FOLLICULARITY in LYMPHOMA
Reactive Follicular Hyperplasia
Follicular Hyperplasia – irregular follicles
Follicular Hyperplasia – dark and light zones
Light Zone

Dark Zone
Follicular hyperplasia – MIB1
Follicular dendritic cell
CD 21 Hyperplasia
CD 10 Hyperplasia
BCL 6 Hyperplasia
IgD Hyperplasia
Follicular Lymphoma
Follicular Lymphoma

A lymphoma of germinal centre B cells (centrocytes and centroblasts) with typically at least a partially follicular pattern

**Frequency**
40% of adult lymphomas in the United States; 20% worldwide

**Age**
Median, 55-59 years

**Sex**
Male = female

**Clinical features at presentation**
Generalized lymphadenopathy, frequent splenomegaly, often asymptomatic; bone marrow positive in 40%; rare stage I, extranodal or paediatric

**Morphology**
1. Pattern: follicular with or without diffuse areas, or interfollicular involvement, extracapsular extension, sclerosis, vascular invasion
2. Cytology: centroblasts and centrocytes, follicular dendritic cells
3. Grade 1-2, 3A, 3B
**Usual Immunophenotype**
Ig+, CD19+, CD20+, CD22+, CD79a+, PAX5+, CD10+, BCL2+, BCL6+, CD43−, CD5−;
nodular meshworks of CD21+, CD23+ follicular dendritic cells

**Genetic features**
Immunoglobulin genes rearranged, mutated, intraclonal heterogeneity; t(14;18)(q23;q32) and IGH/BCL2 rearranged

**Postulated normal counterpart**
Germinal-centre B cells

**Clinical course**
Indolent, incurable: median survival 8-10 years; prognosis based on histologic grade (grade 1 to 2 indolent, grade 3 aggressive), Follicular Lymphoma International Prognostic Index

**Treatment**
Symptomatic for grade 1 to 2, aggressive for grade 3
## Grading of Follicular Lymphoma

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 to 2 (low grade)*</td>
<td>0-15 centroblasts/hpf†</td>
</tr>
<tr>
<td>Grade 1</td>
<td>0-5 centroblasts/hpf†</td>
</tr>
<tr>
<td>Grade 2</td>
<td>6-15 centroblasts/hpf†</td>
</tr>
<tr>
<td>Grade 3</td>
<td>&gt;15 centroblasts/hpf†</td>
</tr>
<tr>
<td>Grade 3A</td>
<td>Centrocytes present</td>
</tr>
<tr>
<td>Grade 3B</td>
<td>Solid sheets of centroblasts</td>
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</tbody>
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**Reporting of Pattern**

<table>
<thead>
<tr>
<th>Reporting of Pattern</th>
<th>Proportion Follicular (%)</th>
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<tbody>
<tr>
<td>Follicular</td>
<td>&gt;75</td>
</tr>
<tr>
<td>Follicular and diffuse</td>
<td>25-75‡</td>
</tr>
<tr>
<td>Focally follicular</td>
<td>&lt;25‡</td>
</tr>
<tr>
<td>Diffuse</td>
<td>0‡</td>
</tr>
</tbody>
</table>

Diffuse areas containing >15 centroblasts/hpf are reported as diffuse large B-cell lymphoma‡ with follicular lymphoma (grade 1 to 2, 3A, or 3B)
Follicle Centre Cells

Interfollicular Cells
CD 21 FDCs & B cells
CD 10 interfollicular staining
a & c Dako BCL2
b & d Epitomics BCL2
Light chains are only sometimes helpful in FL

IgD can be a great help
In situ Follicular Neoplasia

**Definition**
Clonal BCL2+ follicles on an architecturally normal background

**Possibilities**
Nothing
History of follicular lymphoma
Concurrent follicular lymphoma
Heralds Follicular lymphoma

Do NOT make diagnosis of FL on the basis of this finding

Clinical assessment required
In situ follicular neoplasia (ISFN): reactive looking follicles
MALT lymphoma is an extranodal lymphoma comprising morphologically heterogeneous small B cells, including marginal-zone (centrocyte-like) cells, cells resembling monocytoid cells, small lymphocytes, and scattered immunoblast and centroblast-like cells.

There is plasma cell differentiation in a proportion of cases. The infiltrate is in the marginal zone of reactive B-cell follicles and extends into the interfollicular region.

In epithelial tissues, the neoplastic cells typically infiltrate the epithelium, forming lymphoepithelial lesions.
MALT lymphomas account for 7% to 8% of all B-cell lymphomas and at least 50% of primary gastric lymphomas
MALT Lymphoma sites

• Gastrointestinal tract
  • Stomach
  • Intestine (including immunoproliferative small intestinal disease)
• Salivary glands
• Respiratory tract
  • Lung, pharynx, trachea
• Ocular adnexa
  • Conjunctiva, lacrimal gland, orbit*
• Skin
• Thyroid gland
• Liver
• Genitourinary tract
  • Bladder, prostate gland, kidney
• Breast
• Thymus
MALT lymphomas only rarely arise from native MALT

Usually arise from MALT that has been acquired as a result of a chronic inflammatory disorder at sites normally devoid of MALT such as the stomach, salivary gland, lung, thyroid gland, and ocular adnexa.

MALT lymphomas of the salivary gland and thyroid gland, organs normally containing no lymphoid tissue, are always preceded by an autoimmune lymphoid infiltrate - Sjögren’s syndrome and Hashimoto’s thyroiditis, respectively
Infectious agents

H. Pylori (gastric MALT lymphoma))

Campylobacter jejuni (immunoproliferative small intestinal disease – Middle East, India, Cape region of South Africa)

Borrelia burgdorferi (cutaneous MALT lymphoma)

Chlamydia psittaci (Ocular adnexal MALT lymphoma)

*NB Association is not proof of aetiology*
Lymphoepithelium of Peyers patch
Gastric MALT Lymphoma
Gastric MALT Lymphoma - Lymphoepithelial lesions
Cell morphology gastric MALT lymphoma – centrocyte like
Cell morphology gastric MALT lymphoma – small lymphocytes
Cell morphology gastric MALT lymphoma – monocytoid cells
But be careful......
Each of these represents a follicular lymphoma!
What’s this one?
kappa  lambda
Answer: NLPHL
Mantle cell lymphoma (MCL)

*Definition*

Mature B-cell neoplasm generally composed of monomorphic small to medium-sized lymphoid cells with irregular nuclei that carries 11q13 translocations, leading to overexpression of cyclin D1.

Neoplastic transformed cells (centroblasts), paraimmunoblasts, and pseudofollicles are absent.
Extranodal involvement is frequent in MCL. Gastrointestinal infiltration has been reported in 10% to 25% of patients, either at presentation or during the course of the disease. A peculiar manifestation of this involvement is lymphomatoid polyposis.

Other extranodal sites commonly involved are Waldeyer’s ring, lung, and pleura (5%-20%).

Less common localizations are skin, breast, soft tissue, thyroid, salivary gland, peripheral nerve, conjunctiva, and orbit.

Leukaemic phase can occur
MCL Architectural Patterns

Mantle zone

Nodular

Diffuse
MCL – diffuse pattern
MCL - histiocytes
MCL – Nodular pattern
MCL - Mantle zone pattern
MCL – centrocyte like cells
MCL – small lymphocytes
MCL – pleomorphic variant
MCL – blastoid variant
kappa

lambda
What’s this one?
Two more follicular tricksters.......
Answer: Angioimmunoblastic T cell lymphoma
What’s this one?
Answer: CLL / SLL
Other lymphomas with a marginal zone pattern

1. Follicular lymphoma
2. Mantle cell lymphoma
3. Peripheral T cell lymphoma
4. Lymphoplasmacytic lymphoma

(Benign proliferation)