REACTIVE LYMPHOID LESIONS

a. Lymphoid Hyperplasia

b. ALHE

1) **LYMPHOID HYPERPLASIA**
   - Proliferation of lymphocytes without cellular atypia.
   - Mitotic figures restricted to germinal center.
   - Occasionally mimic **starry sky appearance**
   - Difficult to distinguish from (neoplastic lymphoblastic proliferation)

   - Site: postero-lateral portion of the tongue, anterior floor of mouth, anterior tonsillar pillar & posterior part of soft palate.

   - Clinical Features:
     Aggregations of lymphoid tissue are part of the foliate papillae or lingual tonsil.
     Sometimes these papillae become inflamed or irritated with associated enlargement and tenderness.

   - Histopathology:
     Reactive Lymphoid Hyperplasia (enlarged germinal center with mitosis & macrophages)

2) **ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA (ALHE)**
   - Nodular subcutaneous benign disease
   - Aggregates of lymphocytes and eosinophils.
   - Blood eosinophilia

   - Site: 85% in head & neck, rare intra-orally (lip)

   - Size: 1-2cm

   - Clinical Features: Solitary, or multiple painless and mobile submucosal nodule which enlarge gradually.

   - Histopathology:
     Circumscribed lesion
     Hyperplastic lymphoid tissue (well-developed follicle with germinal center)
     Eosinophilic and lymphatic infiltrate
     Proliferating dilated capillaries

   - Differential Diagnosis:
     Minor Salivary Gland (Reactive or Neoplastic)
     Lipoma or Schwannoma
     Eosinophilic Granuloma

   - Treatment:
     Surgical Excision
     Intra-oral steroid injections.

DEVELOPMENTAL LYMPHOID LESIONS

a. Oral Lymphoepithelial Cyst

b. Cervical Lymphoepithelial Cyst

NEOPLASTIC LYMPHOID LESIONS

a. Lymphoma (Hodgkin / Non-Hodgkin's lymphomas)

b. Myeloma / Plasmacytoma

1) **HODGKIN'S LYMPHOMA**

- Characteristics:
  Affect bone of soft tissue
  Painless enlargement of lymph nodes
  Rarely affect oral cavity:
  - Unilateral tonsillar enlargement (early phase)
  - Extranodal: Submucosal swelling with mucosal ulceration.

- Staging: Ann Arbor Staging System
  - **Stage I**: Involvement of single lymph node region
    - **Stage IE**: or a single extranodal site or organ
  - **Stage II**: Involvement of 2 or more lymph nodes region on same side of diaphragm
    - **Stage IIE**: or localized involvement of extra nodal site or organ and one or more lymph node.
  - **Stage III**: Involvement of lymph node regions of both sides of the diaphragm.
    - **Stage IIIE**: with localized extranodal site
    - **Stage IIIS**: with splenic involvement
    - **Stage IIISE**: both
  - **Stage IV**: Diffuse or disseminated involvement of one or more distant extranodal organ

  - **Subclassification**:
    - **A**: without symptoms
    - **B**: with systematic symptoms: unexplained fever >38^{o}C, unexplained weight loss > 10% of body weight in past 6 months, night sweats.

- Histology:
  Reed Sternberg Cells must be present for diagnosis of HL. There are lymphocytic origin cells, characterized by **large size & bilobed nucleus**, each lobe contain a large **amorphous or eosinophilic nucleolus.**
  Non-neoplastic inflammatory cell infiltrate.
  Classic HL comprises 4 entities (Likes- Bulter Histologic Classification):
  - **Lymphocytic -rich**: most favorable diagnosis
  - **Nodular Sclerosis**: most common form (50%) collagen fibers penetrate into LN subdividing it into islands of tumors
  - **Mixed Cellularity**: contains combination of lymphocytes, many RS cells, PMNs, plasma cells & macrophages.
  - **Lymphocytic depletion**: least favorable prognosis

- Treatment:
  External radiotherapy
  Chemotherapy

2) NON-HODGKIN'S LYMPHOMA

- Characteristics:
  Affect middle-aged and elderly
  Gradual, asymptomatic focal enlargement of lymph nodes.
  Variable account for <5% of oral malignancies

- Site: Arise in nodal & extranodal sites
  Most common extranodal:
  1. GIT
  2. Head & Neck is second most common site (**Waldeyer's Ring**) especially in HIV+
  3. B-cell Lymphoma are the most common phenotype in extranodal site.

- Ann Arbor Classification**:**
  - **Nodular Lymphoma**:
    - Poorly Differentiated
    - Mixed lymphocytic-histiocytic
    - Histiocytic (least favorable prognosis)
  - **Diffuse Lymphoma**:
    - Lymphocytic (well or poorly differentiated)
    - Histiocytic
  - **Mixed**

- Histological Types (in Head & Neck):
  - **Large B-Cell Lymphoma**: Burkitt's Lymphoma
  - **T-Cell & NK Lymphoma**: Midline Lethal Granuloma
  - **Extra nodal marginal zone lymphoma**: Unique, arise in LN present in salivary glands.

- Etiology: Genetic predisposition, Immunodeficiency, Chromosomal Translocation

- Clinical Features:
  Mass or **ulcerated mass** resemble SCC or Salivary Gland Neoplasms (**Waldayer's Ring**)
  Burkitt's Lymphoma show a **striking predilection for primary involvement of bone.**
  Bone loss, tooth mobility, swelling, pain and lip numbness
  Three broad groups of NHL can be discerned on basis of biological behavior:
  - **Indolent**: Slow growth, wide dissemination, long natural history, relative incurability
  - **Aggressive**: Rapid growth, localized presentation, short natural history.
  - **Highly Aggressive:** Rapid growth, localized presentation, short natural history.

  Most lymphomas in adults are **diffuse B-Cell** or **Follicular Lymphoma** (predominant tumor of lymph nodes, rare in oral cavity)
  In Children: **Aggressive and highly aggressive lymphoma** are most common with Burkitt's

- Treatment: Radio & Chemotherapy (frequent responsiveness to chemotherapy)

LARGE (DIFFUSE) B-CELL LYMPHOMA

- Aggressive, rapidly growing neoplasm of large lymphoid cells.
- Arise de novo or as transformation of lower grade lymphomas.
- Lymphadenopathy
- Extranodal involvement: **Bone – Extensive Destruction**
- Histology: Sheets of large lymphoid cells with abundant cytoplasm and reactive histiocytes.

EXTRANODAL MARGINAL ZONE LYMPHOMA

- Indolent lymphoma occurring in mucosal sites of extranodal tissue like: CNS, ano-rectal, oral cavity, GIT, SG, Thyroid Gland and skin.
  Orally: Fauces or gingiva are most commonly affect sites.
- Localized with protracted course before dissemination
- Rapidly growing mass &/ teeth mobility
- Poor prognosis
- B-cell type predominate, although T-cell lymphoma also seen.
- Most of B0cell type are immunoblastic or Burkitt's like lymphoma
- Predisposing Factors: Hashimato's Thyroiditis, Sjogren Syndrome, H.P. Gastritis
- Histology: **Centrocyte-like cells** resemble a range of lymphocytes to monocytoid cells.

NASOFACIAL NK/T-CELL LYMPHOMA [MIDLINE LETHAL GRANULOMA]

- Progressive, ulcerative destruction of the palate, nose & paranasal structures.
- **Epistaxis**
- Swelling of hard & soft palate – **Ulceration & destruction** of palatal & nasal tissues causing **oroantral fistula.**
- MLG also involves **Wegner's Granuloma**

- Histology:
  Varying amount of granulation tissue & necrosis.
  Medium and large atypical lymphocytes with clear cytoplasm & irregular nuclear outline.
  Angiocentricity & epitheliotropism are most common histopathological features.

- Treatment: Chemo & Radiotherapy

BURKITT'S LYMPHOMA

- Highly aggressive B-cell Lymphoma
- Primarily affects children and adolescents

- Radiographically: Poorly marginated radiolucency.
  Cortex: Expanded, eroded or perforated

- Histology: **Monomorphic** sheets of densely packed, medium sized neoplastic lymphocytes that have a deeply basophilic cytoplasm with high mitotic rate (10/HPF).
  Numerous macrophages containing cellular debris give the classic **Starry Sky** appearance

- Treatment: Chemotherapy with 2-years survival.

- Three forms:
  - Endemic (Africa)
    - Diseases of children in Equatorial Africa
    - Endemic Malaria is a pathogenetic co-factor.
    - Associated with EBV infection
    - **Jaw-bone involvement** in up to 50% of cases
    - Other organs involved: Kidney, liver, retroperitoneum & gonads.
  - Sporadic (NA & Europe)
    - Affect young adults
    - Abdominal mass & bone marrow involvement
    - Jaw lesions are less common (10%)
  - Associated with immuno-deficiency.
    - Tumor present in lymph node and at extranodal sites (CNS, BM, GIT)

3) **GRANULOCYTIC SARCOMA (EXTRAMEDULLARY MYELOID TUMOR)**

- Orally: Localized soft tissue mass that occurs in three setting:
    - Patients previously known to have Acute Myeloid Leukemia (AML) as a sign of blast transformation
    - In patients with Chronic Myeloid Leukemia (CML) or other myeloproliferative diseases.
    - In patients who was previously ill.

- Difficult to diagnose histologically from:
    - Large Cell Lymphoma
    - Poorly Differentiated Carcinoma
    - Plasmacytoma
    - Granulocytic Sarcoma & AML (due to Auer Rods)

- **Auer Rods**: Crystalline, rod-like intracytoplasmic acidophilic bodies can establish diagnosis of both granulocytic sarcoma & AML
- Poor prognosis.