, cohesive, monotonous pattern, starry sky appearance

CD20+, CD10+, bcl6+, slgG + 100% proliferation rate



(t 8;14)
FISH





CLL / SLL

Begins bone marrow and blood → leukemia
 lymph node → lymphoma

Ends bone marrow (BM), lymph node, liver, spleen, blood

Non destructive growth, BM infiltration > 70 % --> symptoms

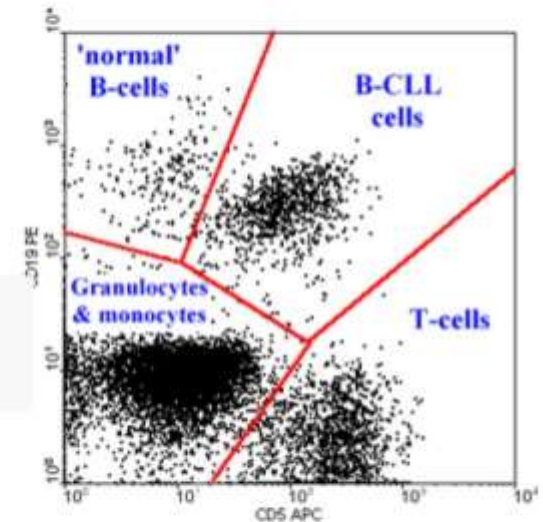
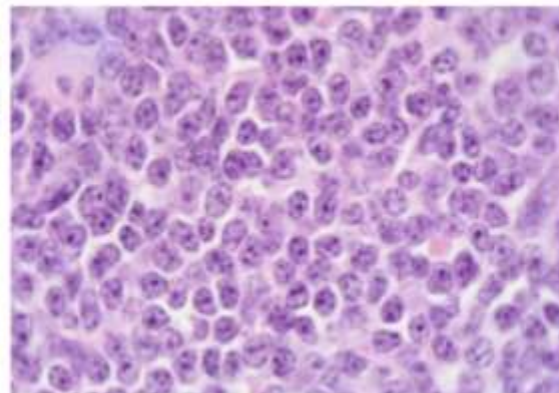
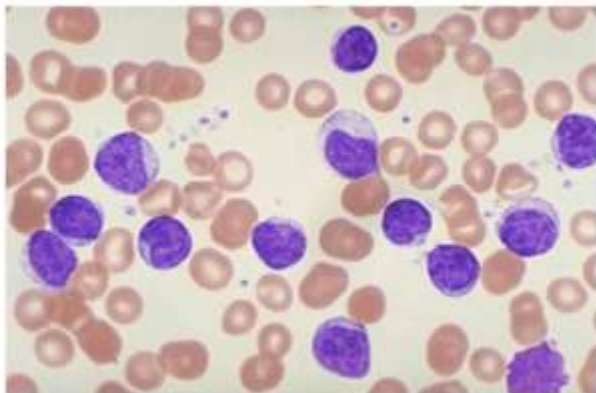
Indolent 5-20 years

Fast 3

elderly

young

Prognosis: stage, tumor biological markers (mutation status, immunophenotype, cytogenetic aberrations, proliferation index), general condition of the patient



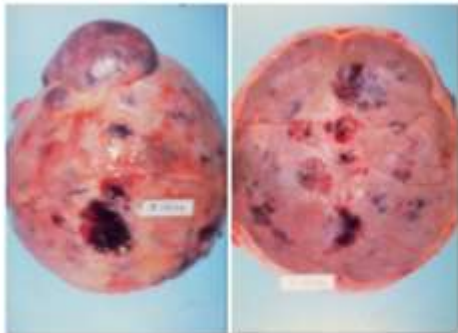
CD19+, CD20+, CD23+,
 CD5+, CD23+



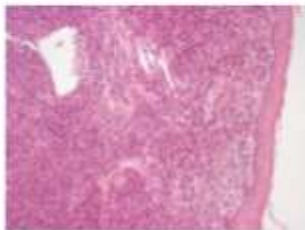
B 56/06



Multiple myeloma



AIDS
oral
plasma
blastic



Plasma
cytoma,
gingiva

Terminally differentiated, IgG and IL-1b producing tumor

Bone marrow tumor – BM stromal cells produce IL6 and attract plasma cells

Paraprotein

Hypercalcemia

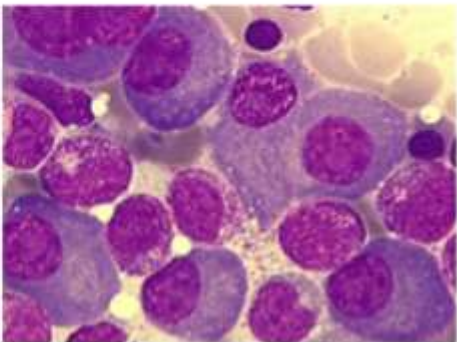
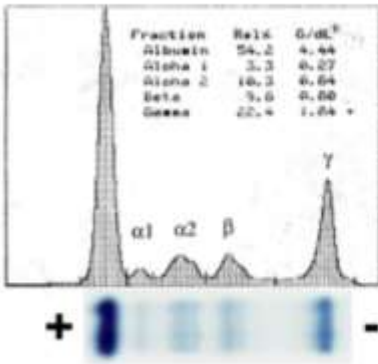
Bone pain

Amyloidosis

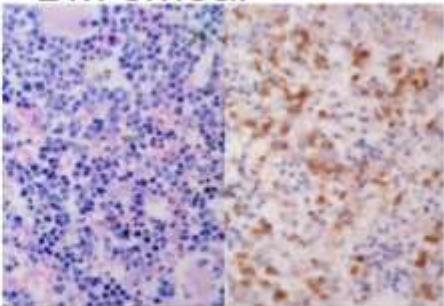
Pathologic fractures, lytic lesions

Monoclonal light chain (Bence-Jones protein) proteinuria – renal insufficiency

Hyperviscosity – High sedimentation rate



BM smear



BM biopsy, κ chain



Kidney amyloidosis, polarisation



Other plasma cell tumors



Extranodal NK / T- cell lymphoma, nasal type

Rare in Europe, frequent in Asia

Nasopharyngeal region, midline

Lethal midline granuloma

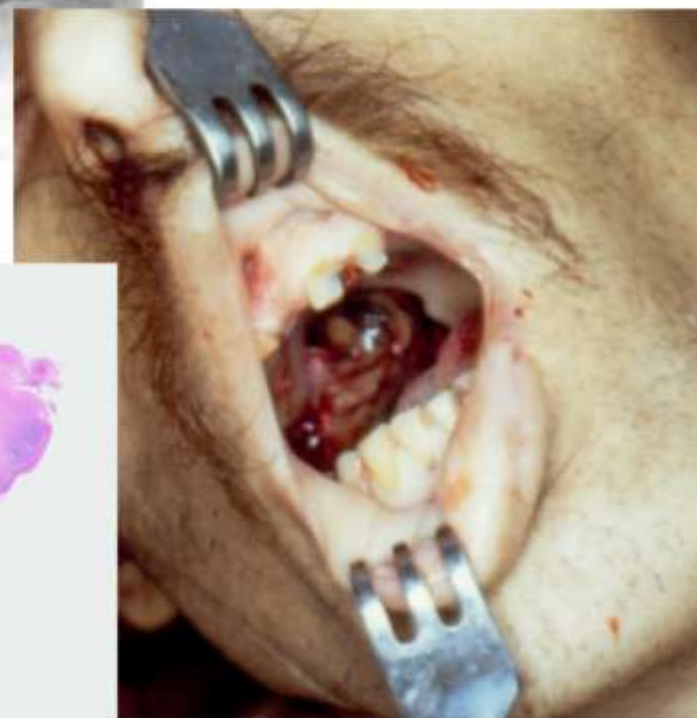
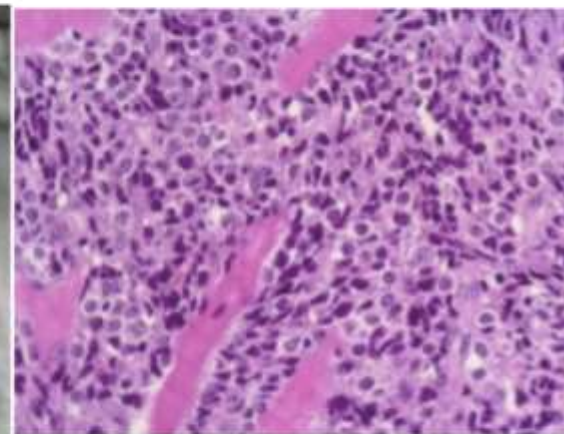
Epistaxis, airway obstruction

Angiocentric, angiodestructive

EBV - related lymphoma

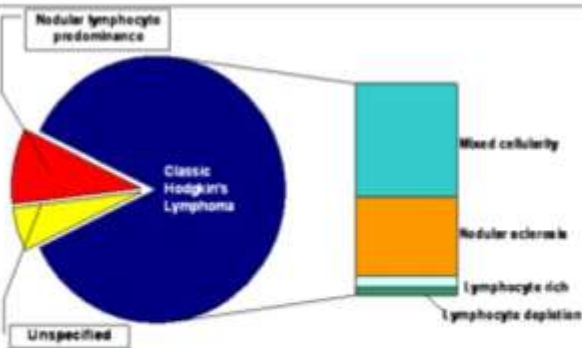
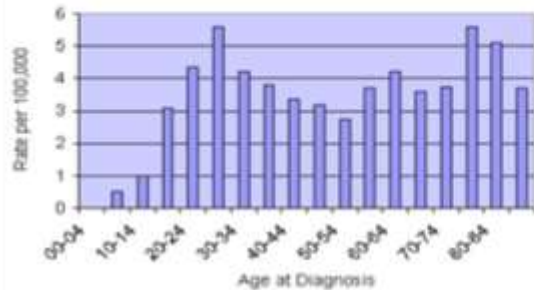
sCD3-, cyCD 3+, CD 56+,
CD 8 +/-, CD4-, TIA +

Variable clinical course,
aggressive/ responds well
to therapy





Approximate Cases of Hodgkin's Disease/Lymphoma per 100,000 People (U.S.)



Lymphocyte predominant Hodgkin lymphoma (Nodular paragranuloma)
cells: popcorn cells +



Background is composed of T- and B-lymphocytes

Classical Hodgkin lymphoma

Subtypes:

lymphocyte rich
nodular sclerosis
mixed cellularity
lymphocyte depleted

Cellular composition:

Sternberg – Reed cells

+

Background consists of T-lymphocytes, eosinophil granulocytes, plasma cells, fibroblasts, reticulum cells

Behaves like a low grade lymphoma

Neck, thoracic, abdominal lymph nodes, spleen, liver are frequently involved.

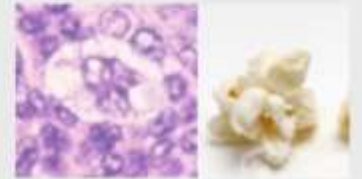
Early stage can be cured in 80% of the cases, in late stages only 50%

Sternberg – Reed cell variants

CD 20 +

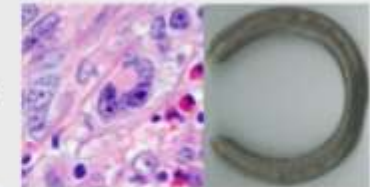
CD 30 –

LCA +



popcorn

CD 30 +



horseshoe



MUM +

LCA –

IgH –

B-cell



lacunar



Mirror image



Acute leukemia : necrotizing stomatitis, gingival hyperplasia



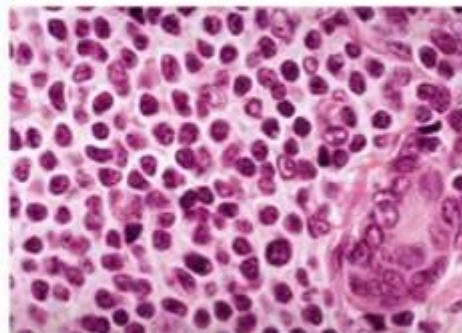
Burkitt lymphoma: destruction of the skull



Plasmablastic lymphoma: gingival tumor



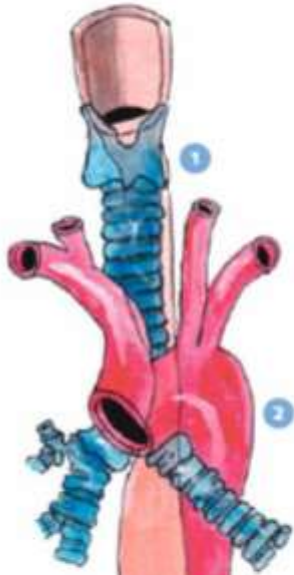
MALT: small salivary glands, parotid tumors – Sjögren syndrome



Lethal midline granuloma



III. DISEASES OF THE ESOPHAGUS



Physiologic narrowings of the esophagus

1. At the esophageal inlet, where the pharynx joins the esophagus, behind the cricoid cartilage (14-16 cm from the incisor teeth).

2. Where its anterior surface is crossed by the aortic arch and the left bronchus (25-27 cm from the incisor teeth).

3. Where it pierces the diaphragm (36-38 cm from the incisor teeth).



Congenital/developmental diseases

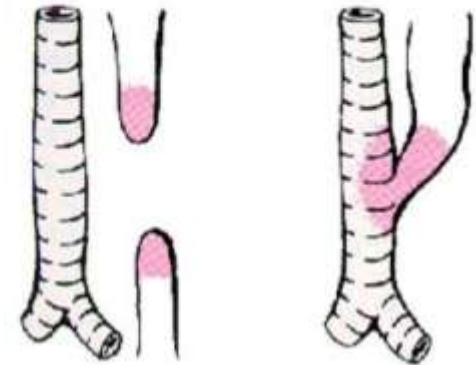
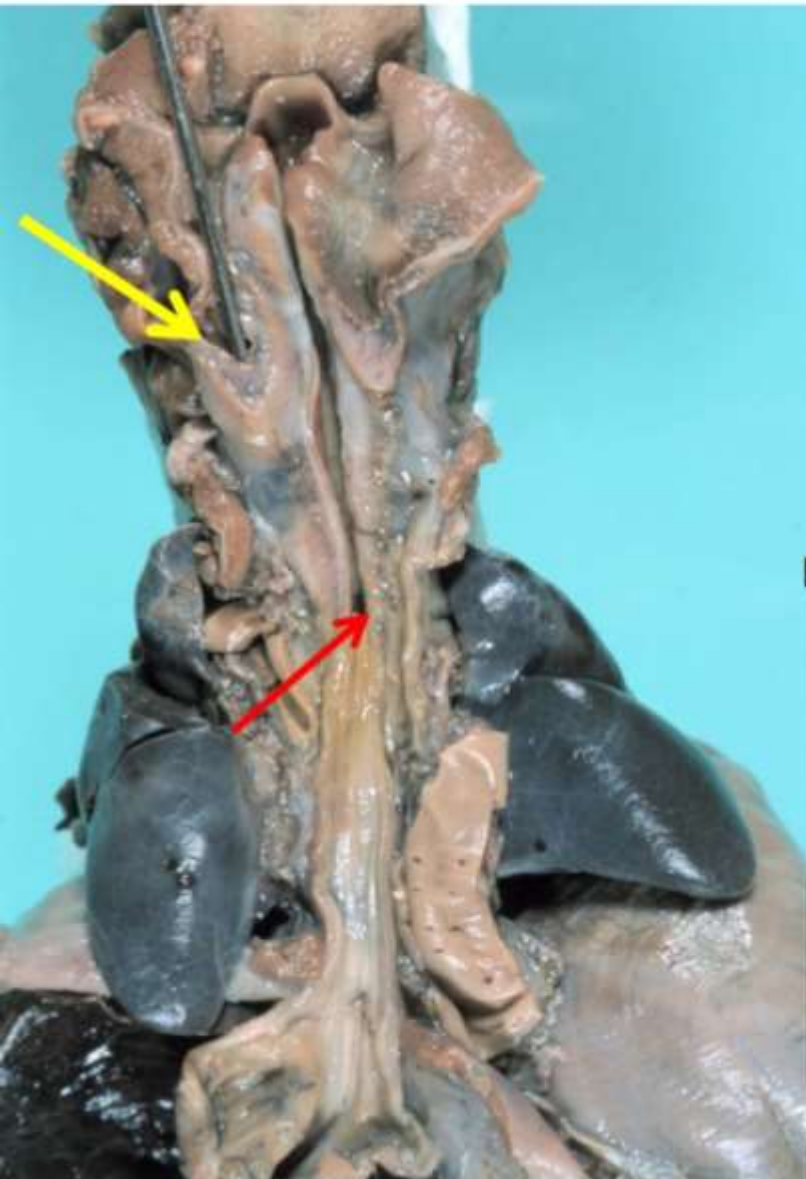
Atresia: failure of embryonal canalisation.

- Several variants exist. The most common is:
 blind upper segment, and fistula between the lower segment and the trachea

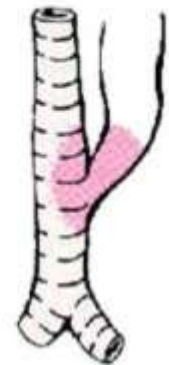
Complications:

Death occurs from aspiration pneumonia

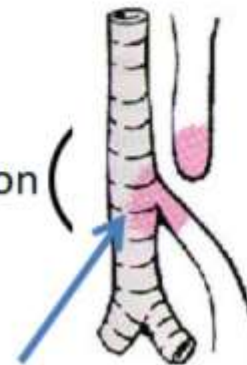
- Short atresias may be repaired surgically
 - oesophago-tracheal fistula
 - oesophago-bronchial fistula



A



B



Most common

Fistula

C



D



E

Oesophageal atresia

Blind upper segment (yellow arrow & probe)
and fistula between
the lower segment and the trachea (red arrow)

- Stenosis
 - Congenital or acquired
 - Oral part is dilated – inflammation, ulcer – perforation
- Diverticulum (Outpouchings of the wall of the oesophagus)
Pathogenesis:
 - Traction D. (pull from outside; e.g., fibrous adhaesions)
 - Pulsion D. (push from inside; e.g., ↑ luminal pressure)
- *Upper oesophagus* / lower pharynx: Zenker's (pulsion) D.
- *Mid oesophagus*: traction D. due to mediastinal and bronchial lesions; e.g., scarring of lymph nodes in tuberculosis
- *Lower oesophagus (epiphrenic)*:
 - pulsion D.
 - associated with diaphragmatic hernia or GERD (gastrooesophageal reflux disease) or achalasia

COMPLICATIONS OF THE DIVERTICULA:

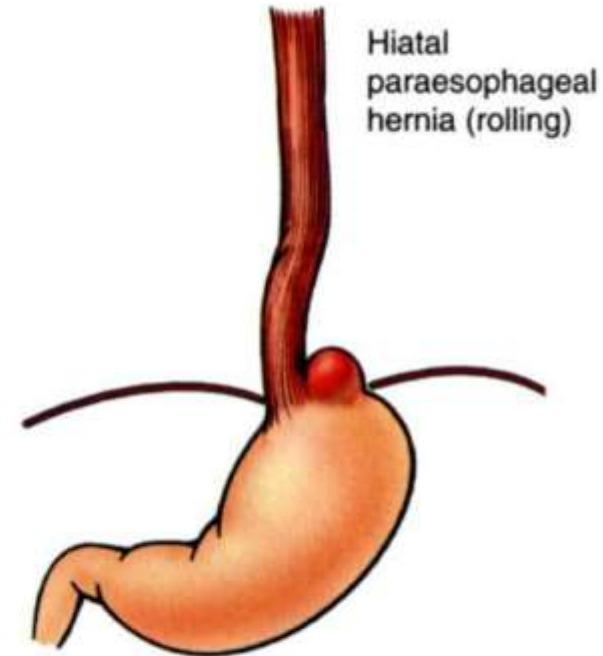
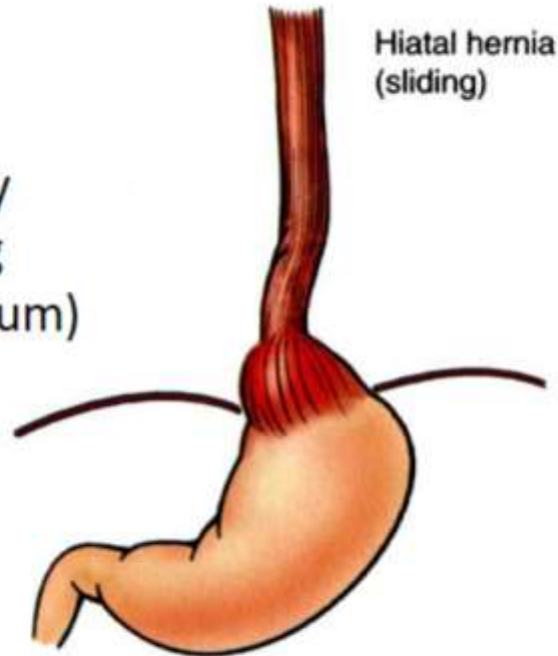
May reach several cm-s and may be the site of food accumulation

⇒ with nocturnal regurgitation and aspiration during sleep

⇒ Aspiration pneumonia

Symptoms:

May be asymptomatic, may cause heartburn (a burning sensation behind the sternum) or dysphagia (difficulty in swallowing) or pain on swallowing.

**HIATAL HERNIA**

Protrusion of the stomach above the diaphragm through a widened diaphragmatic hiatus.

- Sliding hernia - 90%: the gastroesophageal junction is pulled into the thorax.
- Paraesophageal hernia - 10%: a portion of the stomach rolls up into the thorax.

Inflammation of the esophagus

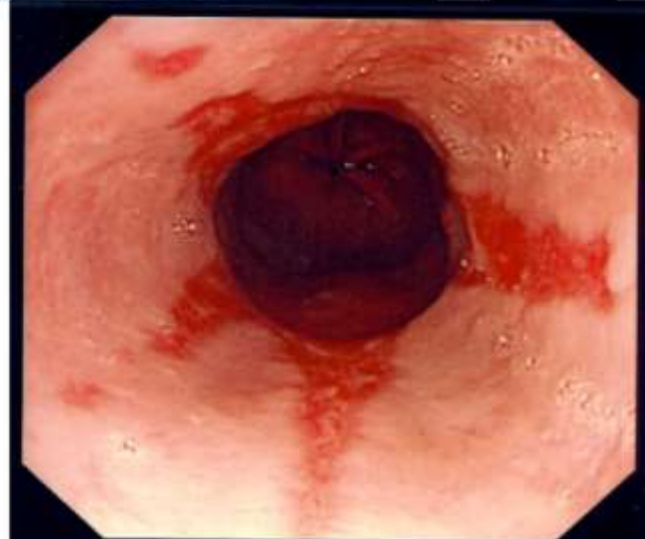
- ACUTE – CHRONIC

Symptoms:

Heartburn

Odynophagy

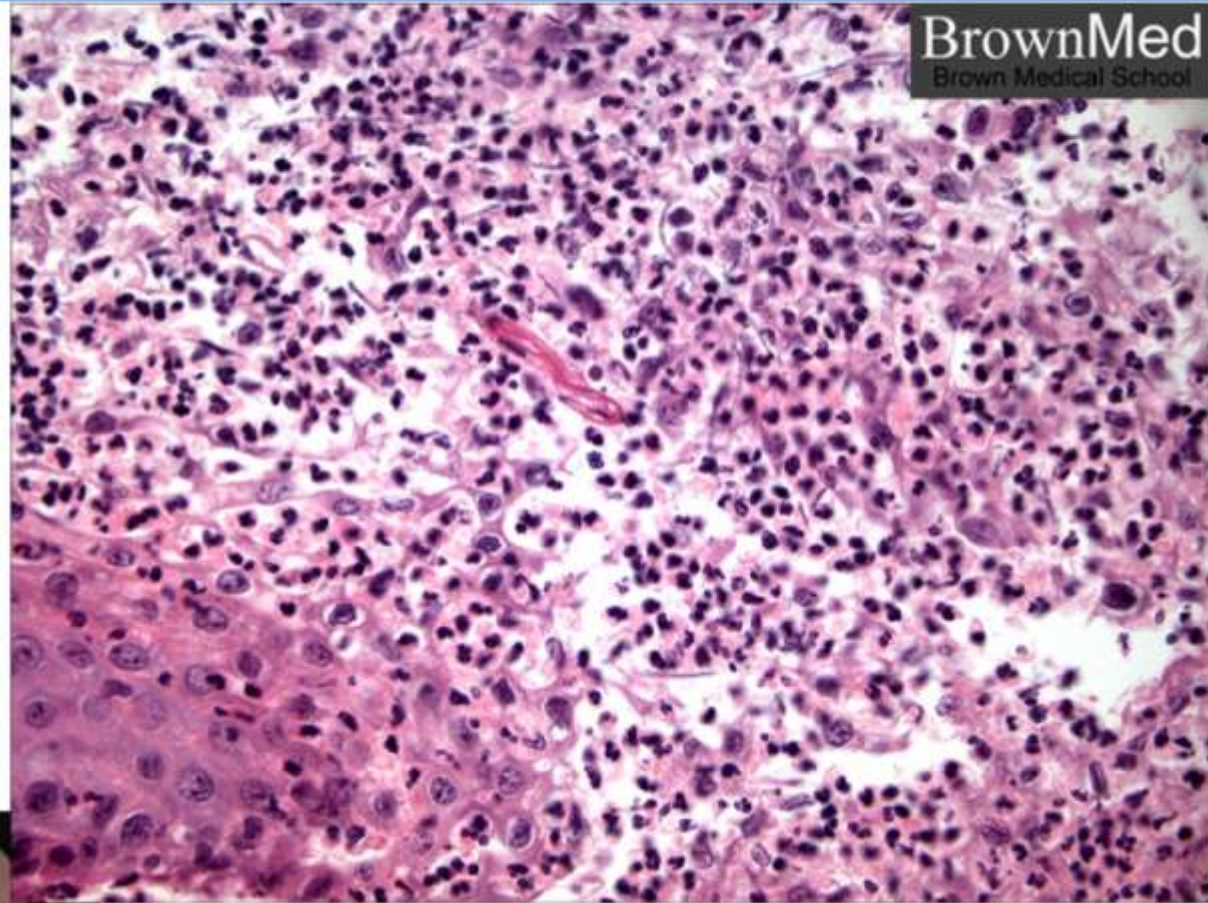
Dysphagy



AETIOLOGY:

- **Reflux of gastric acid** - GERD due to incompetence of the LES (**very common**)
- **Prolonged gastric intubation**
- **Ingestions of irritants:**
 - alcohol,
 - corrosive acids or alkalis;
 - heavy smoking
- **Uraemia**
- **Infections in patients with leukaemias, lymphomas, AIDS (immunocompromized host):**
 - viruses (herpes simplex, cytomegalovirus)
 - fungi (Candida)

CANDIDIASIS



GERD (Gastrooesophageal reflux)

- Gastric content regurgitates
- Many causes:
 - LES tone decreases
 - Drugs
 - Hypothyreoidismus
 - Gravidity
 - Alcoholism, Smoking
 - Hiatal hernia
- Morphology:
 - Erosion
 - Inflammation
 - Reactive epithel proliferation
 - Ulcer
 - Bleeding
 - Scarring
 - **Barrett**

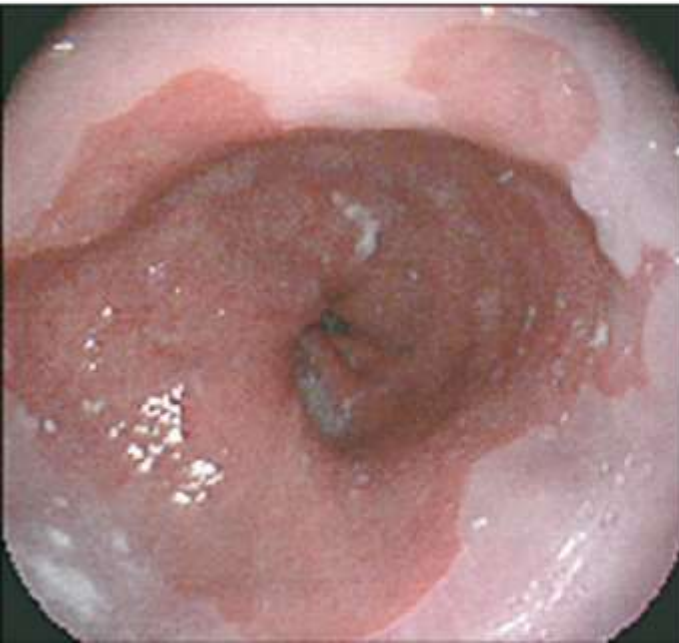
Complication of the reflux oesophagitis:

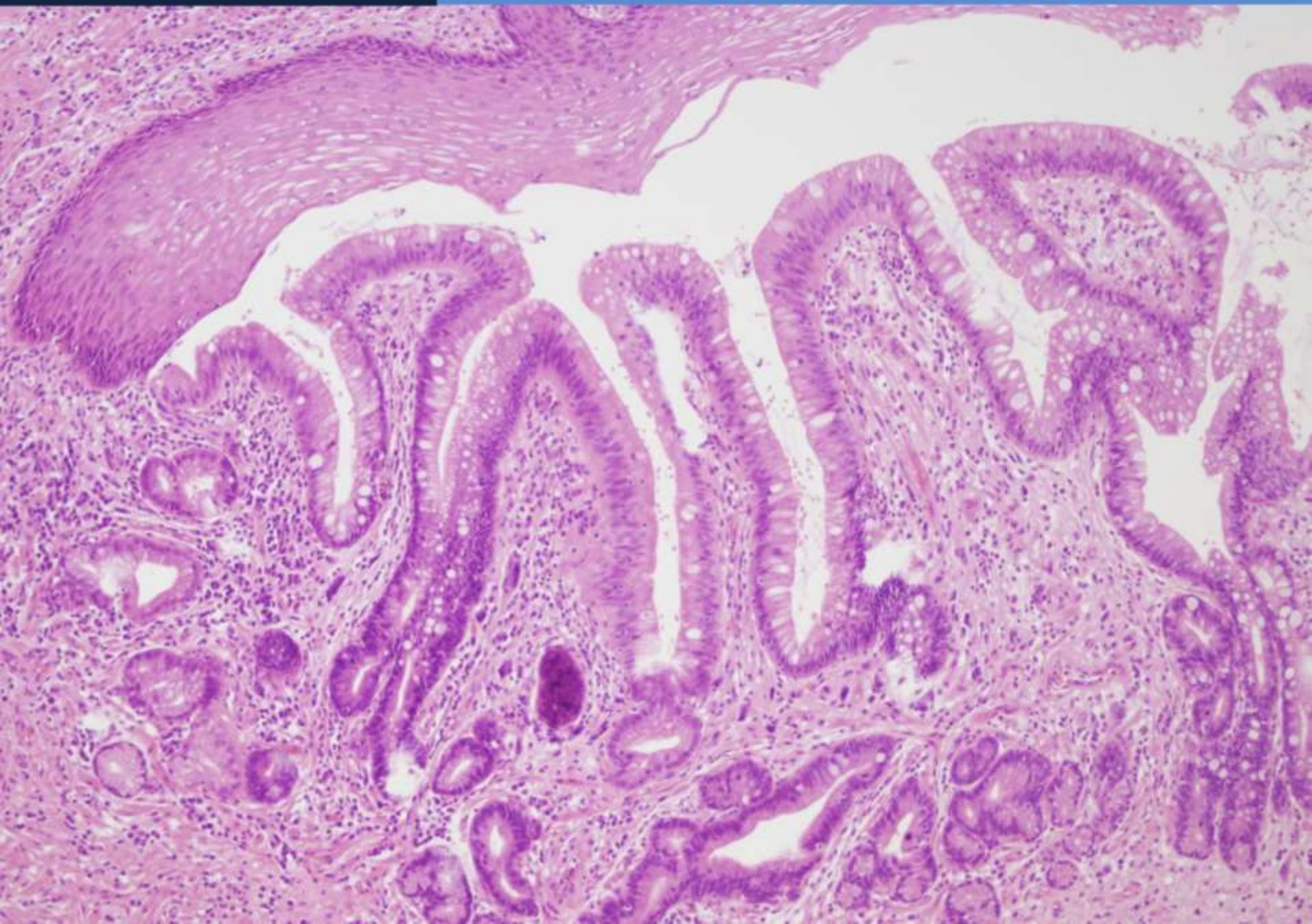
- Mucosal injury \Rightarrow severe acute inflammation, necrosis and ulceration with the formation of granulation tissue \Rightarrow eventual fibrosis & stenosis (stricture)
- Long-standing GE reflux \Rightarrow replacement of distal squamous mucosa by metaplastic gastric or intestinal epithelium:
- **Barrett's oesophagus:**
 - peptic ulcer** may develop
 - dysplasia may develop \rightarrow **adenocarcinoma**

Barrett metaplasia

Barrett oesophagus is an acquired precancerous lesion, where the epithelial lining of the esophagus will change from squamous epithelium into cylindrical epithelium.

Goblet cells will be present in the cylindrical epithelium.





Squamous cell cancer

- Genetic
- Esophageal constrictions
- Dysplasia
- Environmental factors
- usually in males over 50 ys of age
- Geographical difference

Europe: smoking & alcohol consumption

Far East: deficiency of vitamins A, B, C, and trace metals (zinc, molybdenum) and/or fungal contamination of foodstuffs and/or high content of nitrites/nitrosamines

SYMPTOMS

- Dysphagia (difficulty swallowing)
- Odynophagia (painful swallowing)
- Heartburn-like pain in the epigastrium
- Hoarse-sounding cough, a result of the tumor affecting the recurrent laryngeal nerve.
- Nausea and vomiting, regurgitation of food, coughing and an increased risk of aspiration pneumonia.

METASTASIS

Liver metastasis could cause jaundice and ascites lung metastasis could cause shortness of breath, pleural effusions.

Evolution: dysplasia \Rightarrow cc in situ \Rightarrow invasive cc

Localization:

20% in the upper third

50% in the middle third

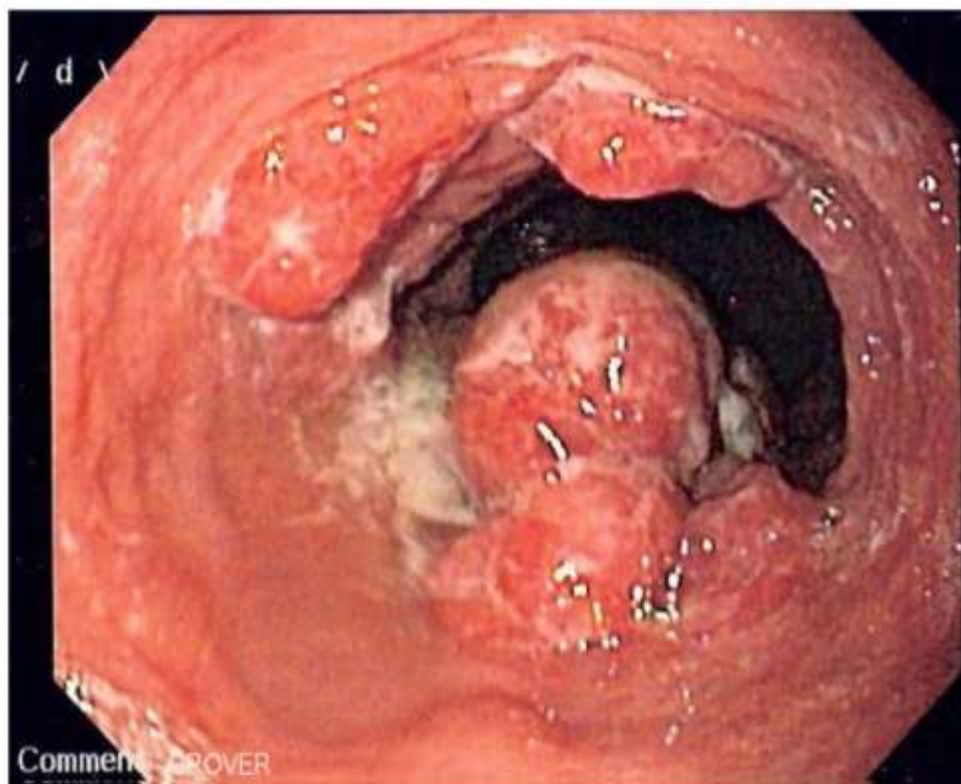
30% in the lower third

Gross:

polypoid-fungating lesion

flat, diffusely infiltrative

Lesion ulcerative-excavating
lesion



Microscopically: moderately diff. squamous cell cc

Lymph node metastasis:

upper third: cervical nodes

middle third: mediastinal, paratracheal, and tracheobronchial nodes

lower third: gastric and coeliac nodes

Haematogeneous metastasis: **lungs**

Complications:

- cancerous esophagotracheal fistula
- aspiration pneumonia
- sepsis
- direct invasion of the mediastinum
- bleeding
- extreme weight loss