

An update on lymphomas of the upper GI tract

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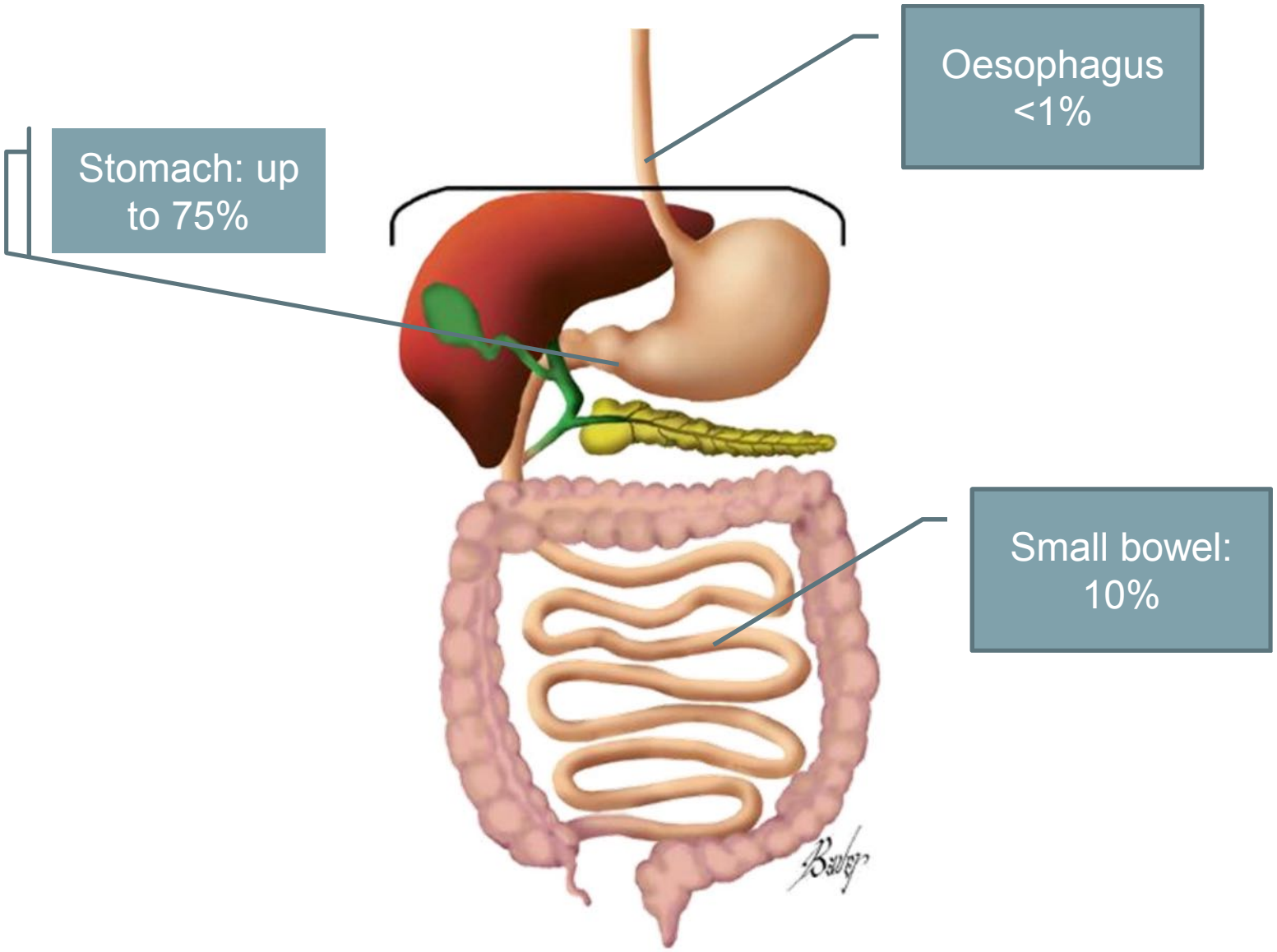
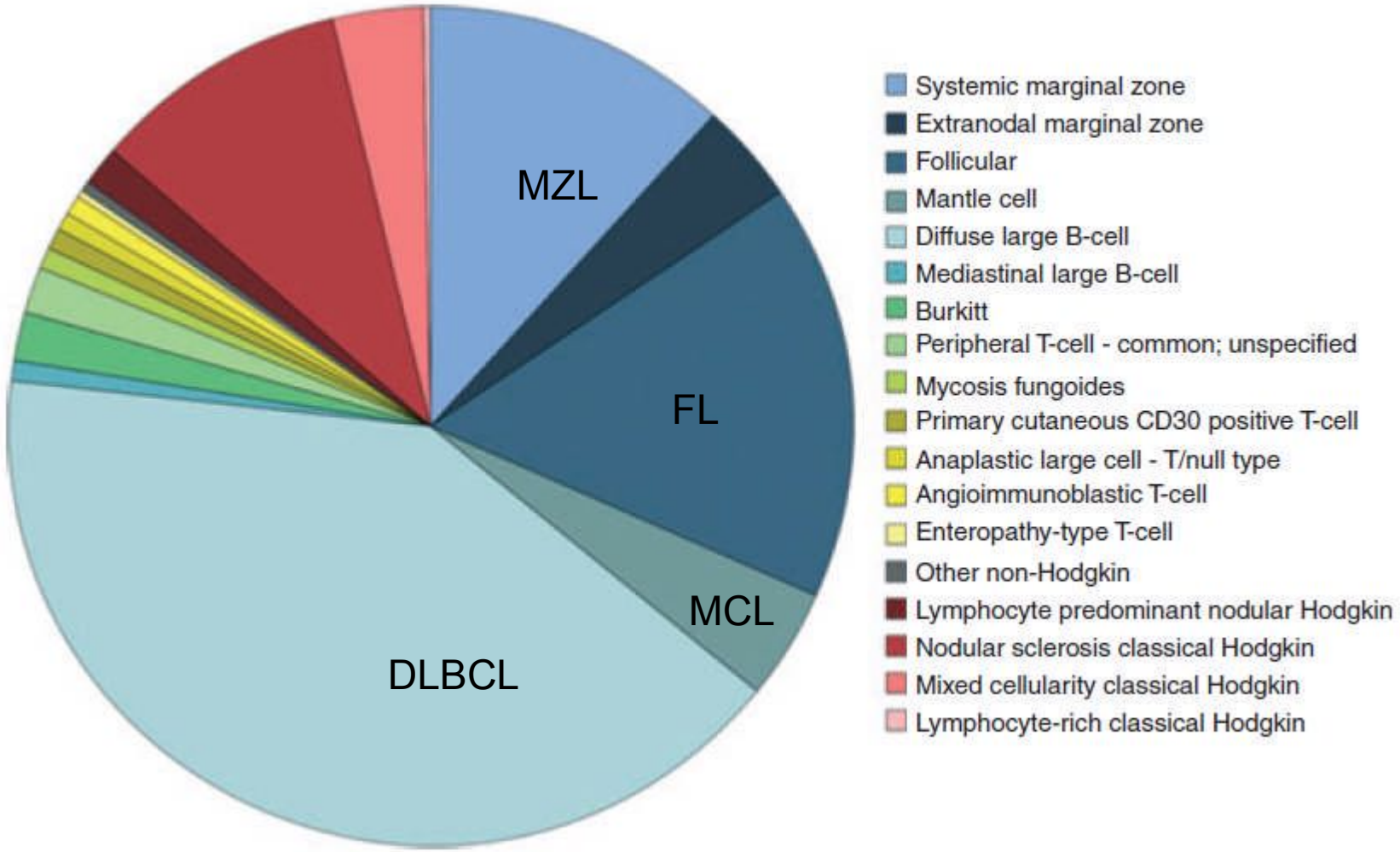
SYMPOSIUM ON UPPER GI & PANCREATOBILIARY PATHOLOGY
2-3 December 2016

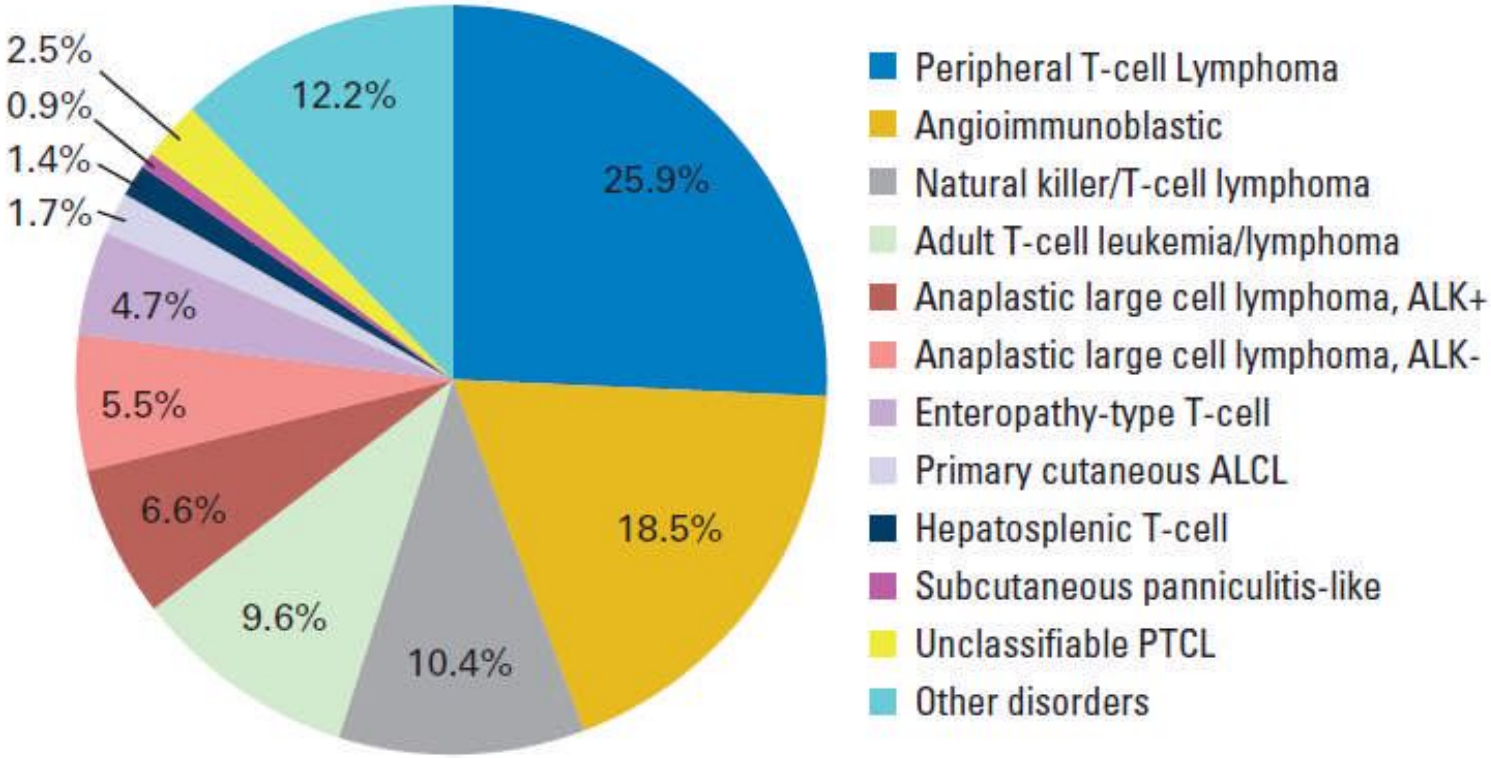
- Primary GI lymphomas account for 1-4% of all GI tumors
- The **GI tract is the most common site of extranodal lymphomas** (4-20% of all NHL)
- Most commonly these are **Non Hodgkin's lymphomas**. Hodgkin's disease usually involve the GIT secondarily.
- In the GI tract they may be associated with other pathologies and complicate the clinical course of the primary pathology (e.g. increase incidence of NHL in IBD patients on **immunosupressive therapy**, lymphomas associated with **HIV infection**…)



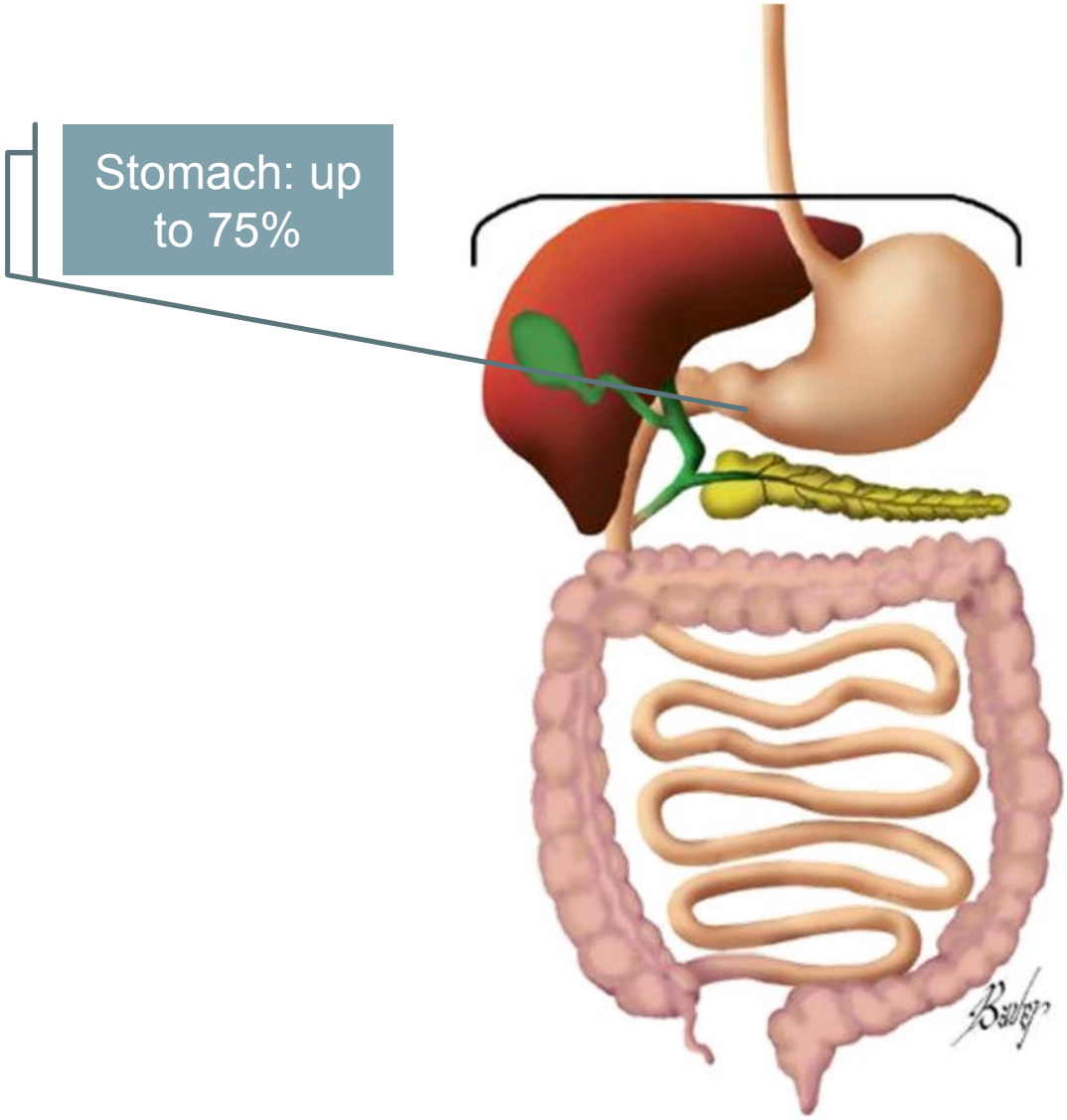
Multifocal or >1 site: 6%



Source: Haematological Malignancy Research Network.



HMRN Haematological Malignancy Research Network


Stomach: up to 75%

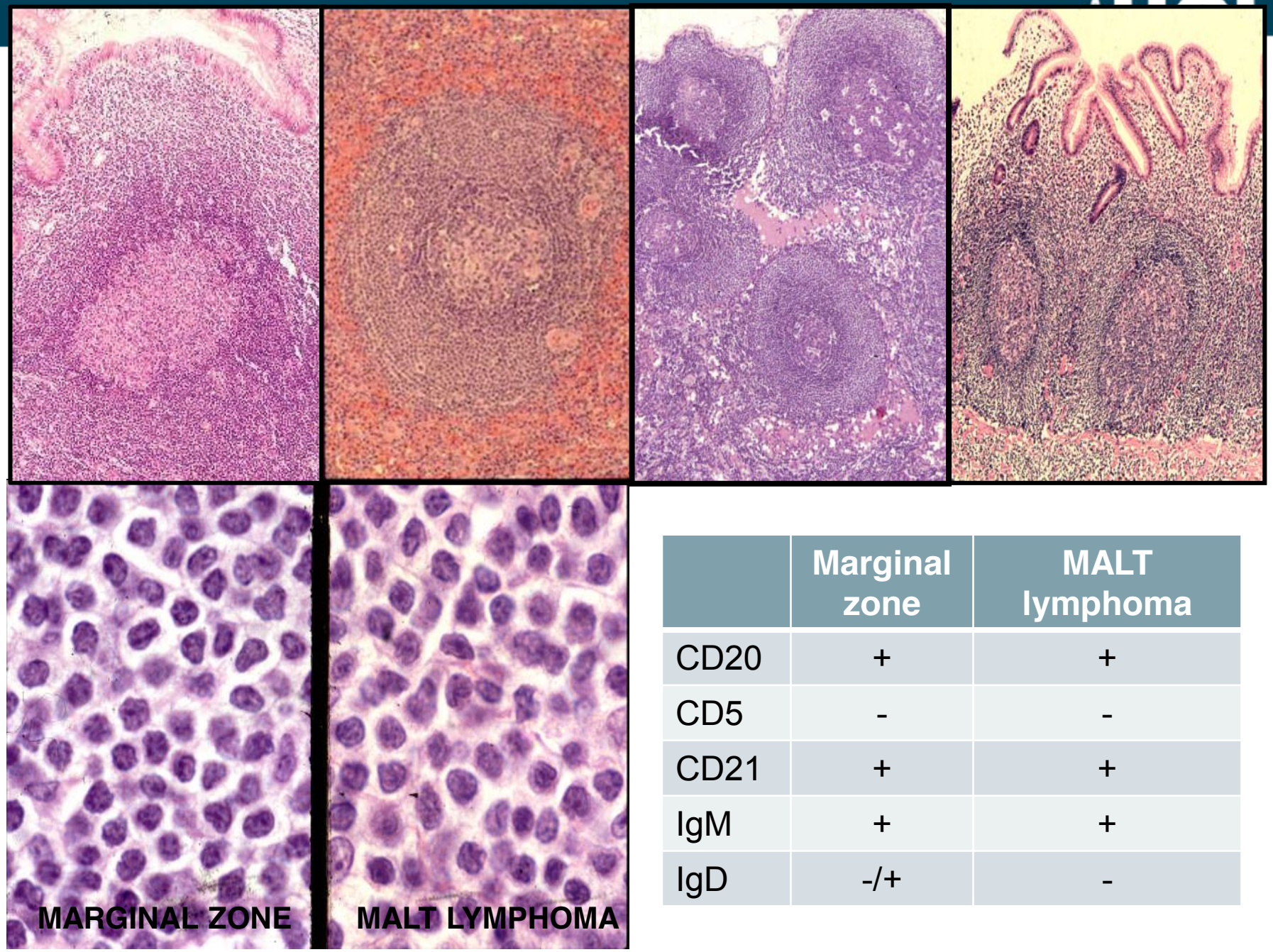
MALT lymphomas

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT)

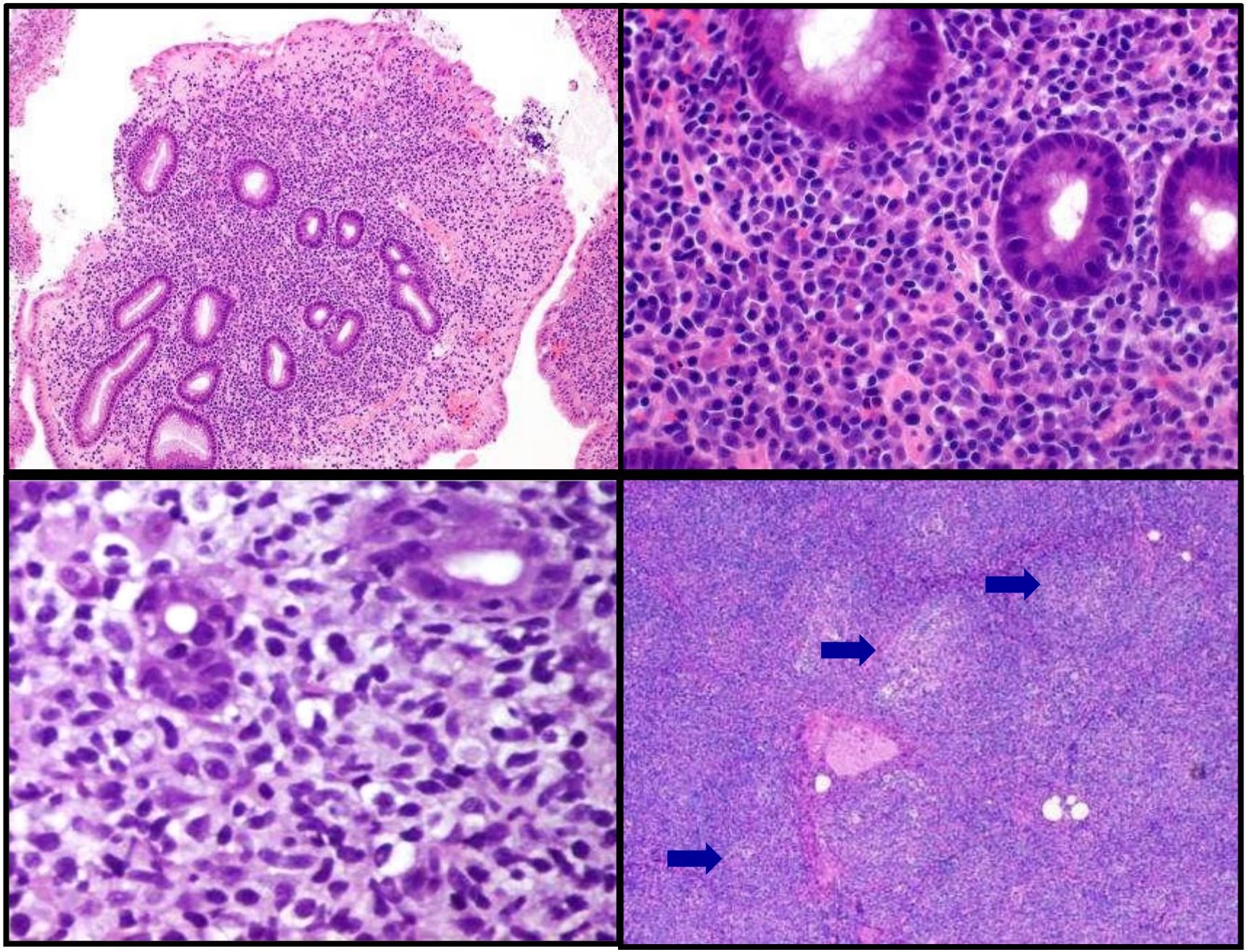
Epidemiology: 7-8% of all B-cell lymphomas
50% of primary *gastric* lymphomas

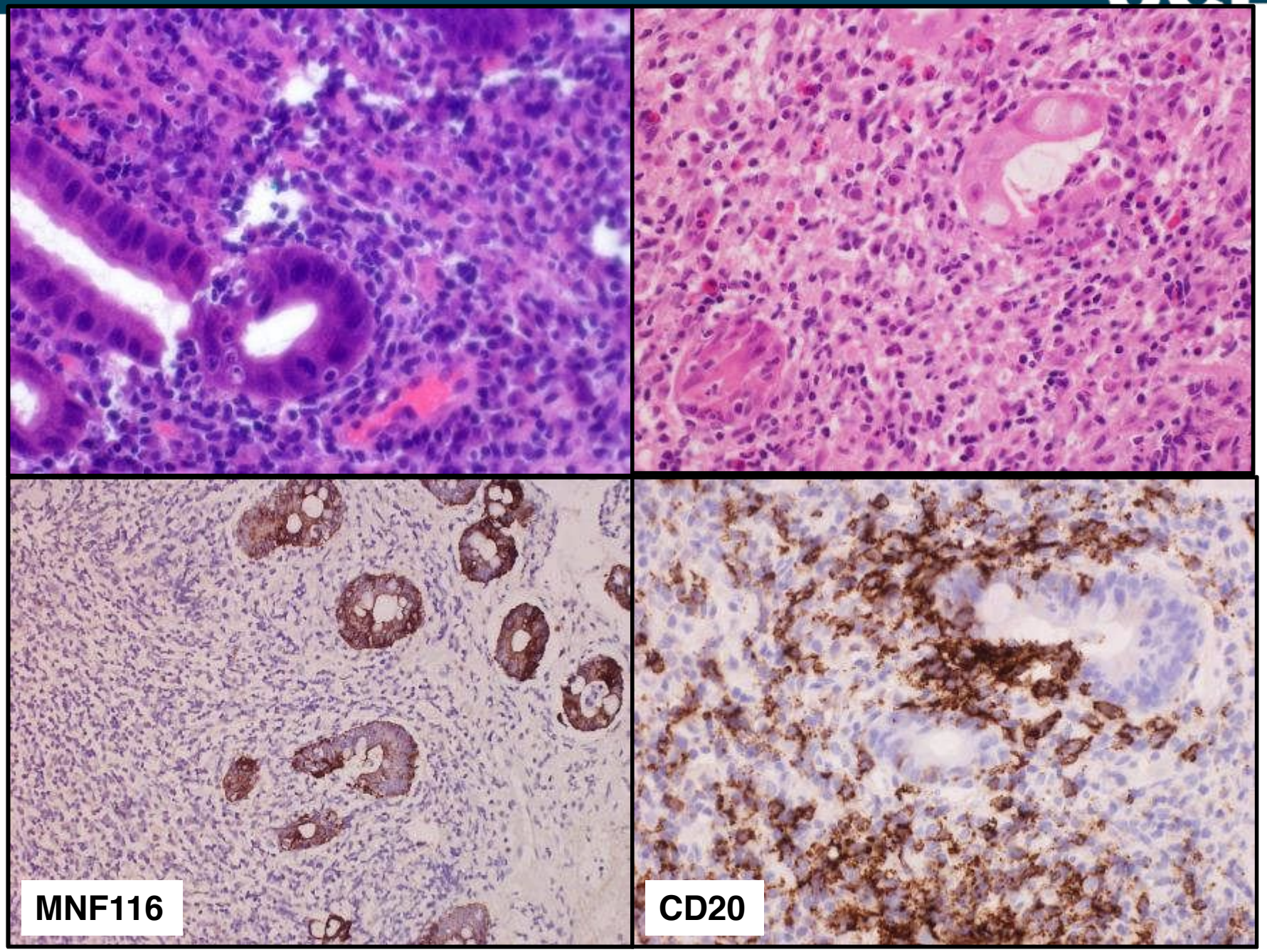
Histopathology:

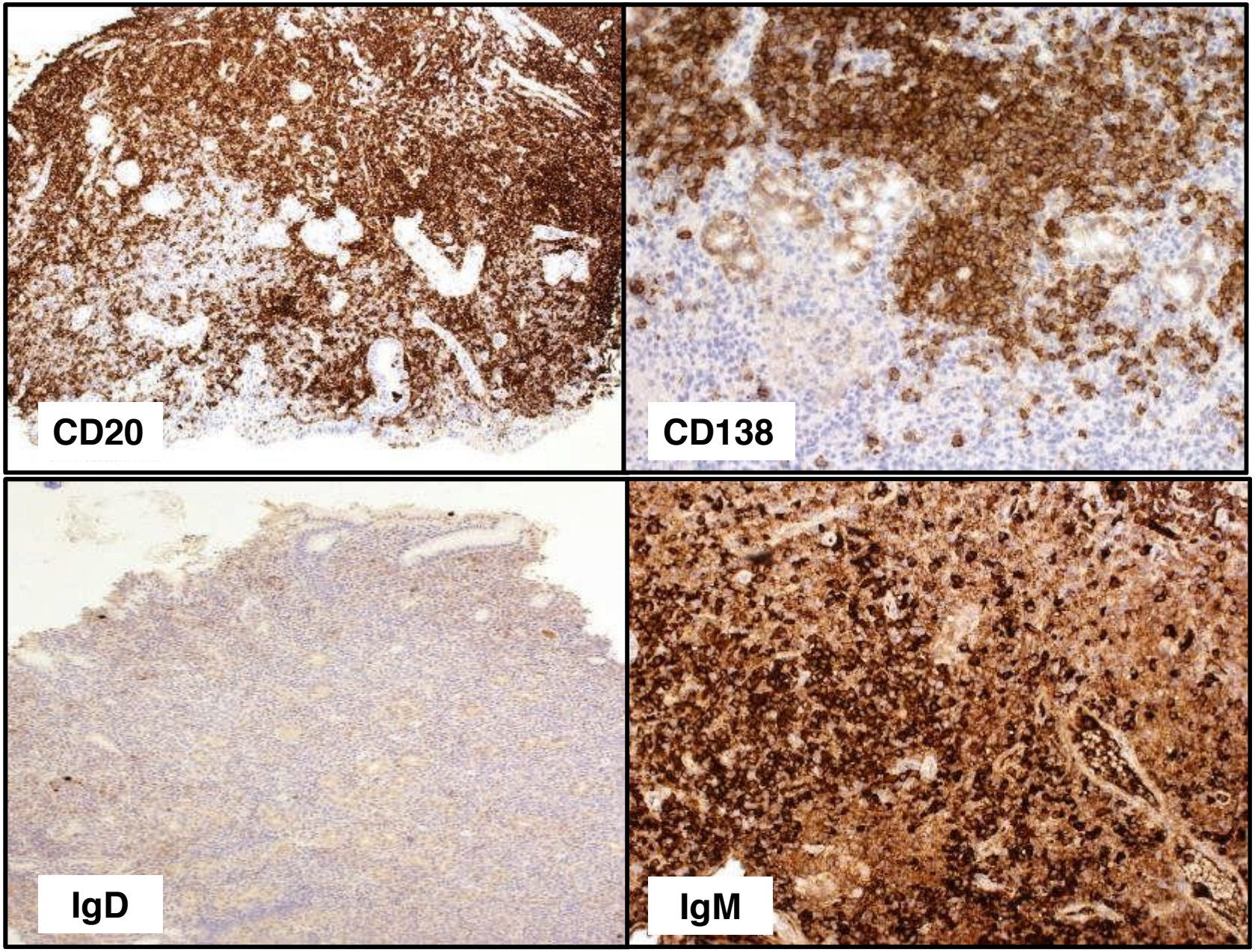
- Heterogeneous population (centrocyte-like cells monocytoid cells, scattered larger cells, plasma cell differentiation)
- Lymphoepithelial lesions

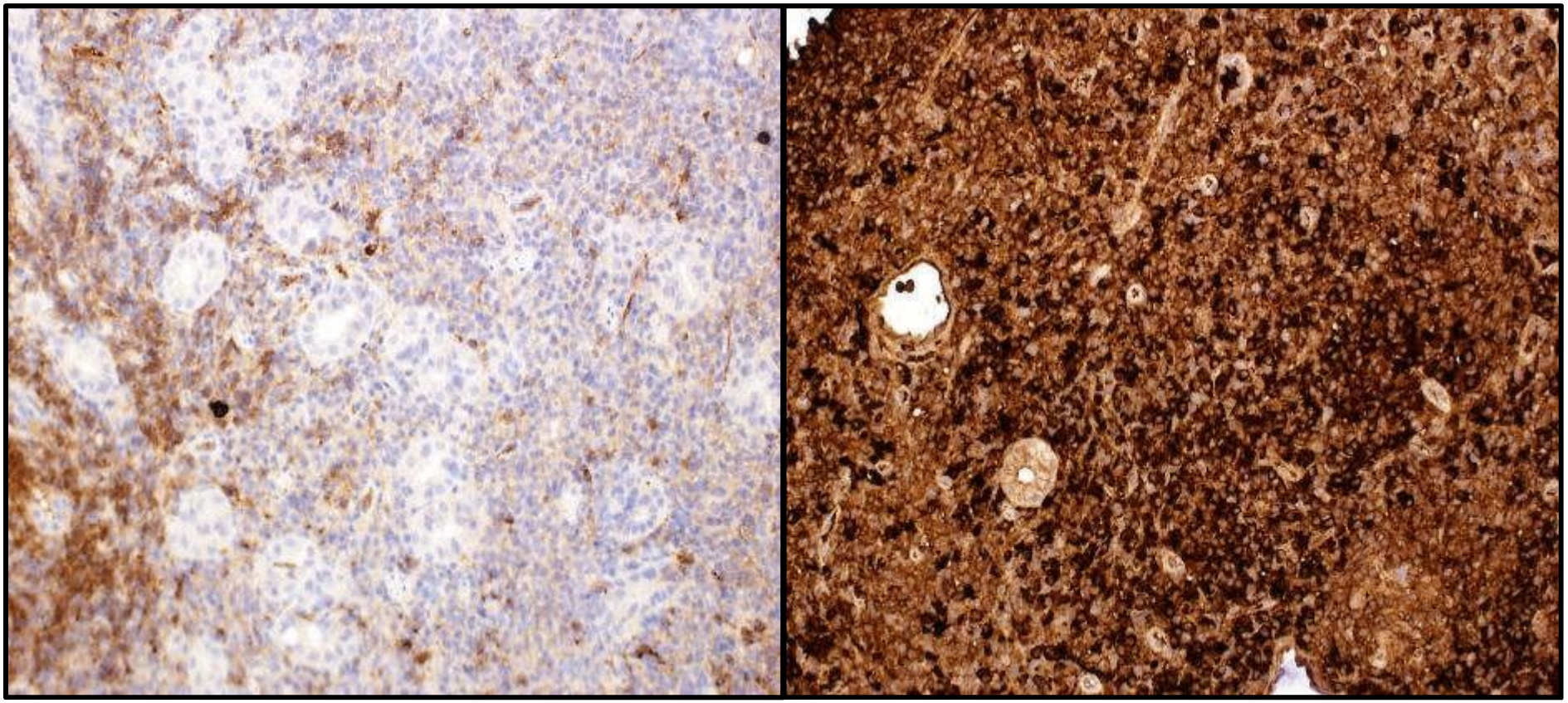


	Marginal zone	MALT lymphoma
CD20	+	+
CD5	-	-
CD21	+	+
IgM	+	+
IgD	-/+	-




MNF116
CD20


CD20
CD138
IgD
IgM



κ λ

	Description	Histological features
0	Normal	Scattered plasma cells in lamina propria (LP). No follicles
1	Chronic active gastritis	Clusters of lymphocytes in LP. No follicles. No lymphoepithelial lesions (LEL)
2	Chronic active gastritis with florid lymphoid follicle formation	Lymphoid follicles with surrounding mantle zone and plasma cells. No LEL
3	Suspicious lymphoid infiltrate, probably reactive	Lymphoid follicles surrounded by small lymphocytes that infiltrate LP and occasionally into the epithelium.
4	Suspicious infiltrate, probable lymphoma	Lymphoid follicles surrounded by marginal zone cells that infiltrate diffusely LP and into epithelium in small groups
5	MALT lymphoma	Dense diffuse infiltrate of marginal zone cells in LP with prominent LEL

To do IHC +/- molecular

Interobserver variation in the histopathological assessment of malt/malt lymphoma: towards a consensus

Blood Cells, Molecules, and Diseases 34 (2005) 6–16

Disease category (0–4)	Pathologist		
	H	GI	General
1. Simple gastritis	Fair (κ 0.38)	Fair (κ 0.35)	Moderate (κ 0.42)
2. Florid hyperplasia*	Fair	Moderate	Fair
Low- grade MALT	(κ 0.35)	(κ 0.42)	(κ 0.30)
Low-grade MALT with increased blasts			
3. High-grade lymphoma	Fair	Fair	Moderate
with low-grade component	(κ 0.31)	(κ 0.28)	(κ 0.40)
High grade lymphoma			
Other lymphoma			
4. Undecided	Fair	Slight	Slight
	(κ 0.27)	(κ 0.06)	(κ 0.01)

H = hematologists, GI = pathologists with special interest in gastrointestinal diseases.

karyotypic alterations

- trisomies 3 (30%) and 18
- translocations t(11;18)(q21;q21), 30-40%
- t(1;14)(p22;q32),
- t(14;18)(q32;q21),
- t(3;14)(q27;q32),
- recently described t(3;14)(p14.1;q32).

t(11;18)(q21;q21) → predicts lack of response to H pylori eradication therapy

H pylori eradication and gastric MALT

- HP is a major factor in the development of MALT-lymphoma.
- Eradication leads to durable remissions in about 80% of selected patients.
- t(11;18)+ patients seem to be unresponsive to HP eradication.
- Relapse triggered by re-infection with HP remains sensitive to eradication

High grade B-cell gastric lymphoma with complete pathologic remission after eradication of helicobacter pylori infection: Report of a case and review of the literature

World Journal of Surgical Oncology 2008, **6**:35

- Forty two cases reviewed
- Anecdotal and prospective
- All *H pylori* positive
- Four trials
  - 22/38 (58%)patients achieved complete remission
  - Depth of infiltration and clinical stage important

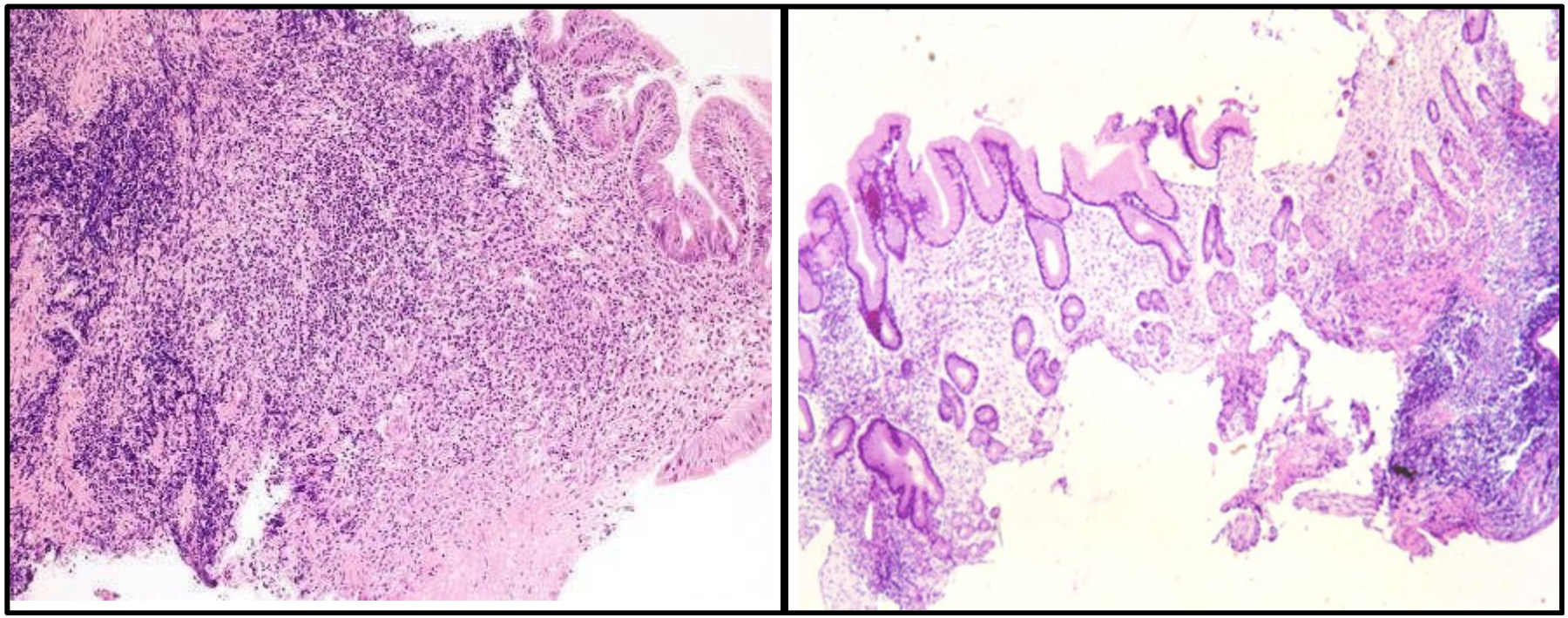
H pylori eradication on non-gastric MALT lymphomas

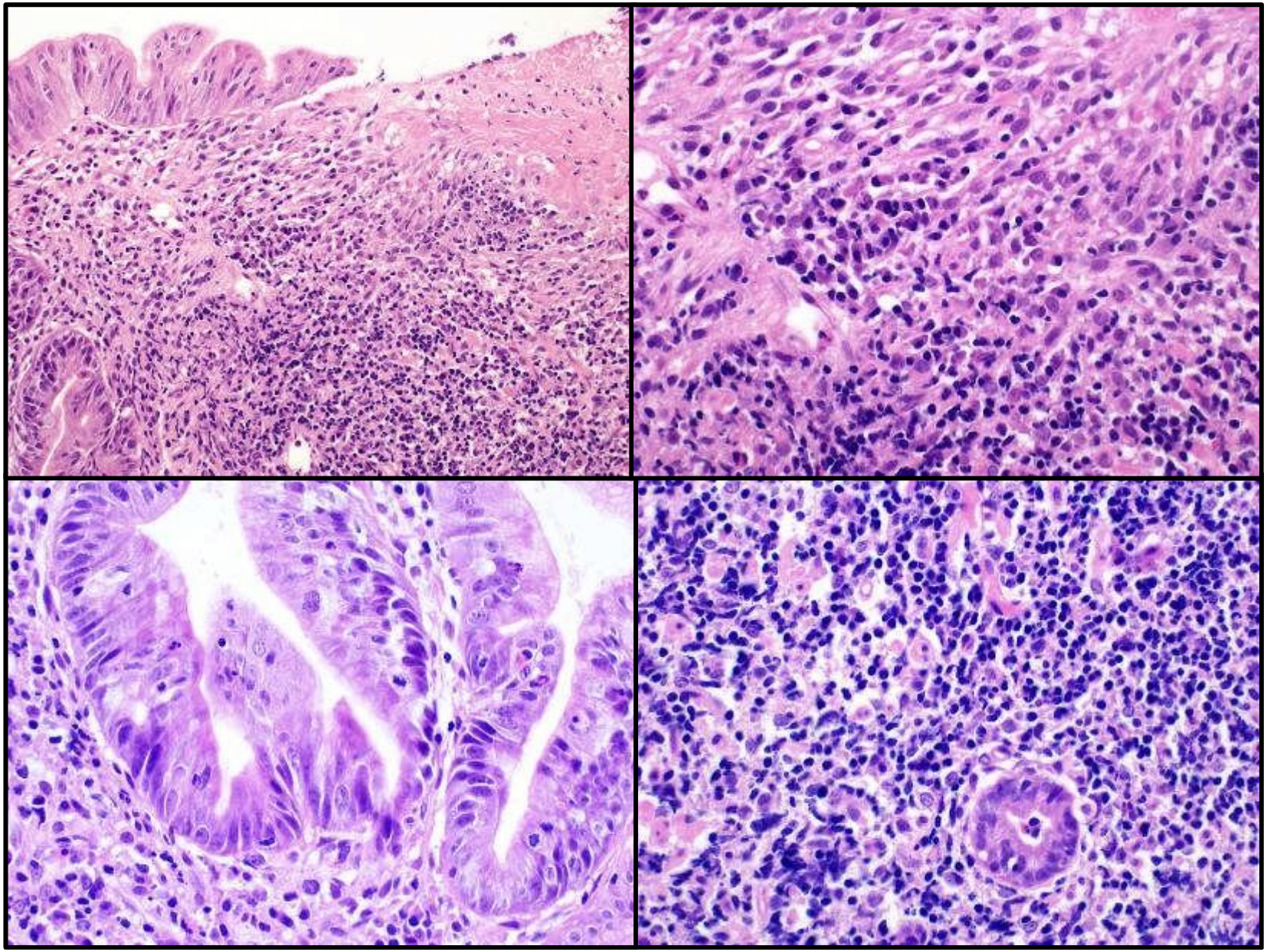
Dig Dis Sci 2004 Mar;49(3):413-6.
Disappearance of rectal mucosa-associated lymphoid tissue lymphoma following antibiotic therapy.
Hori K et al.

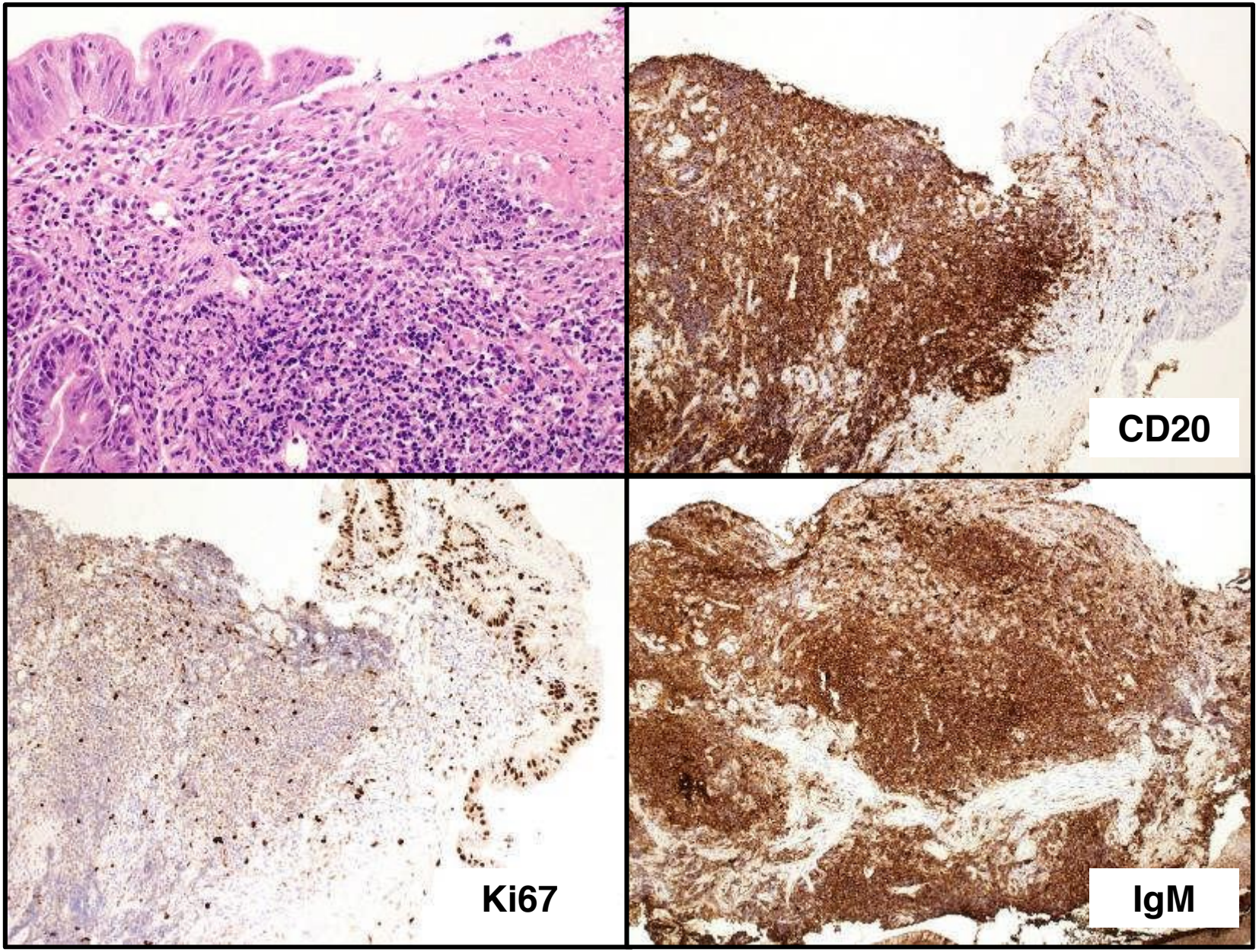
Disappearance of a mucosa-associated lymphoid tissue (MALT) lymphoma of the urinary bladder after treatment for *Helicobacter pylori*

Eur J Haematol 2002: 68: 187–188

Effect of H pylori eradication on gastric MALT





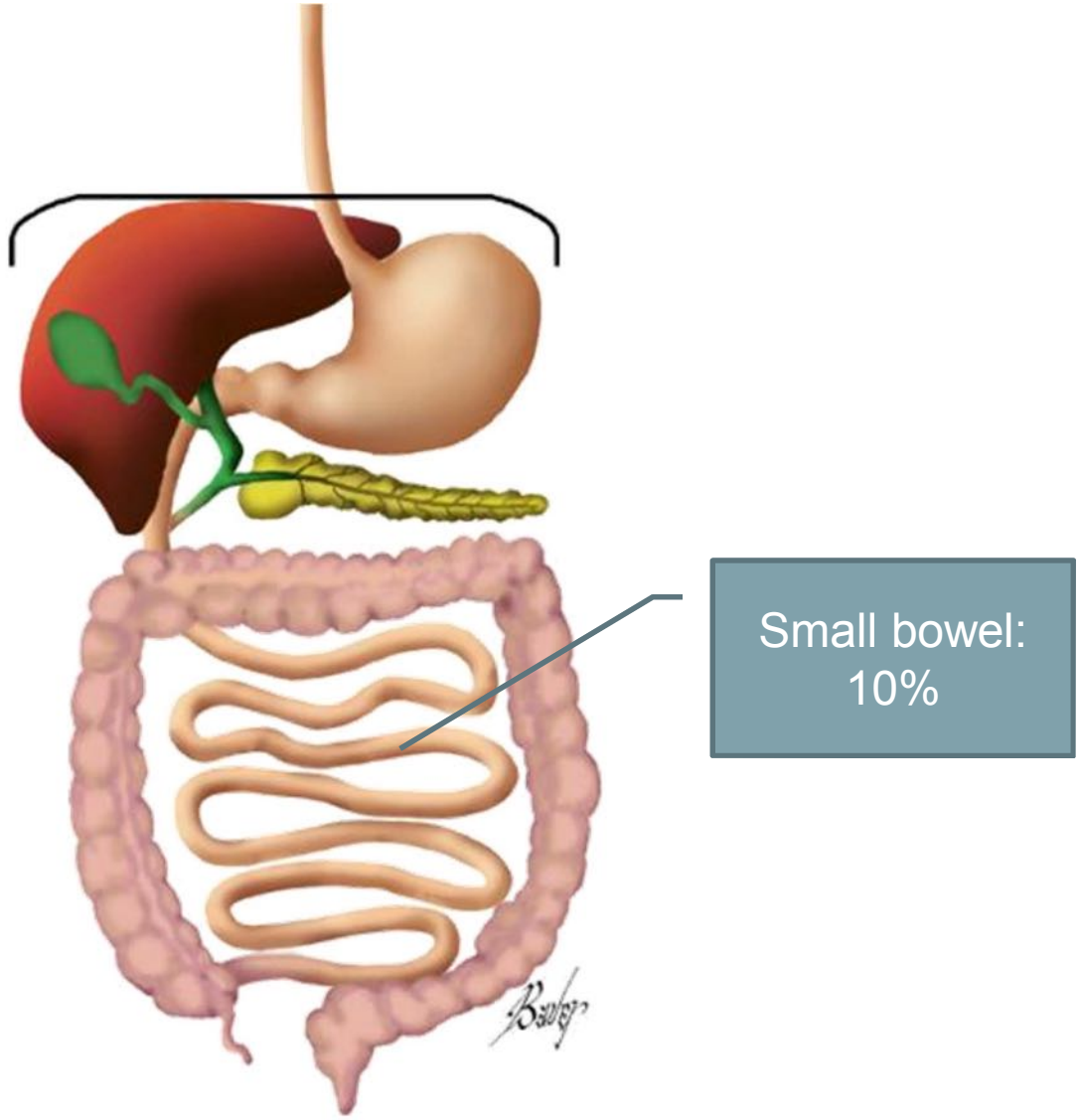

CD20
Ki67
IgM

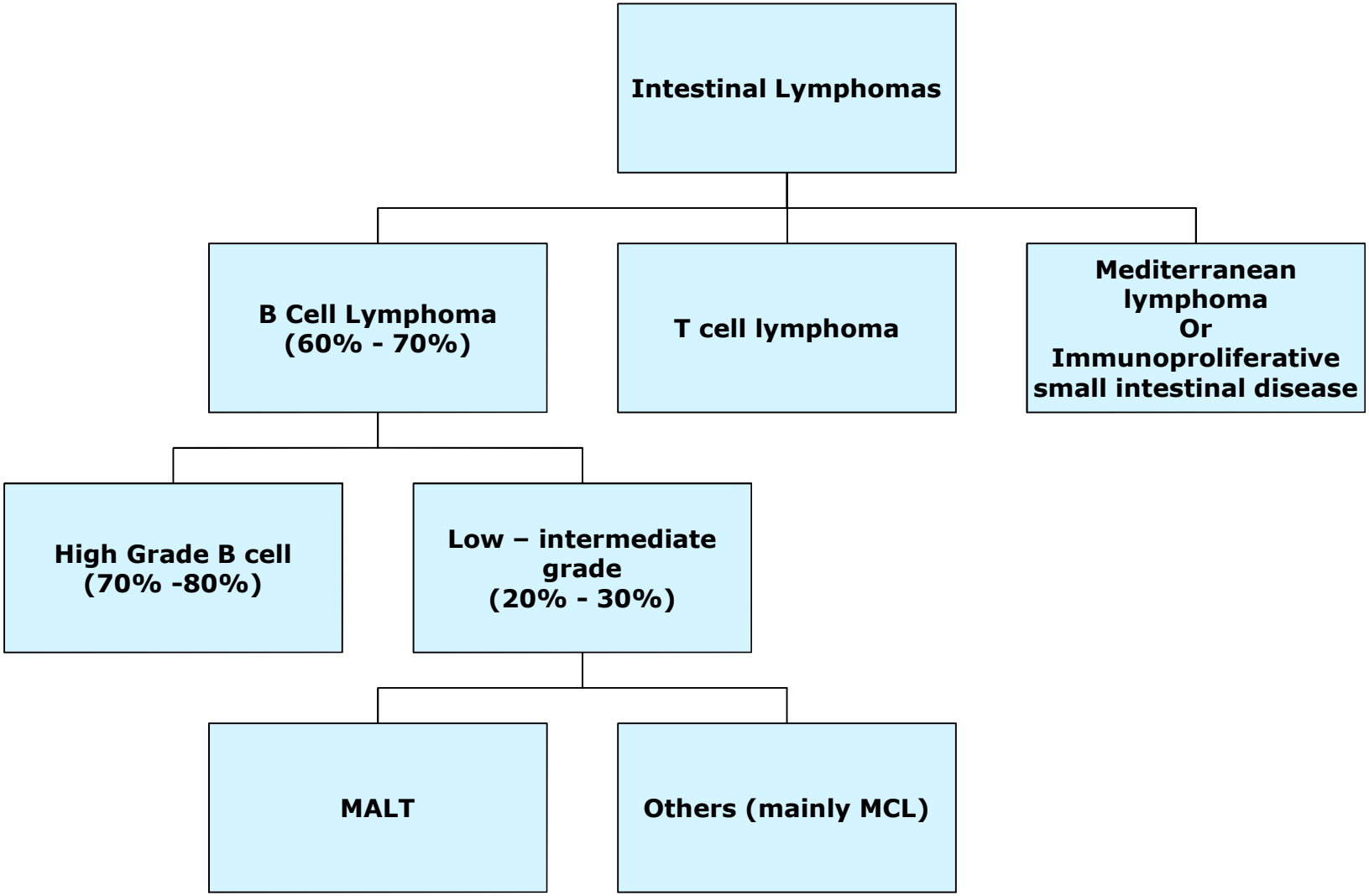
Histological grading system for post-treatment evaluation of gastric MALT lymphoma			
Score	*Lymphoid population*	*LEL*	*Stromal changes*
Complete remission	Absent of scattered plasma cells and small lymphoid cells	-	Normal or empty LP and/or fibrosis
Probable MRD	Aggregates of lymphoid cells/lymphoid nodules in LP / muscularis mucosa and/or submucosa	-	Empty LP and/or fibrosis
Responding residual disease	Dense, diffuse or nodular extending around glands	- / +	Focal empty LP and/or fibrosis
No change	Dense, diffuse or nodular	+	No changes

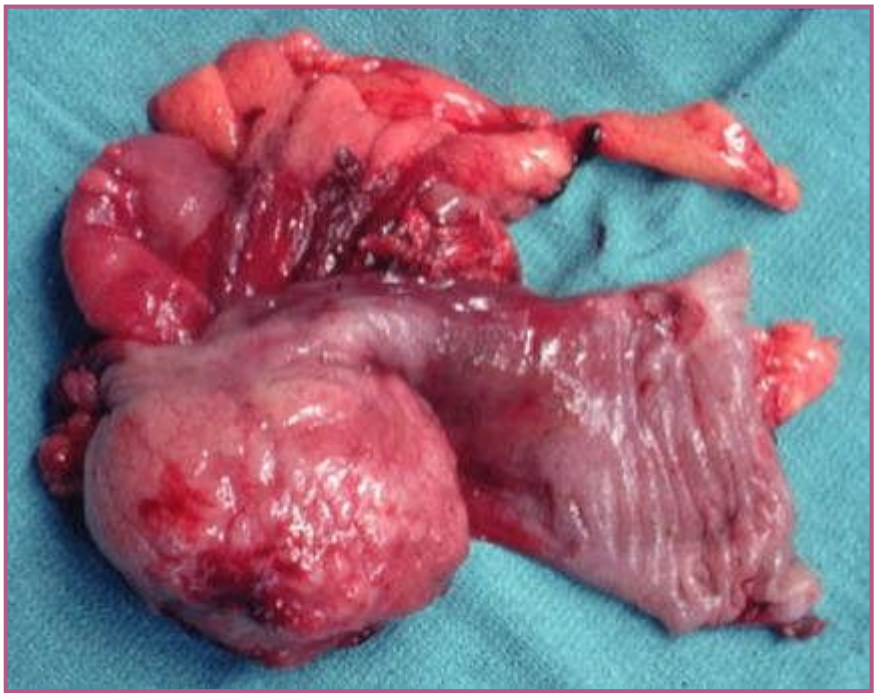
Wotherspoon A, Doglioni C, Diss T, et al. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of *Helicobacter pylori*. *Lancet* 1993; **342:** 575–7.

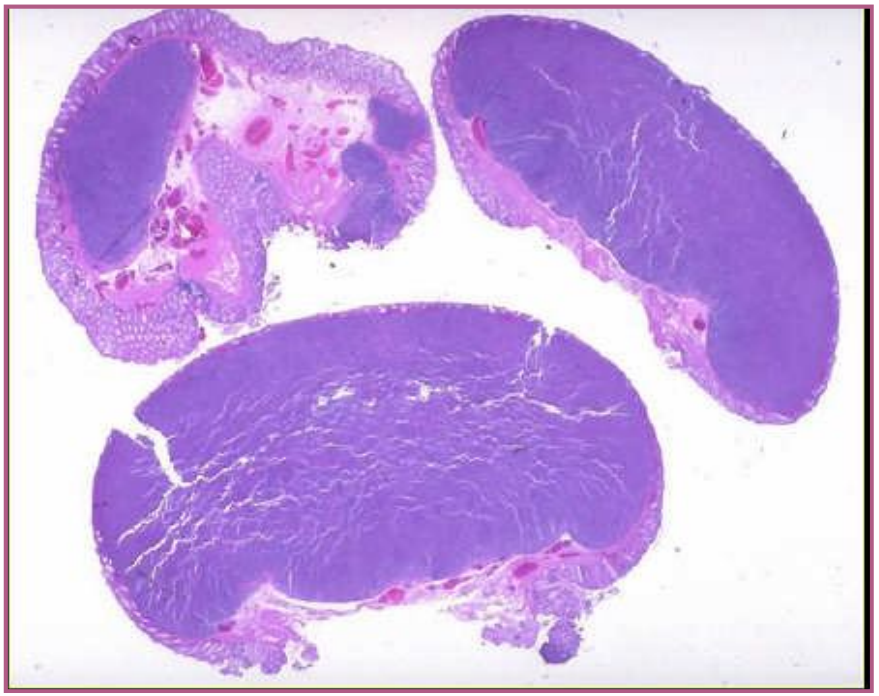
- Demonstration of **monoclonality** (PCR BIOMED-2 protocols) is **not a prerequisite** for the diagnosis of gastric MALT lymphoma.
- **Histology** is the **first diagnostic choice for H pylori infection** since it is the best diagnostic tool in the case of gastric MALT lymphoma.
- H pylori-negative patients with gastric MALT lymphoma can also undergo anti-H pylori treatment.
- Apparent **B cell monoclonality** has been detected in **1-4%** of otherwise **typical chronic gastritis**
- Current evidence does not support a role for assessment of clonality in post-treatment follow-up of gastric MALT lymphomas beyond the research setting.

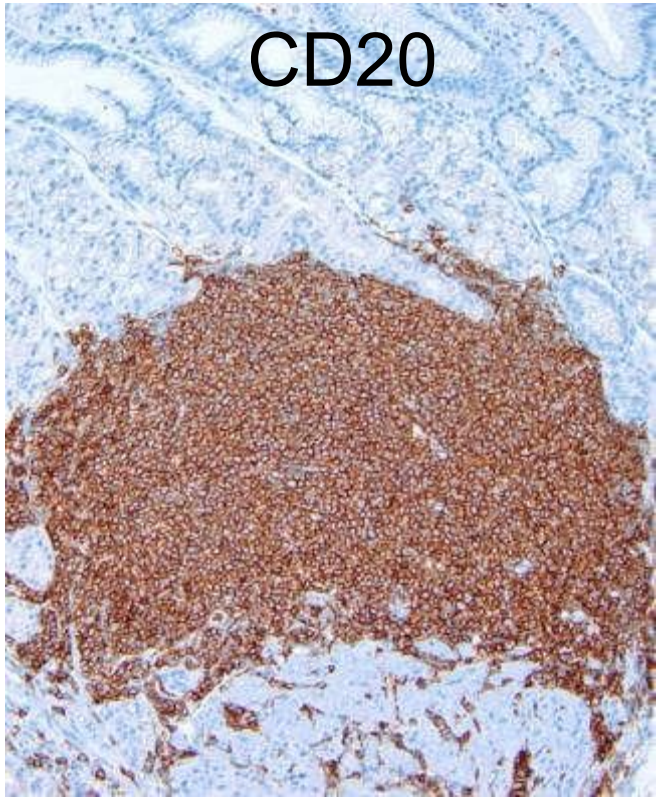
EGILS consensus report. Gastric extranodal marginal zone B-cell lymphoma of MALT
Gut 2011;**60**:747–758. doi:10.1136/gut.2010.224949

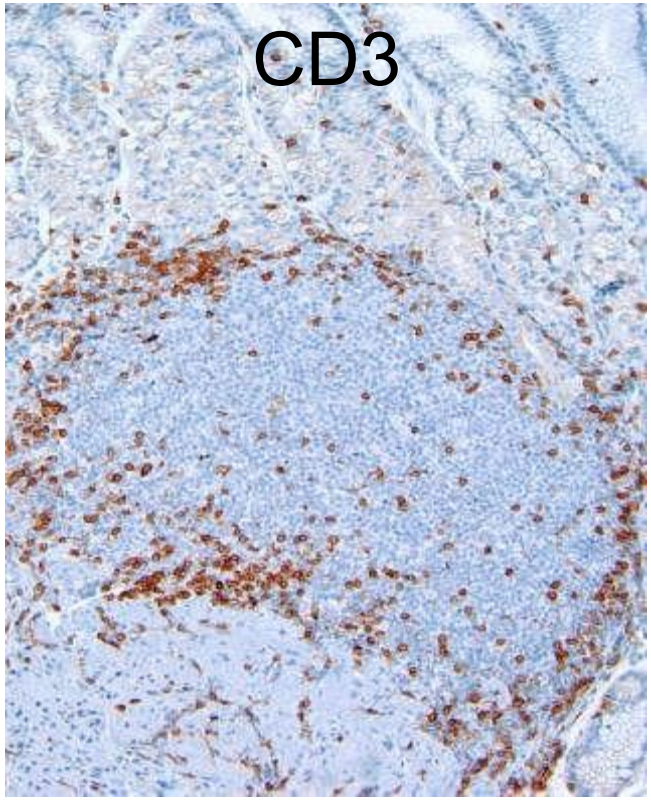

Small bowel:
10%

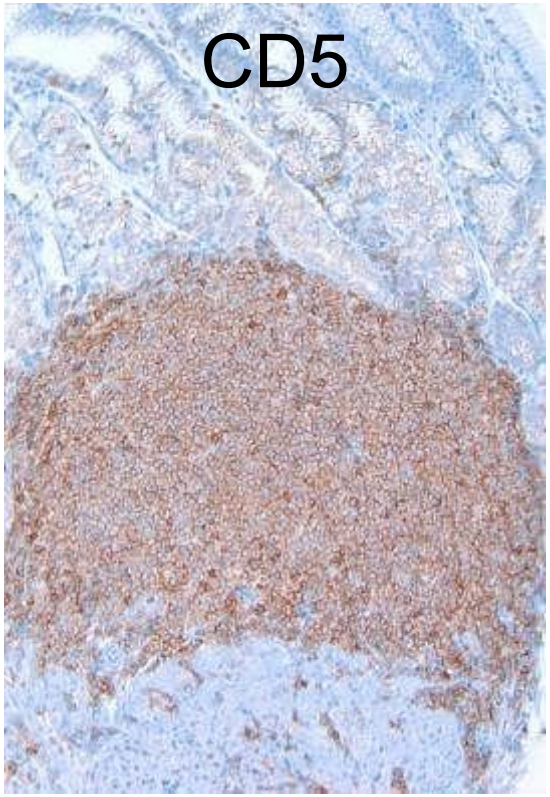

Intestinal Lymphomas
B Cell Lymphoma (60% - 70%)
T cell lymphoma
Mediterranean lymphoma Or Immunoproliferative small intestinal disease
High Grade B cell (70% -80%)
Low – intermediate grade (20% - 30%)
MALT
Others (mainly MCL)






CD20

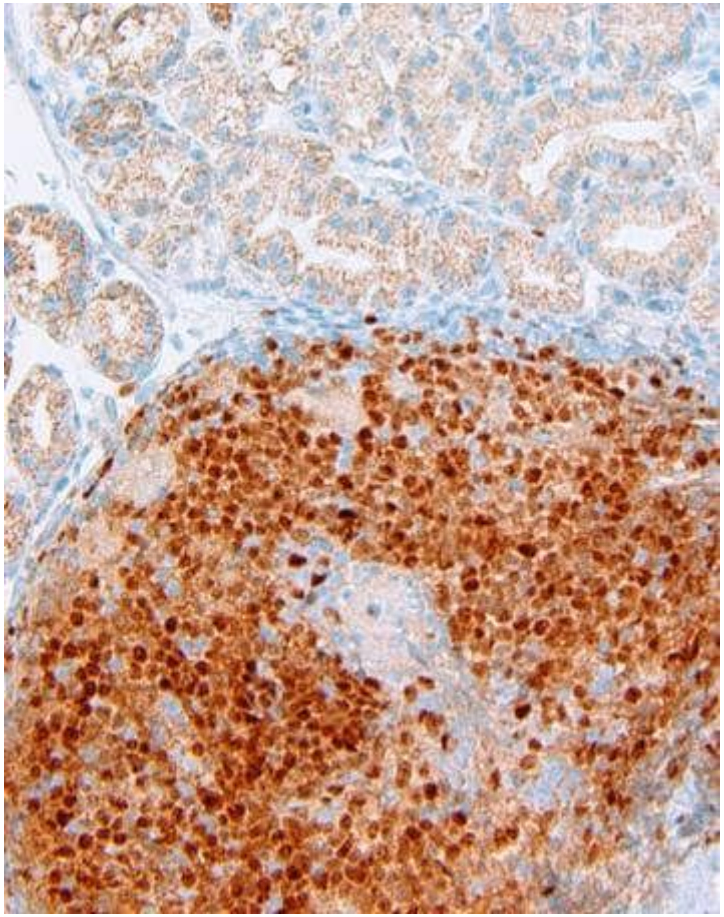

CD3


CD5

Cyclin-D1

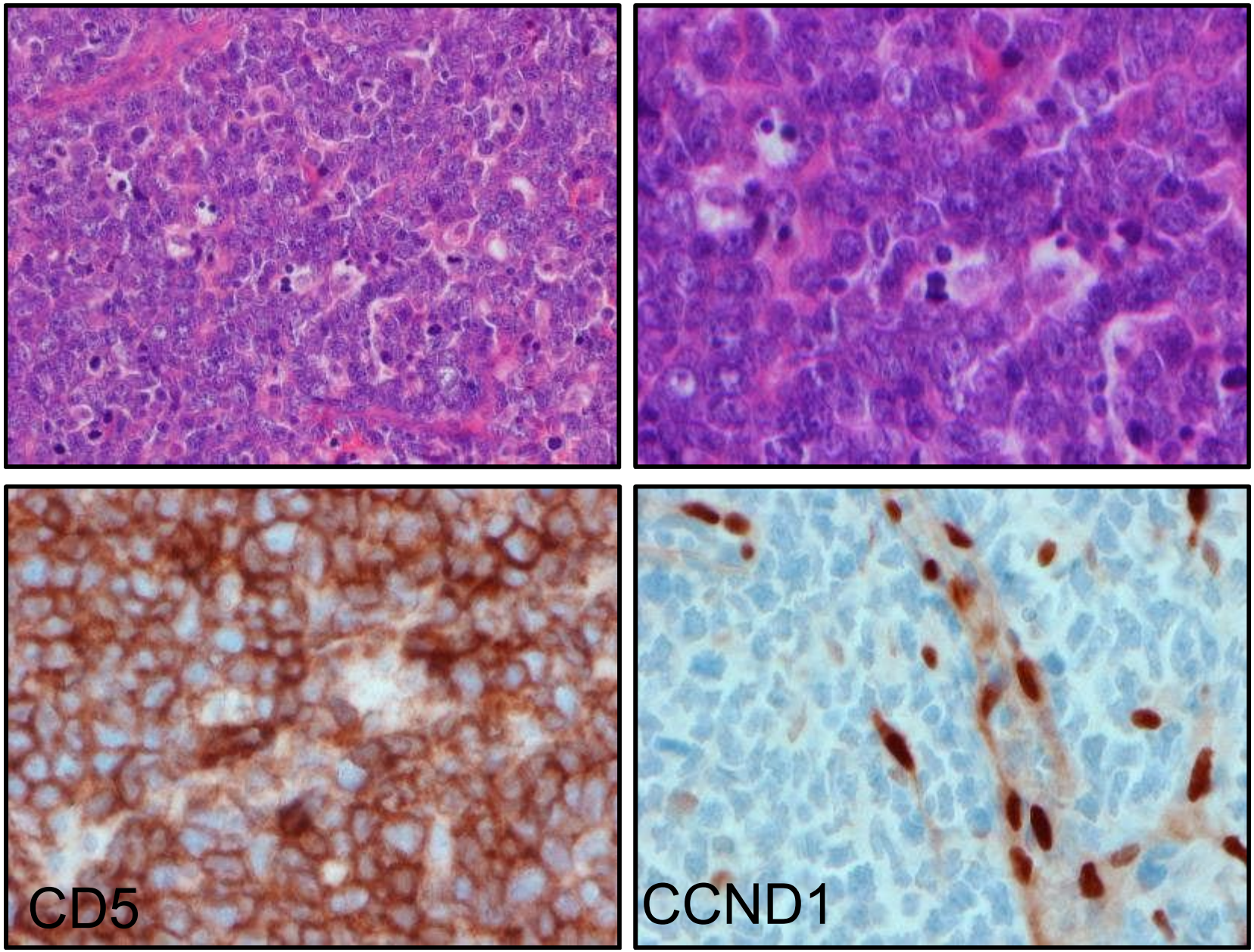
Cyclin D1 is overexpressed in 90% of MCL, as a consequence of the t(11;14)(q13;q32)

Rare cases of mantle cell lymphoma are reported that are negative for cyclin D1, but have a gene expression prolife consistent with mantle cell lymphoma



Mantle cell lymphoma

- MCL involving spleen and bowel: *multiple lymphomatous polyposis* (polyps 0.5-2cm)
- Histology of MCL in small bowel is identical to MCL at nodal sites
- Intestinal glands may be destroyed by MCL but typical LEL are not seen.
- IHC: CD20 (+), CD19 (+), CD5 (+), IgM (+), IgD (+), Cyclin D1 (+)


CD5
CCND1

SOX11 expression is highly specific for mantle cell lymphoma and identifies the cyclin D1-negative subtype

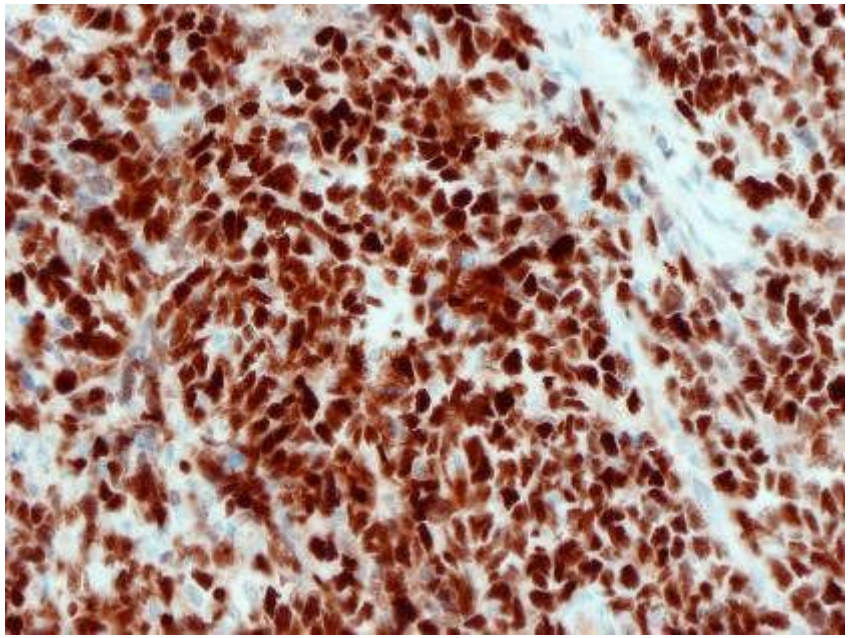
Haematologica 2009; 94:1555-1562. doi:10.3324/haematol.2009.010264

Most MCL are positive including the cases of cyclin D1 negative

(CycD1-,CD5+, Sox11+)

Other “Low grade“ lymphomas are negative

Some Burkitt lymphoma, lymphoblastic lymphomas and T-prolylmphocytic leukemias are postive



SOX11

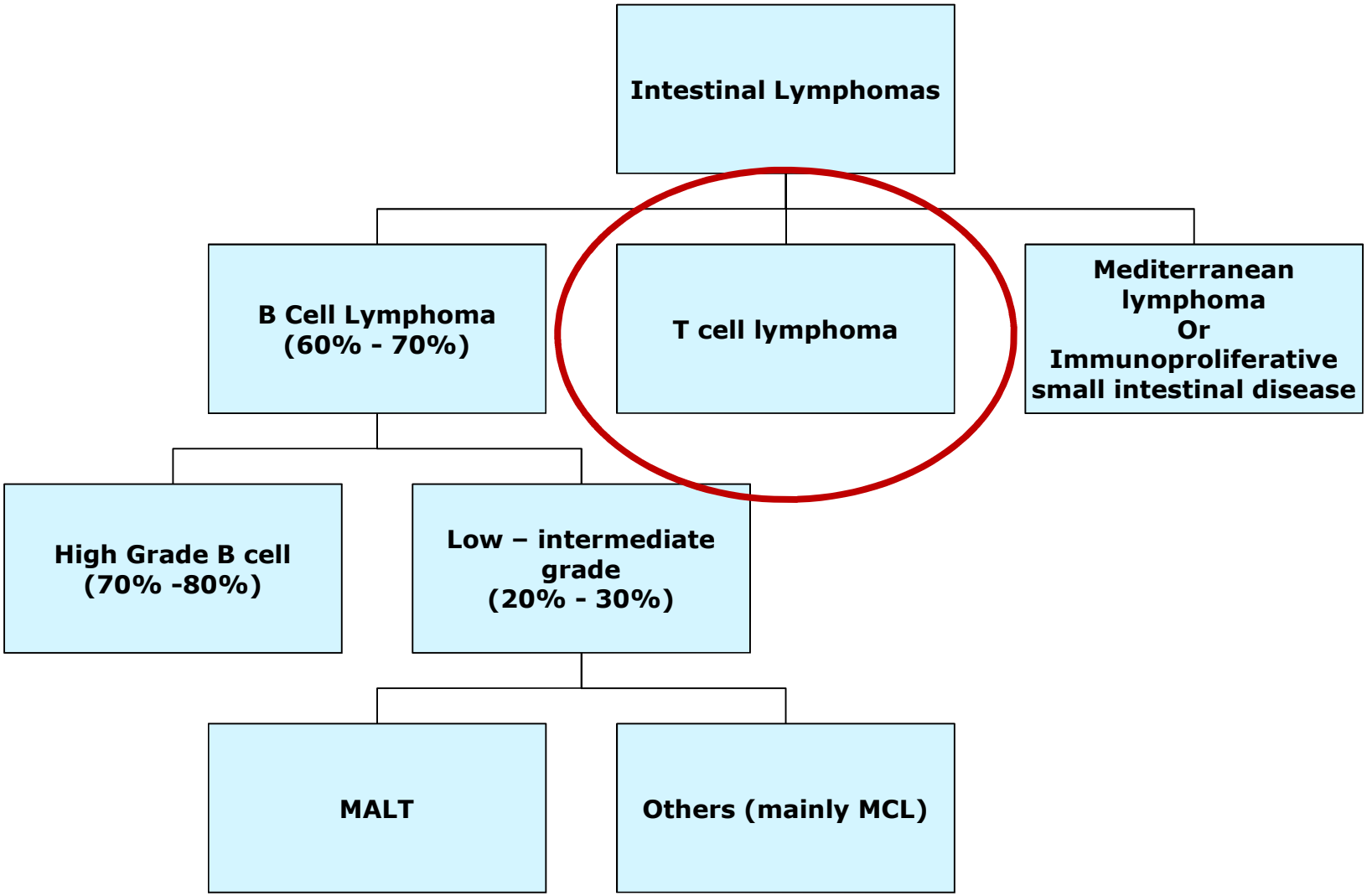
CCND2 rearrangements are the most frequent genetic events in cyclin D1^{-} mantle cell lymphoma

BLOOD, 21 FEBRUARY 2013 • VOLUME 121, NUMBER 8

- 40 cases of cyclin D1 neg MCL
- SOX 11 was positive in all cases
- 55% CCND2 translocation was found
- No alterations were found in CCND3

Table 1. Genetic, morphologic, and immunophenotypical parameters of 40 cyclin D1^{-}/SOX11^{+} MCL patients

Parameter	n	%
***CCND2* translocation**		
IGH-CCND2	3/40	8
IGK-CCND2	10/40	25
IGL-CCND2	5/40	13
CCND2-break*	2/40	5
CCND2-?†	2/40	5
Negative	18/40	45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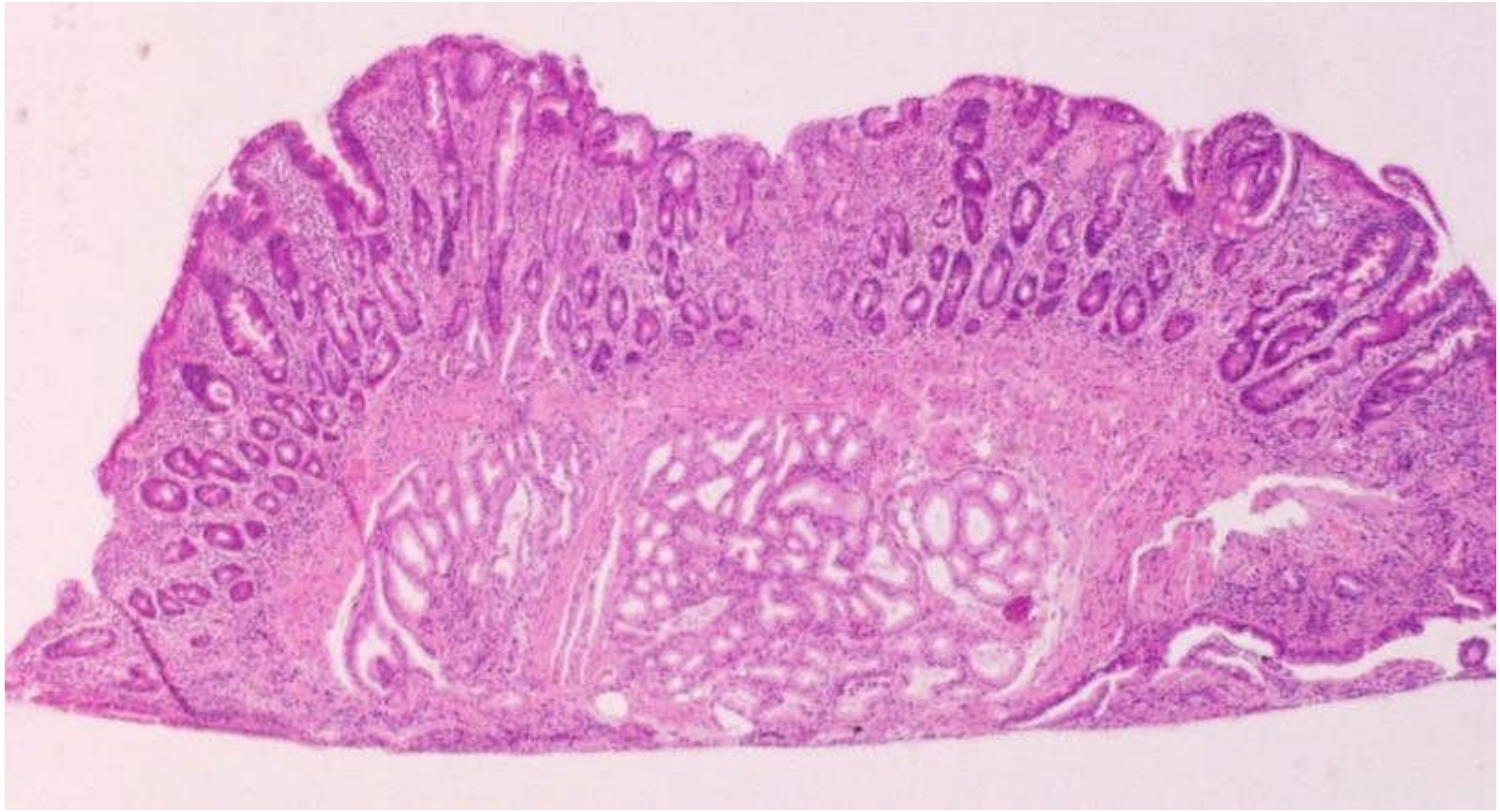
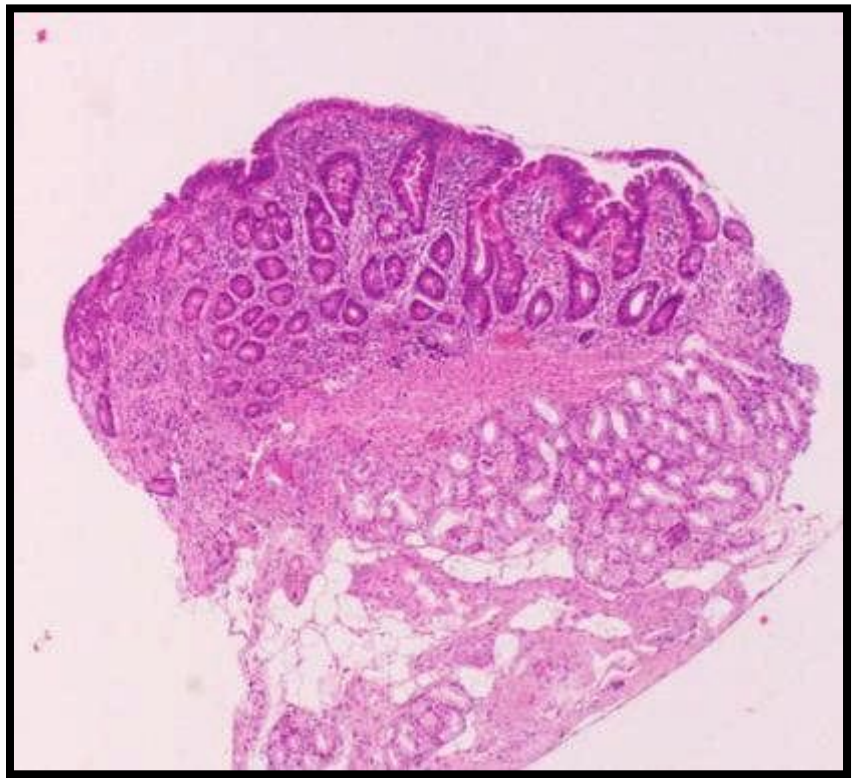
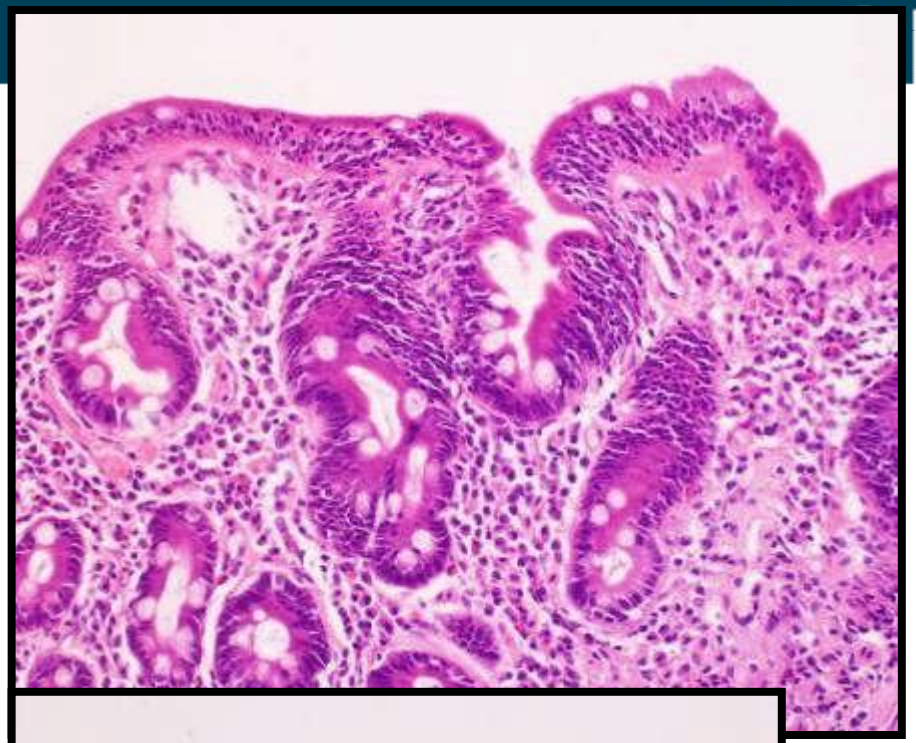
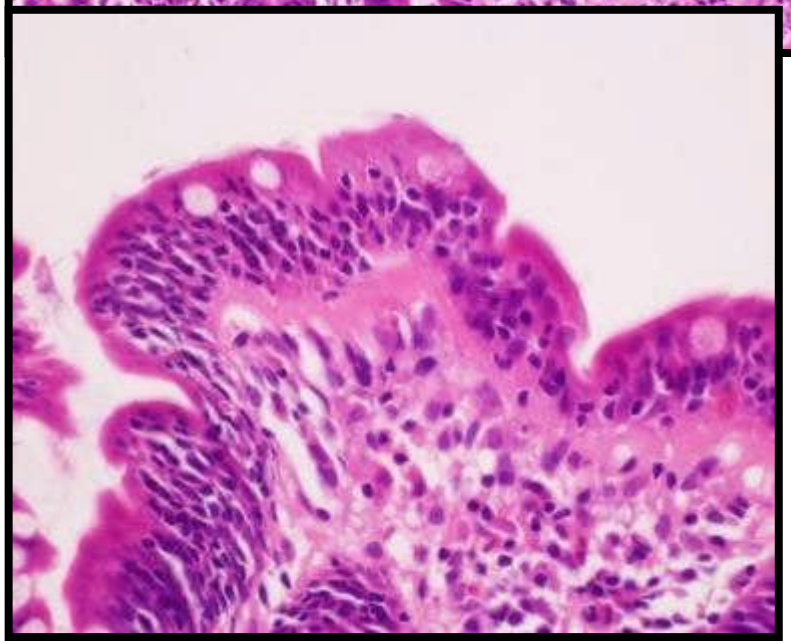
MALT
Others (mainly MCL)

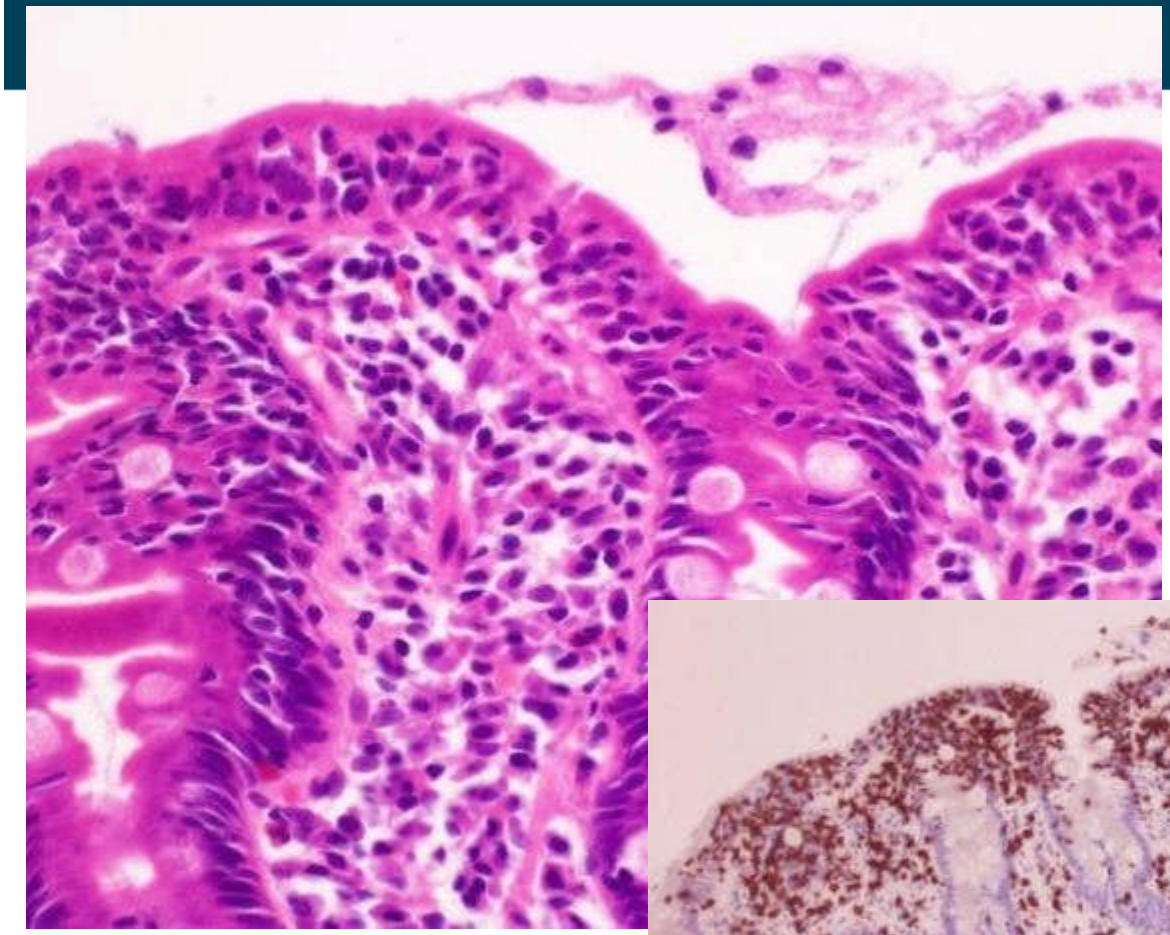
- Rare (only 5% of all GI lymphomas)
- Marked geographic variation in incidence: higher in Northern Europe. Same genetic background that predisposes to Coeliac (Similar HLA haplotypes)
- Proximal jejunum the most frequent site
- Most frequently short history of malabsorption
- Less frequently long history of Coeliac
- Obstruction & perforation (50% -30%)



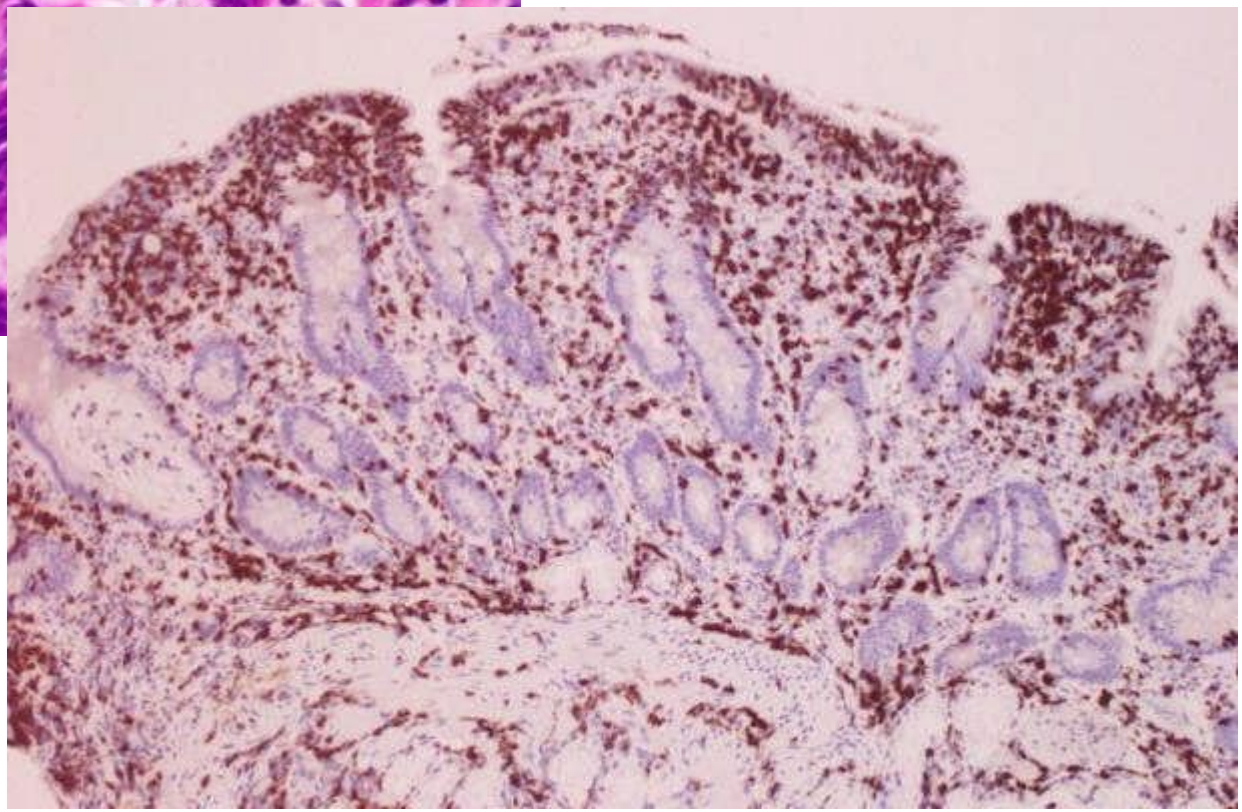


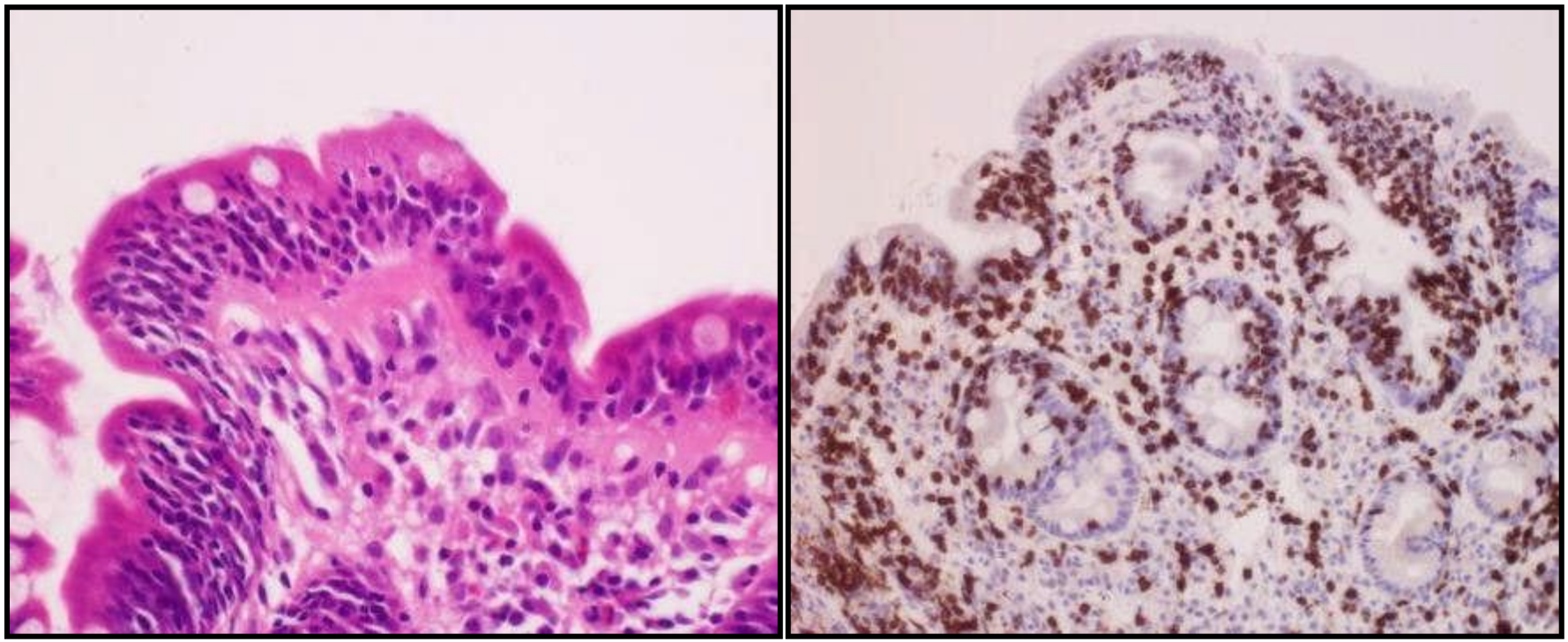




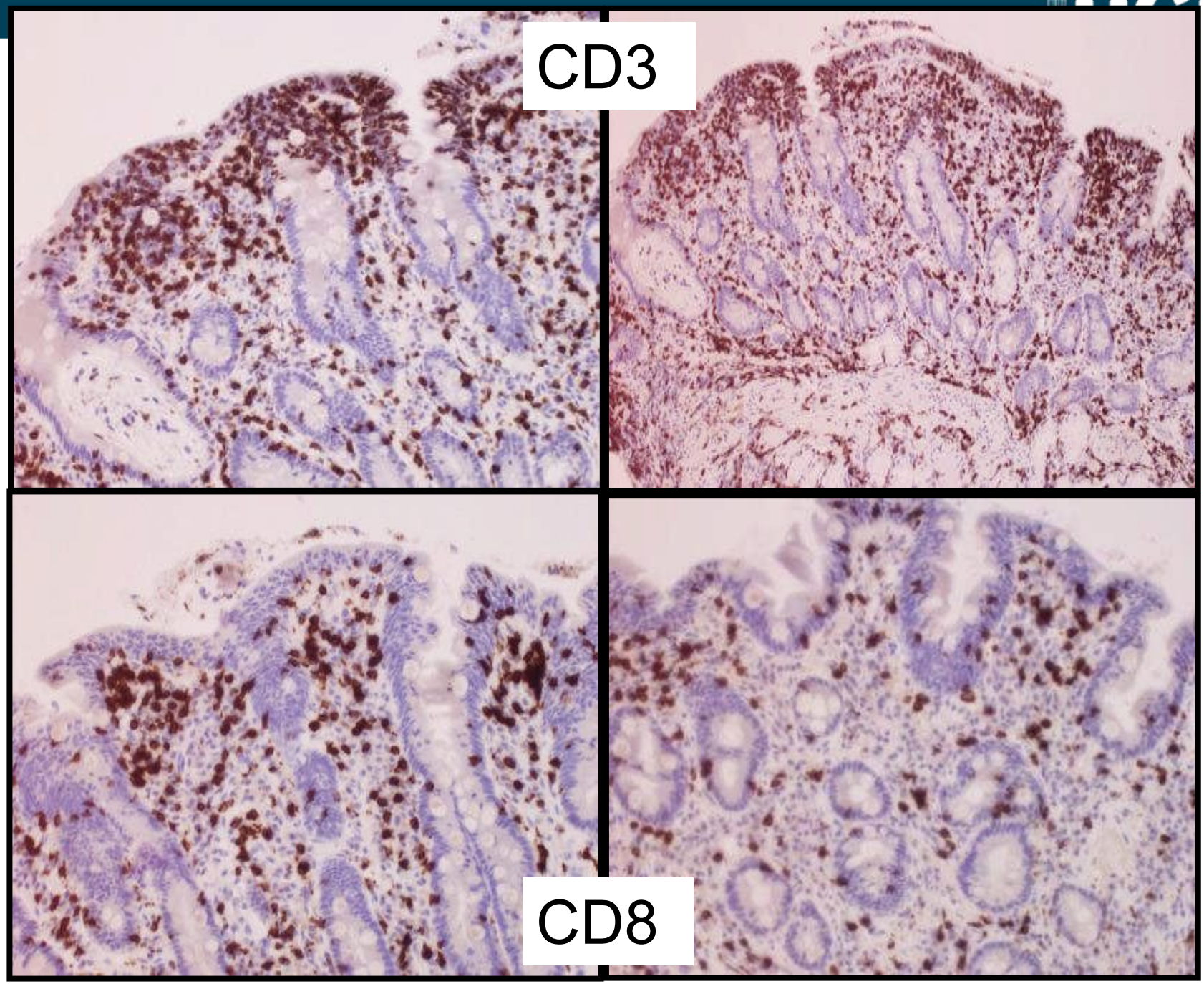


CD3





CD3


CD3
CD8

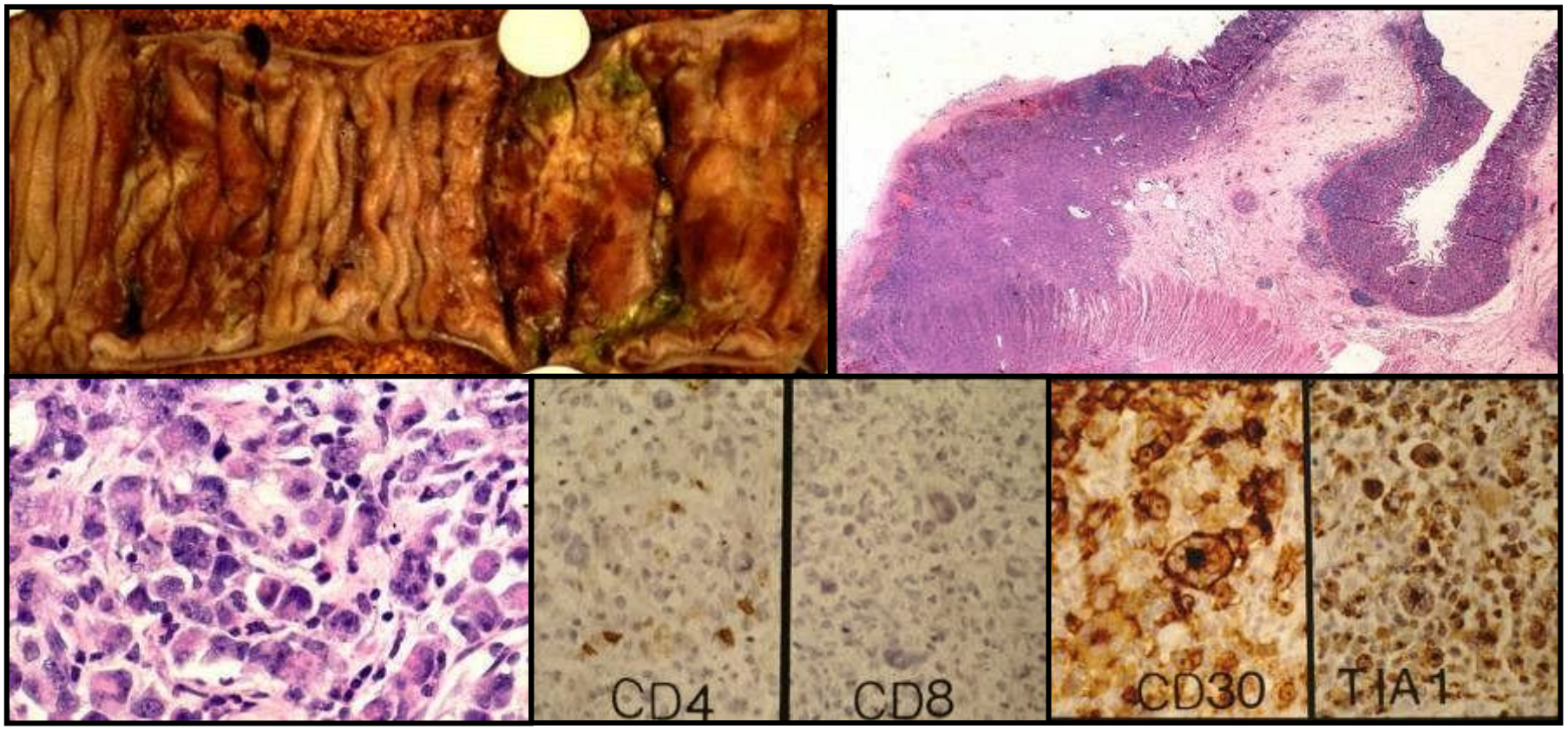
Disease	Histology	IHC / Molecular
CD	↑IELs, Crypt hyperplasia, Villous atrophy, ↑ inflammatory cells LP	IELs: CD3+, CD7+, CD8+ Polyclonal IELs
RCD	Same as CD and: Subcryptal inflammation, mucosal thinning…	IELs: CD3+, CD7+, CD8-, CD4- Monoclonal IELs
EATCL	Medium-sized cells, angular nuclei, nucleoli, occasional anaplastic cells…	CD3+, cytotoxic markers+, CD30(+, anaplastic cells) Monoclonal

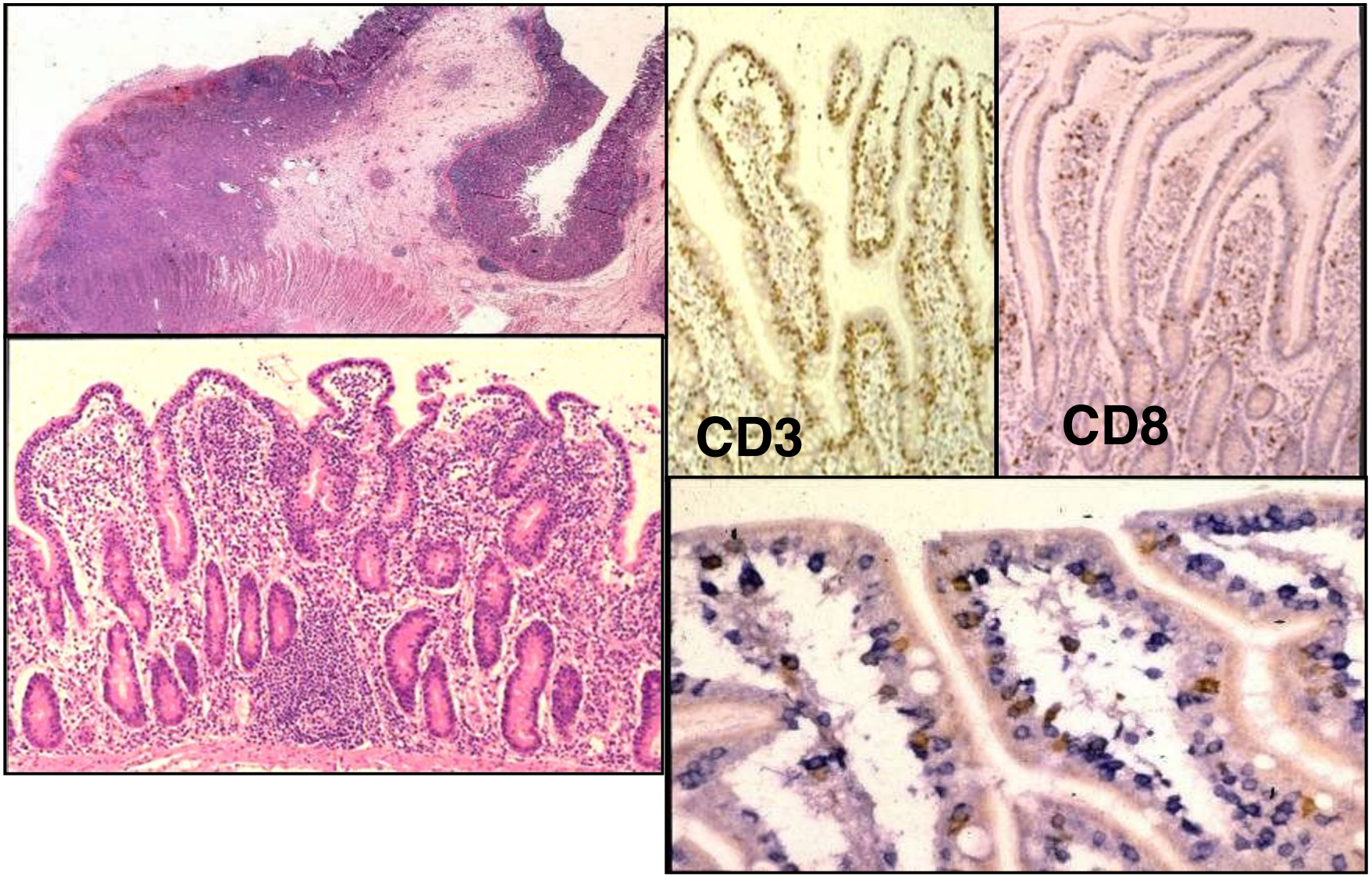
Adapted from Histopathology 2009,54:783-95

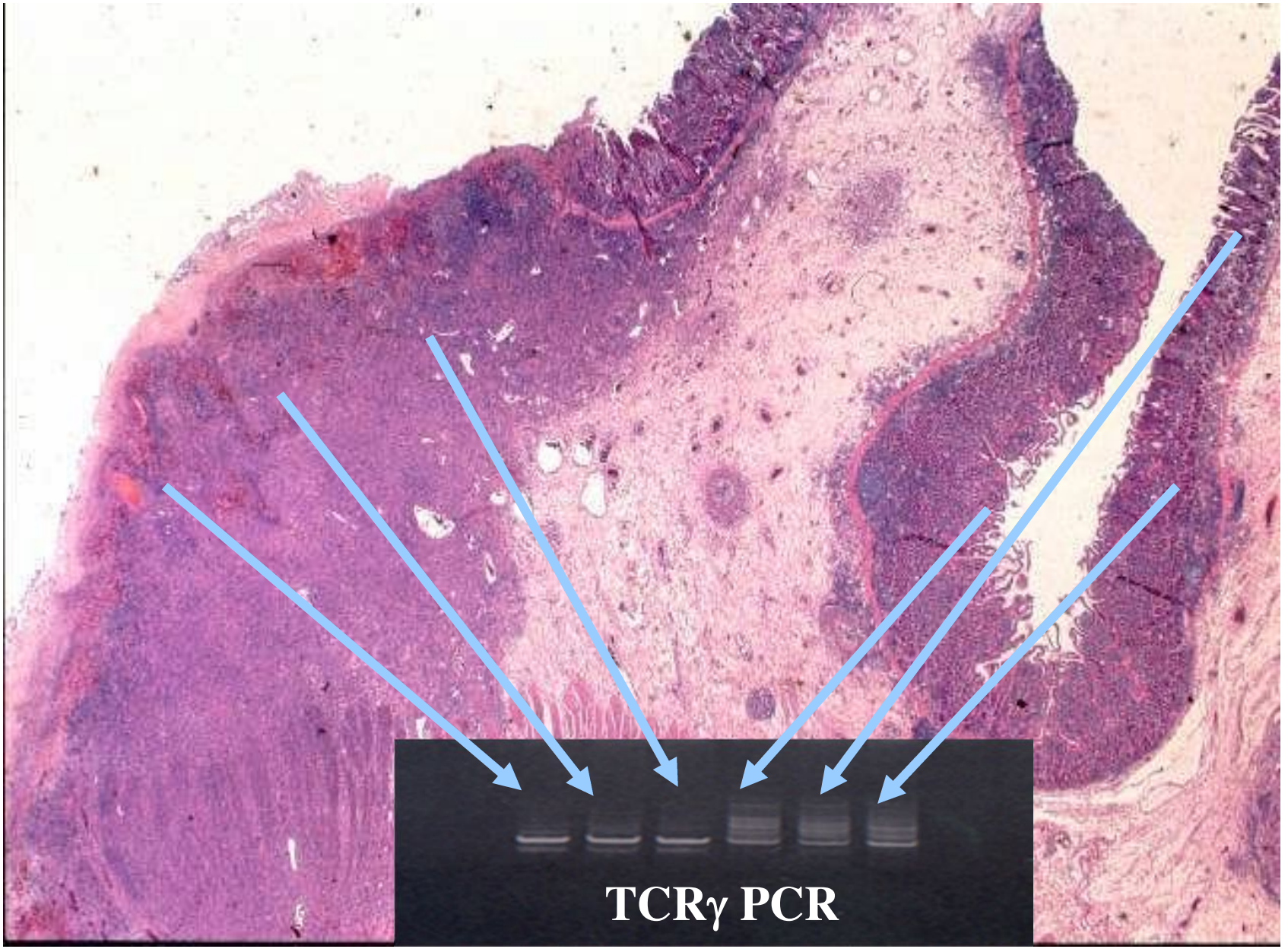
Enteropathy Associated T-cell lymphoma EATL

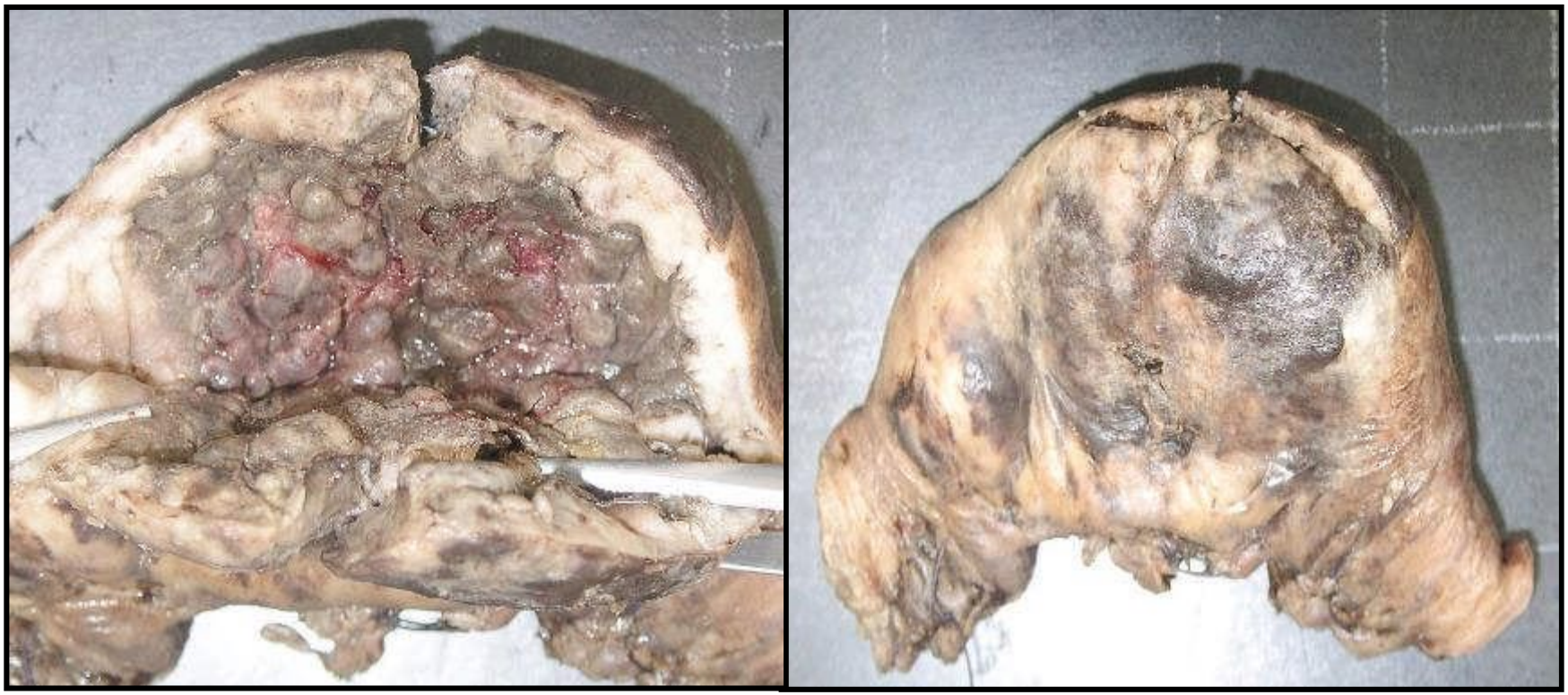
Classical (Type I)

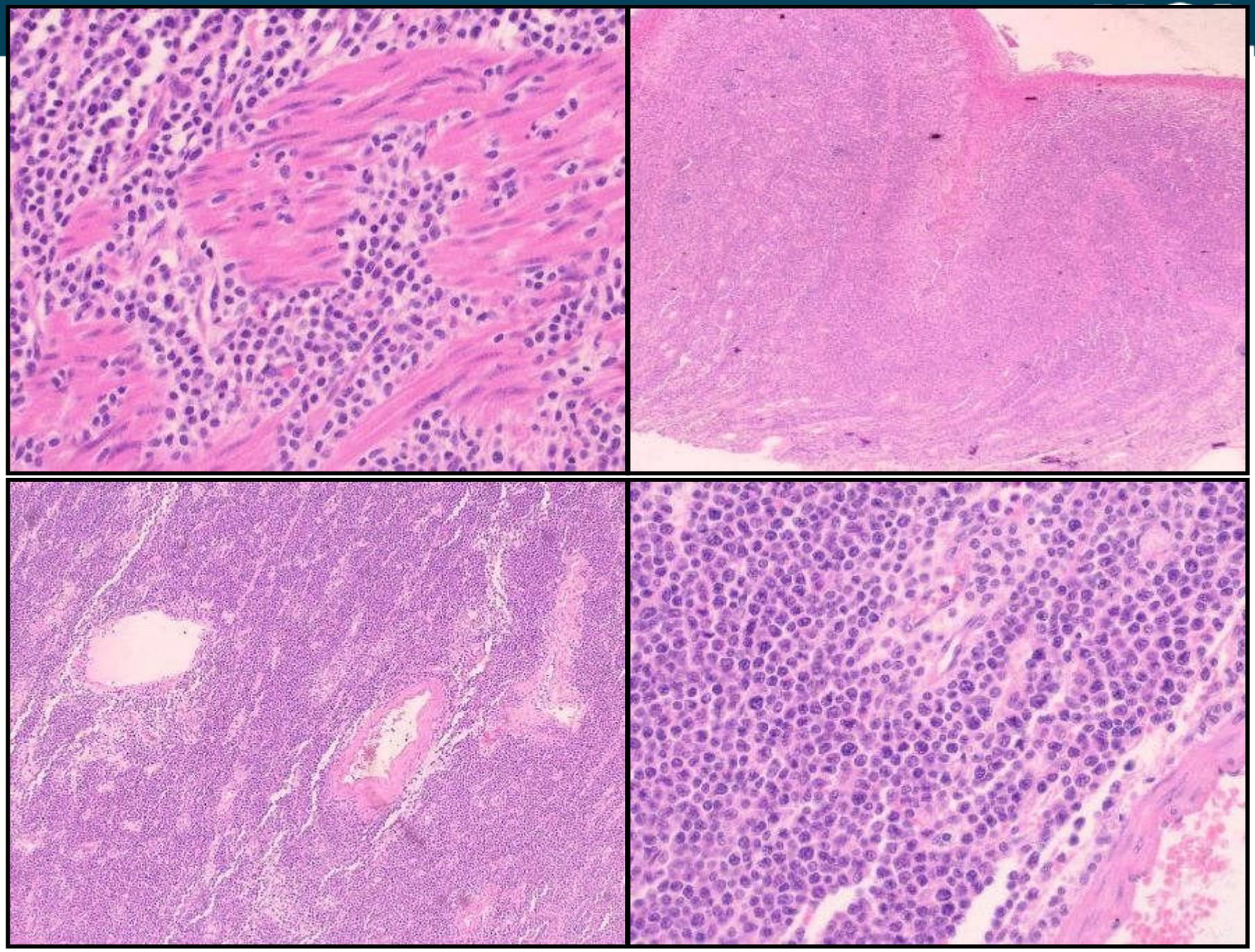
- Large lymphoid cells $CD3^+$, $CD7^+$, $CD5^-$, $CD8^-$ (20% +ve), $CD4^-$, $CD103^+$, cytotoxic granules-associated proteins and some are $CD30^+$
- Closely linked to celiac disease, northern European origin

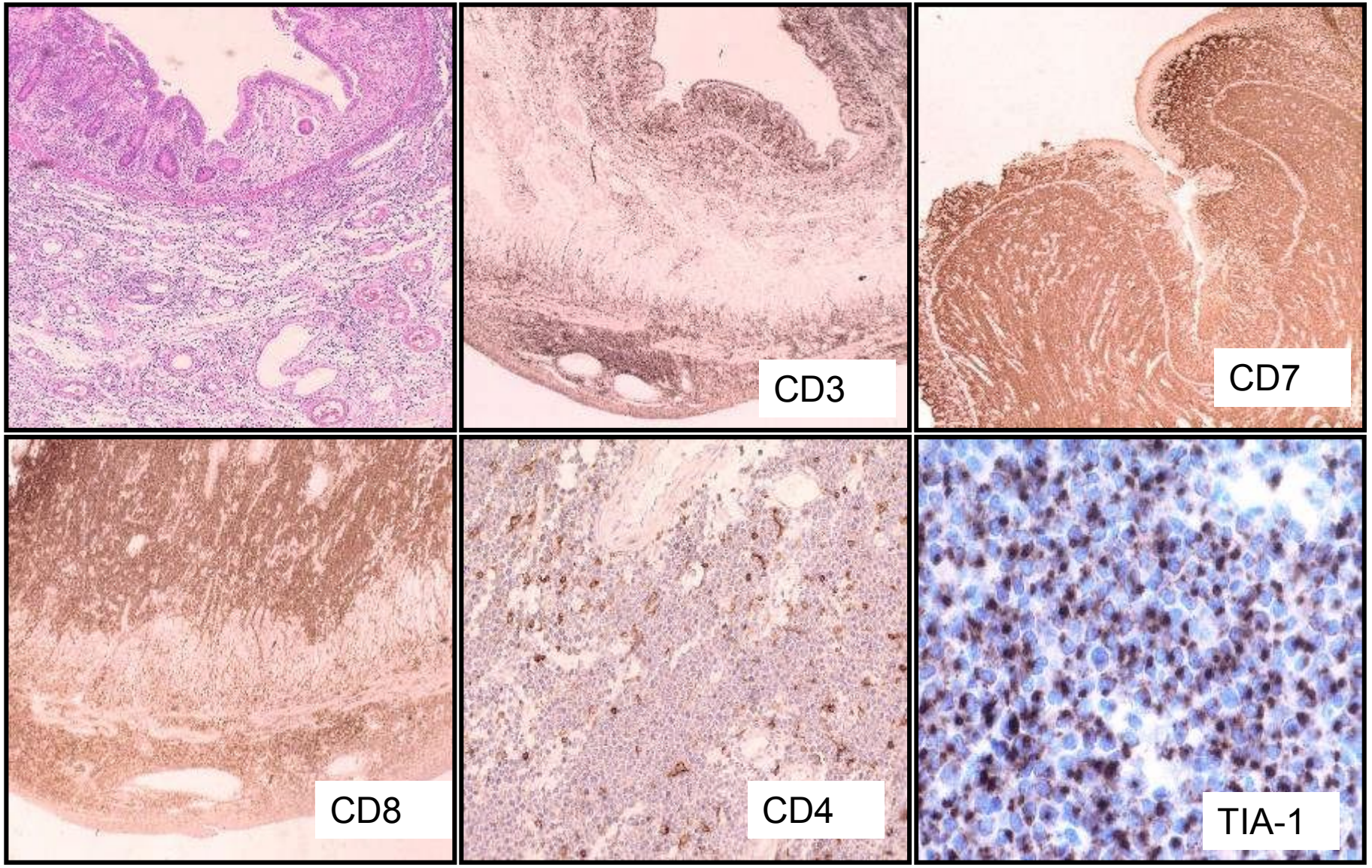



CD3
CD8
CD8/CD3


TCRγ PCR



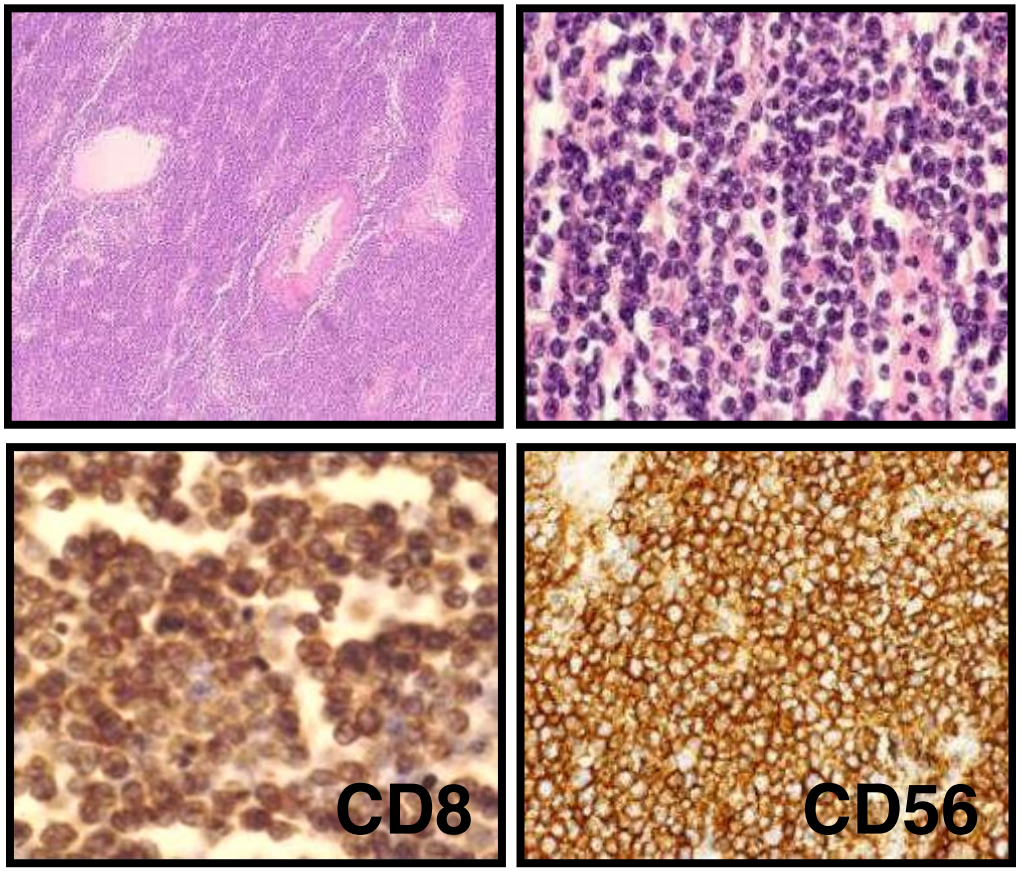



CD3
CD7
CD8
CD4
TIA-1

EATL type II (WHO 2008) – monomorphic (10-20%)

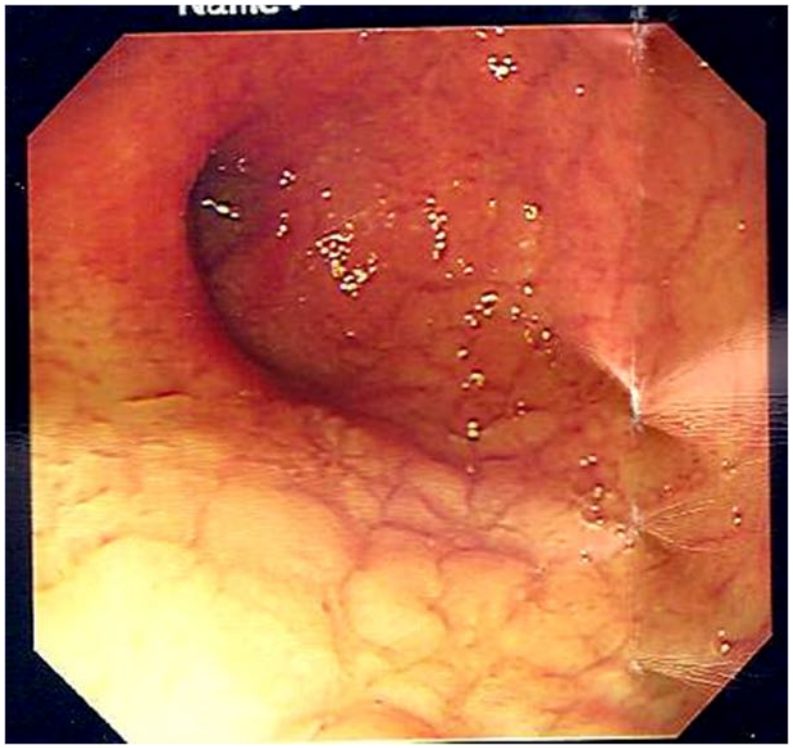
- **MONOMORPHIC EPITHELIOTROPIC INTESTINAL T-CELL LYMPHOMA (MEITL)** (WHO update 2016)

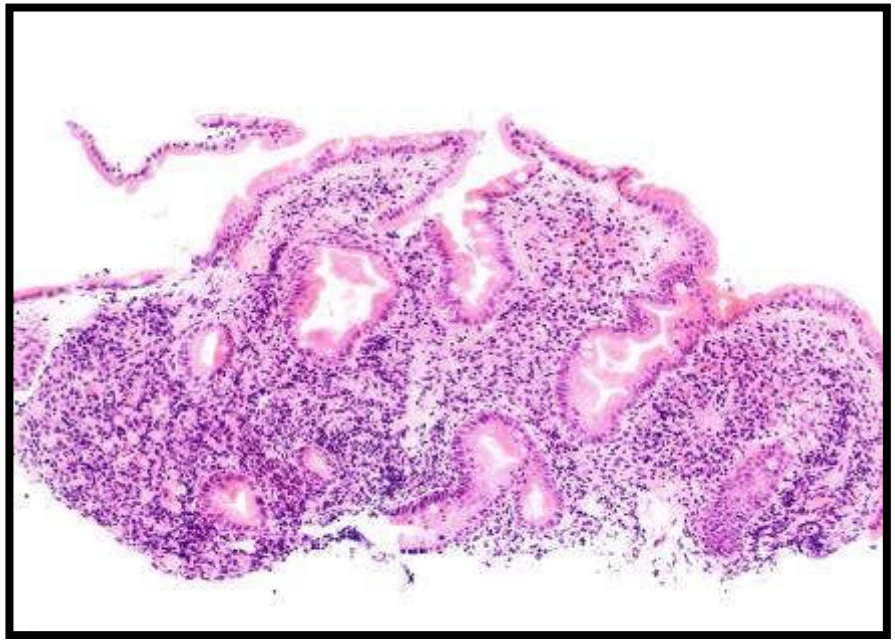
- No association with celiac disease
- Asians, and Hispanic
- Monomorphic, and usually positive for CD8, CD56, and MAPK
- Gains in chromosome 8q24 involving MYC
- From γδ T-cells

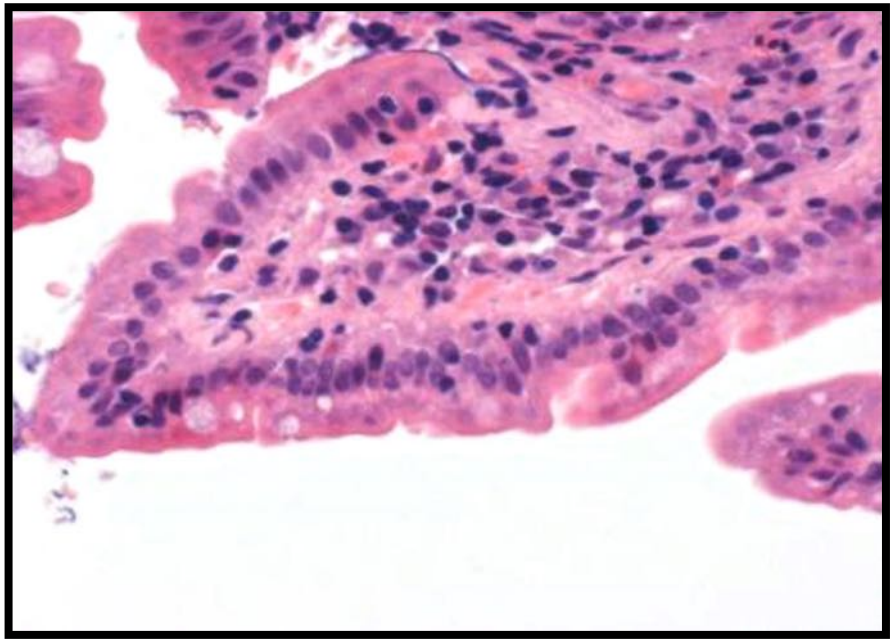


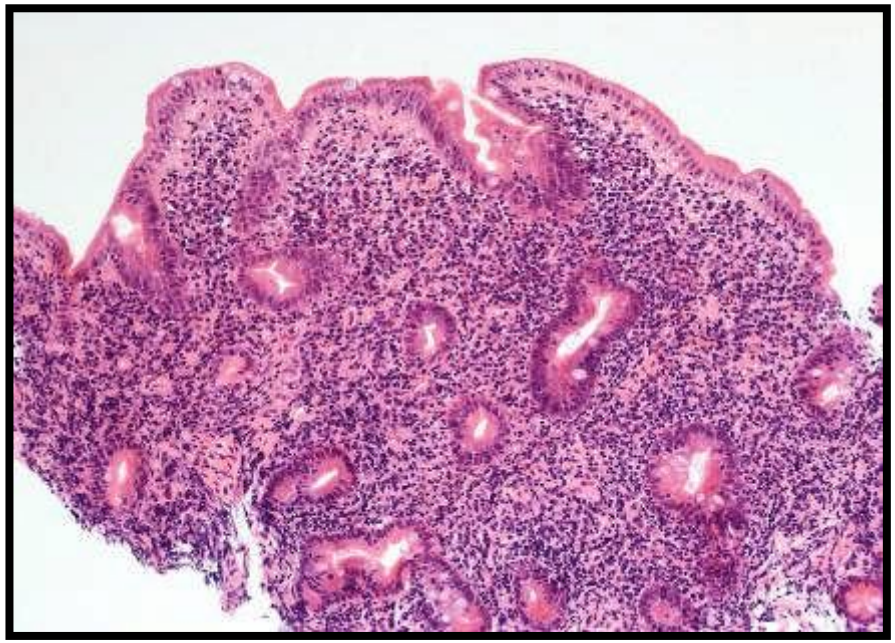
63 Years Old Irish Female

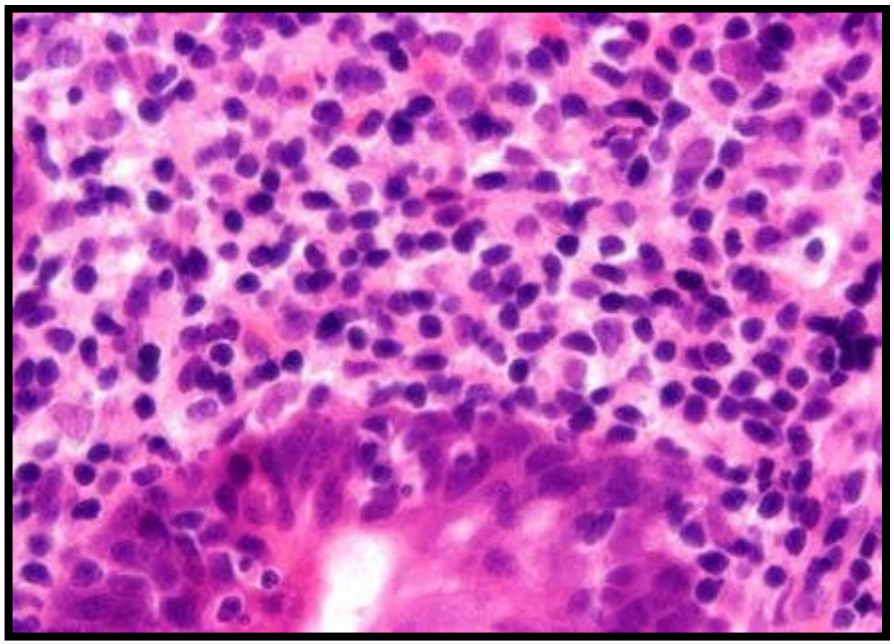
- **Refractory coeliac disease**
- **Cobblestone duodenal mucosa**
- **Duodenal diverticulum**

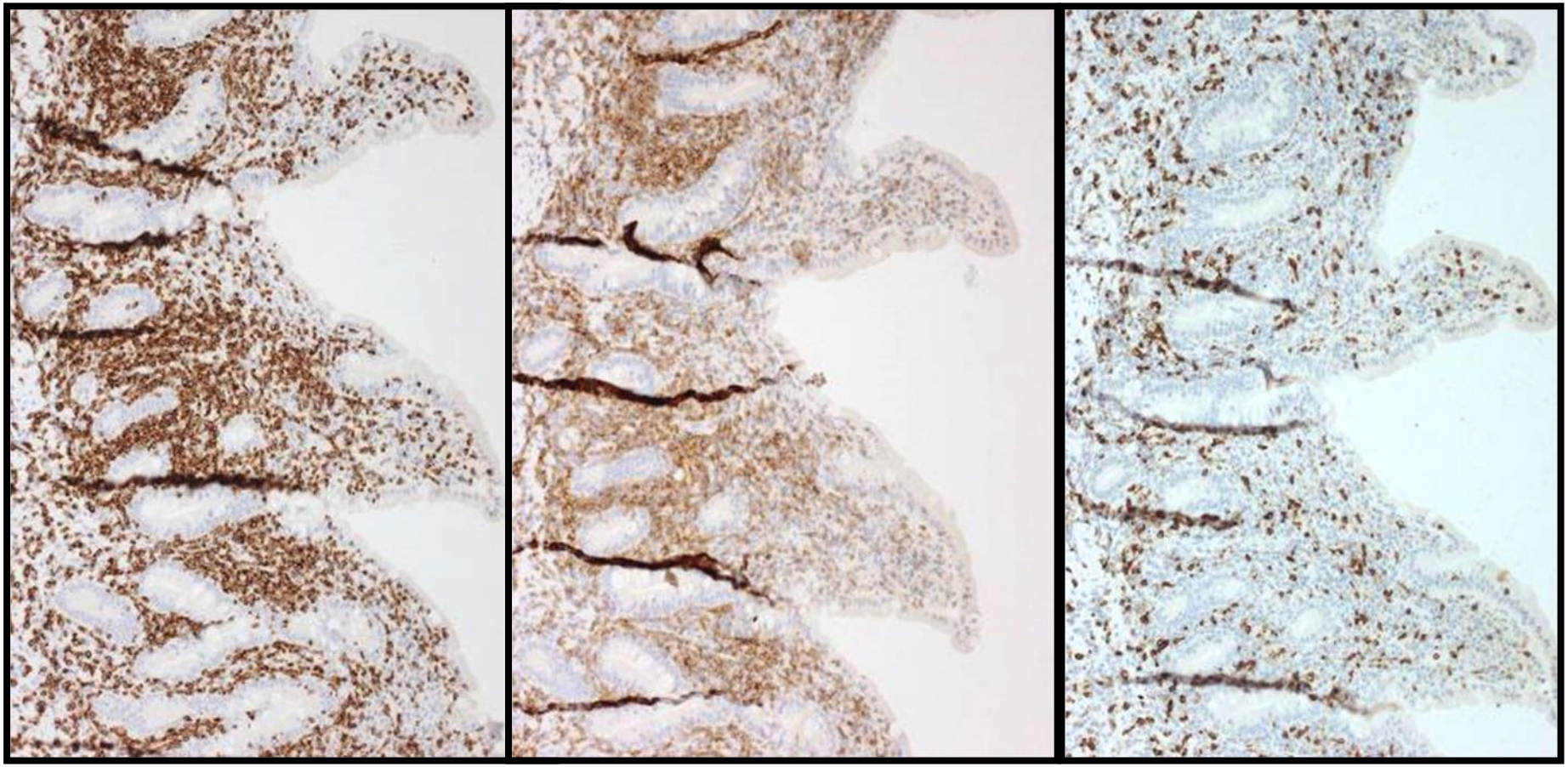




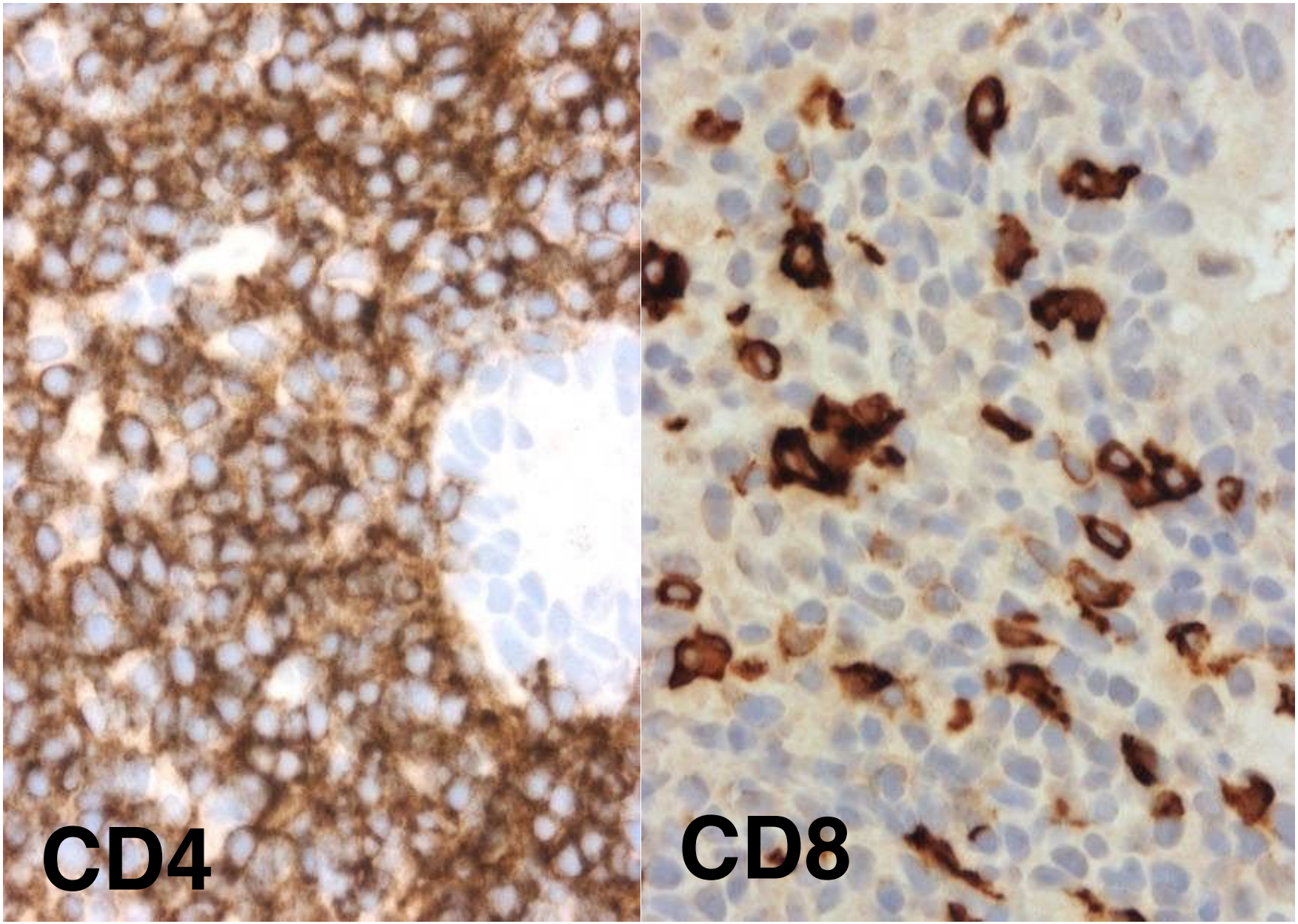


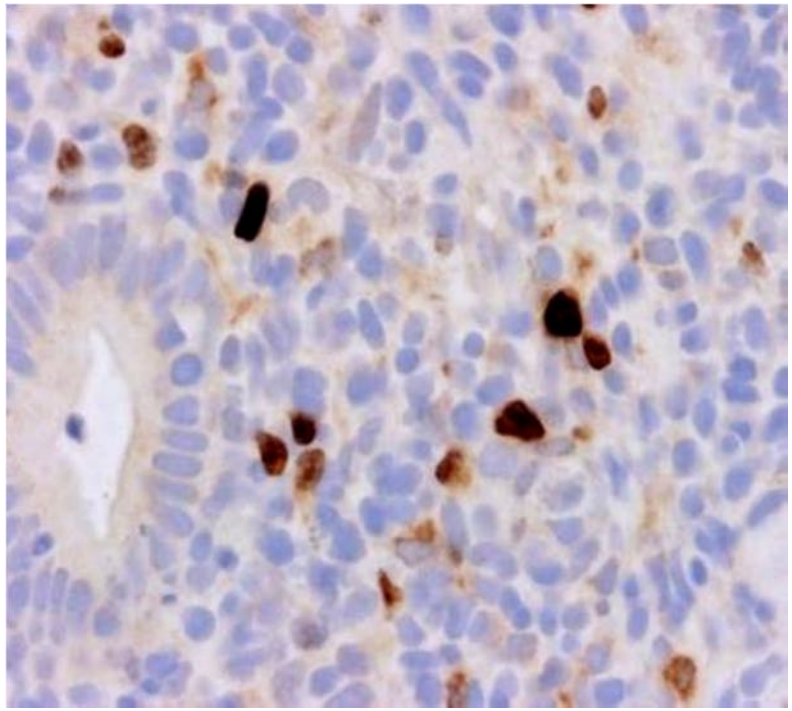




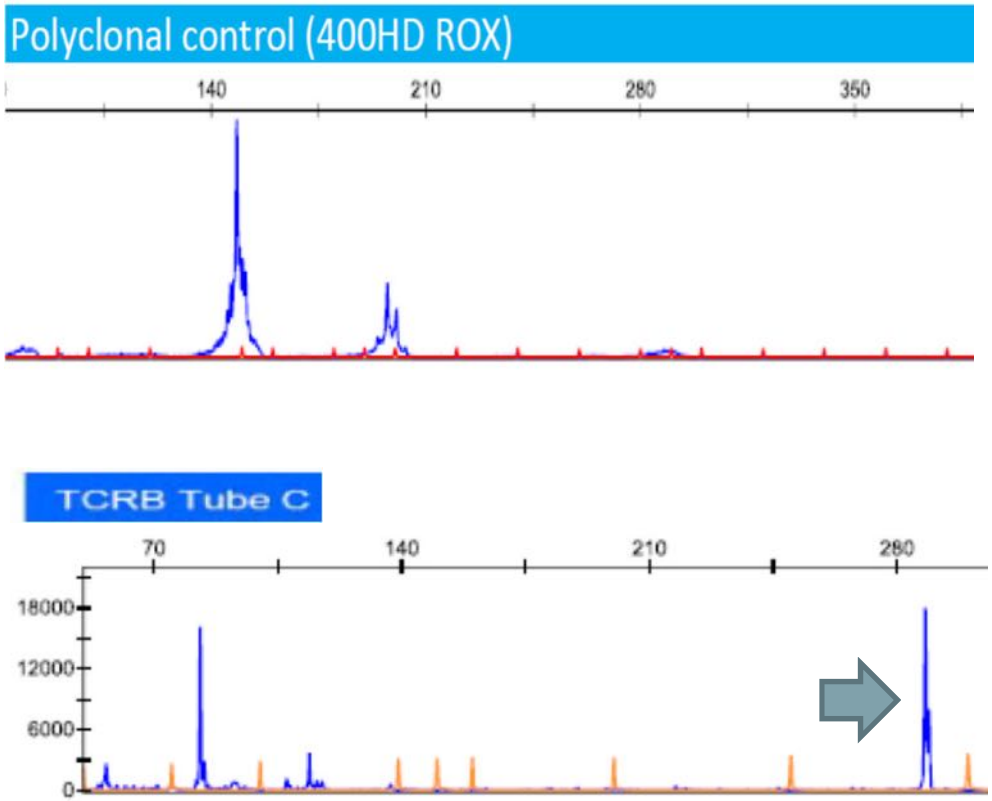


CD3 CD4 CD8


CD4
CD8



Ki-67


Polyclonal control (400HD ROX)
140
210
280
350
TCRB Tube C
70
140
210
280
18000
12000
6000
0

Gut 1999;**45**:662–667

The clinicopathological features of extensive small intestinal CD4 T cell infiltration

F Carbonnel, H d'Almagne, A Lavergne, C Matuchansky, J C Brouet, F Sigaux, L Beaugerie, J Nemeth, B Coffin, J Cosnes, J P Gendre, J C Rambaud

Small intestinal CD4+ T-cell lymphoma: a rare distinctive clinicopathological entity associated with prolonged survival

Magali Svrcek · Laurent Garderet · Virginie Sebbagh · Michelle Rosenzwajg · Yann Parc · Monique Lagrange · Malika Bennis · Anne Lavergne-Slove · Jean-François Fléjou · Bettina Fabiani

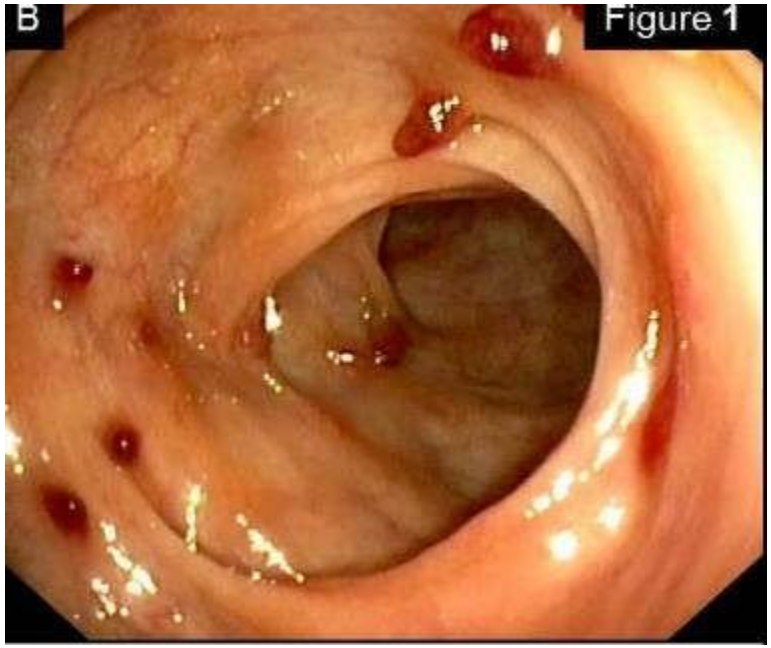
Virchows Arch (2007) 451:1091–1093

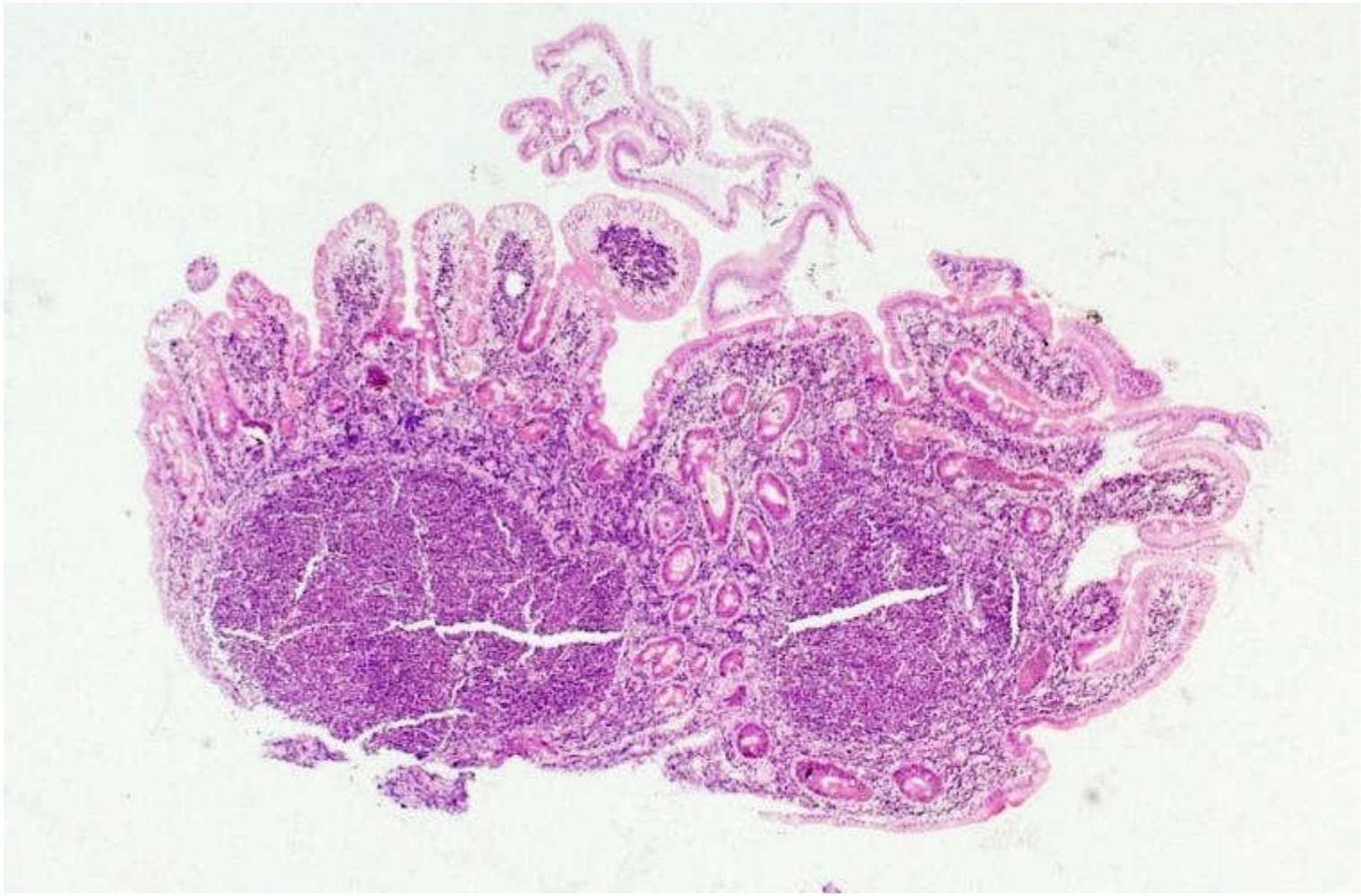
LYMPHOID NEOPLASIA

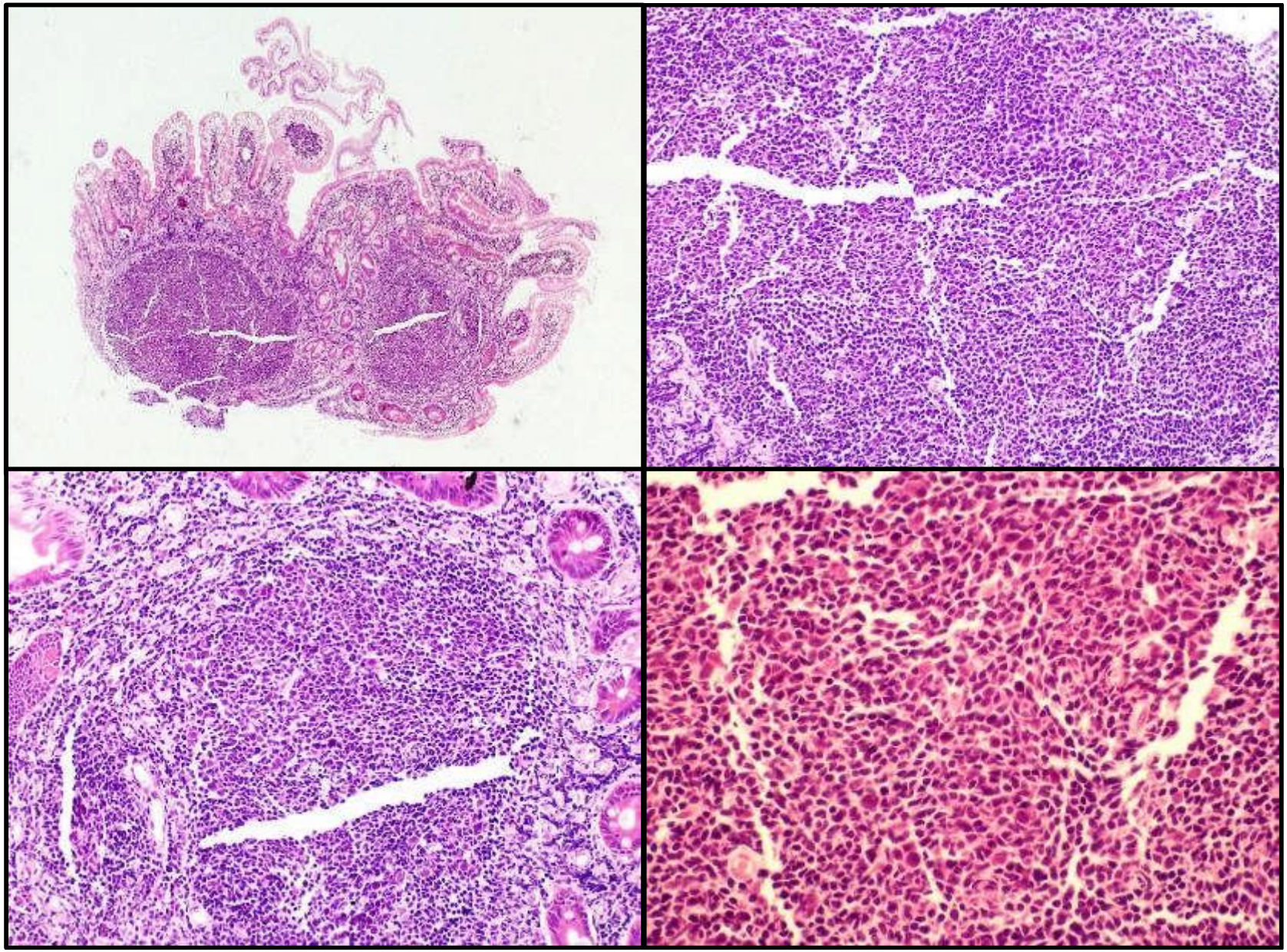
Indolent T-cell lymphoproliferative disease of the gastrointestinal tract

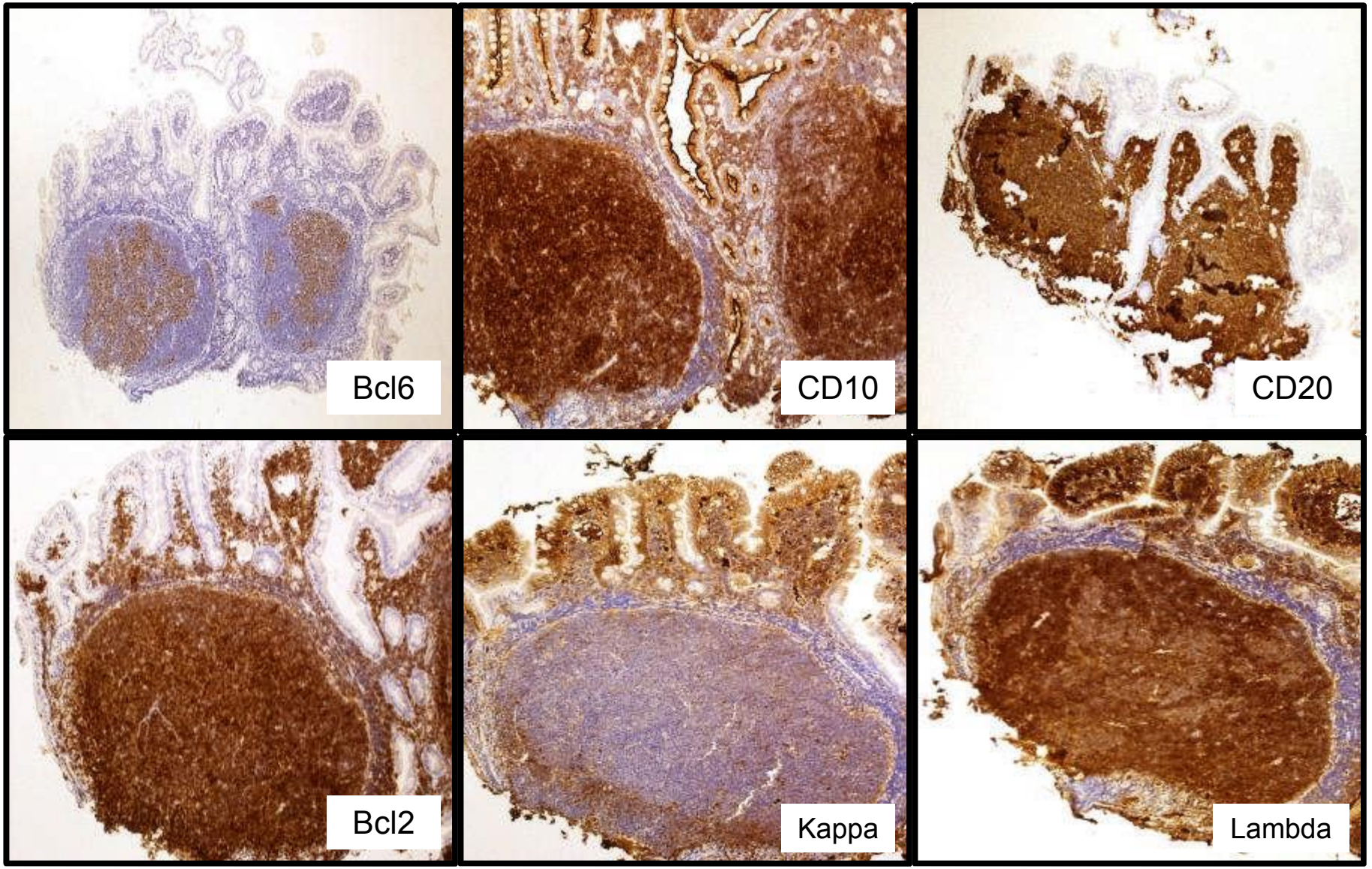
BLOOD, 21 NOVEMBER 2013 • VOLUME 122, NUMBER 22

- Very low proliferation rate
- No destruction of the glands
- No cytological atypia
- Very bland infiltrate
- Superficial infiltrate confined to mucosa. No invasion of the wall
- Multiple mucosal polyps
- Can affect entire GI Tract (most common small intestine and colon)








Bcl6
CD10
CD20
Bcl2
Kappa
Lambda

GI tract follicular lymphoma

Original article

Annals of Oncology 14: 623–629, 2003
DOI: 10.1093/annonc/mdg168

Primary follicular lymphoma of the gastrointestinal tract: a study of 25 cases and a literature review

G. Damaj[1]*, V. Verkarre[1], A. Delmer[2], P. Solal-Celigny[3], I. Yakoub-Agha[5], C. Cellier[4], F. Maurschhauser[5], R. Bouabdallah[6], V. Leblond[7], F. Lefrère[1], D. Bouscary[8], J. Audouin[2], B. Coiffier[9], B. Varet[1], T. Molina[2], N. Brousse[1] & O. Hermine[1]
On behalf of the Groupe d'Etude des Lymphomes de l'Adulte

Primary Follicular Lymphoma of the Gastrointestinal Tract

A Clinical and Pathologic Study of 26 Cases

Jinru Shia, M.D., Julie Teruya-Feldstein, M.D., Dorothy Pan, M.D., Abhijith Hegde, M.D., David S. Klimstra, M.D., R. S. K. Chaganti, Ph.D., Jing Qin, Ph.D., Carol S. Portlock, M.D., and Daniel A. Filippa, M.D.

The American Journal of Surgical Pathology *26(2): 216–224, 2002*

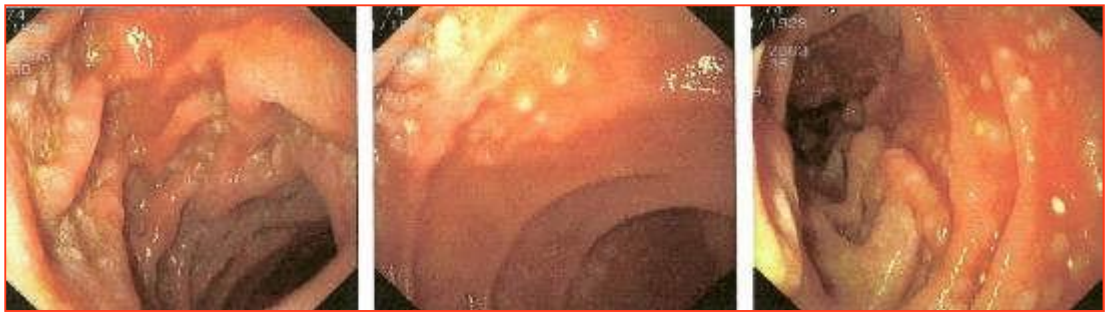
Gastrointestinal tract FL (variant of FL)

- Frequently in the duodenum (2nd portion)
- Usually presenting as multiple polyps, incidental finding on endoscopy
- Morphology, immunophenotype and genetic features similar to those of nodal FL
- Most patient have localized disease and excellent prognosis even without treatment
- FL in GI tract may show lymphoepithelial lesions and can be mis-diagnosed as MALT lymphomas

Primary Follicular Lymphoma of the Duodenum Is a Distinct Mucosal/Submucosal Variant of Follicular Lymphoma: A Retrospective Study of 63 Cases

J Clin Oncol 29:1445-1451. © 2011 by American Society of Clinical Oncology

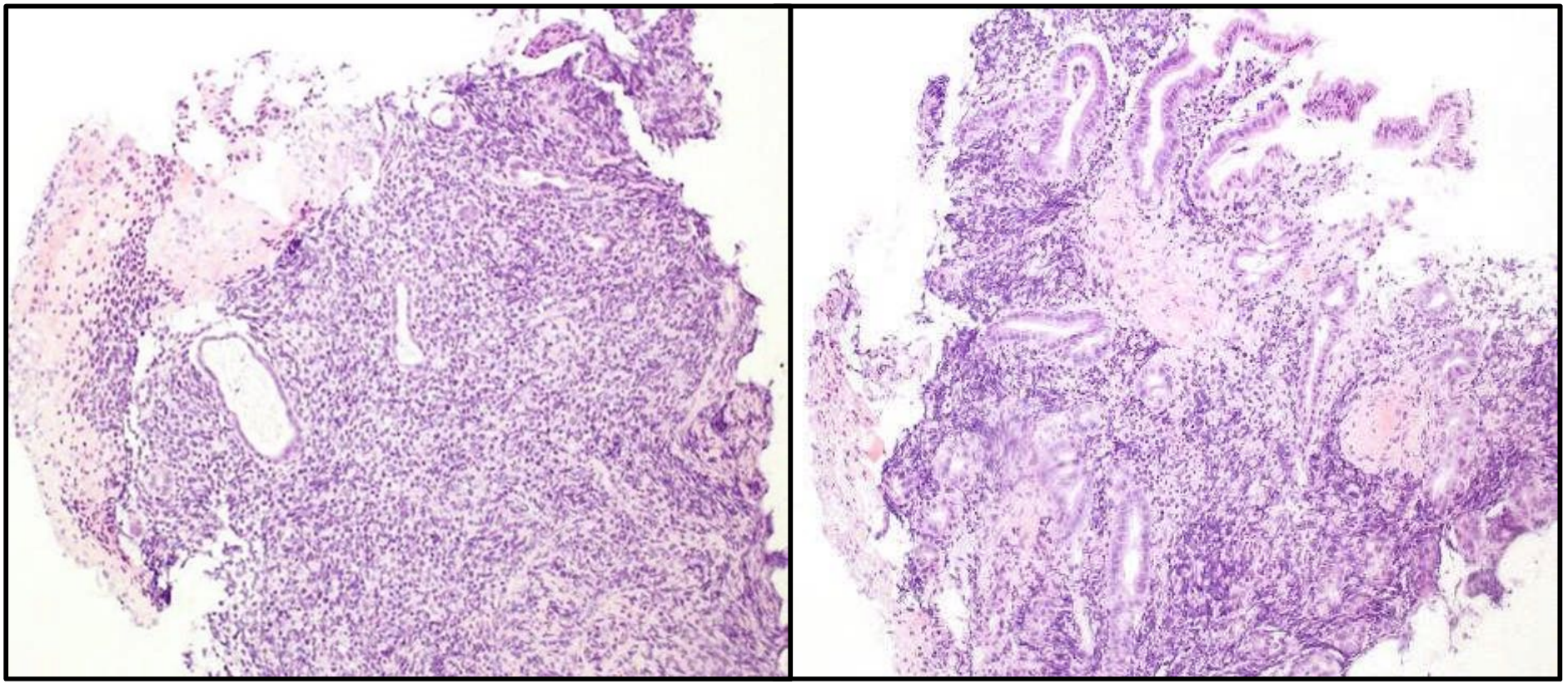
- 63 patients, all stage IE
- Uncharacteristic symptoms
- Usually multiple warty polyps along descending part of duodenum
- Limited to mucosa/submucosa in 19 of 20 cases
- No ulcerations, no obstructive lesions

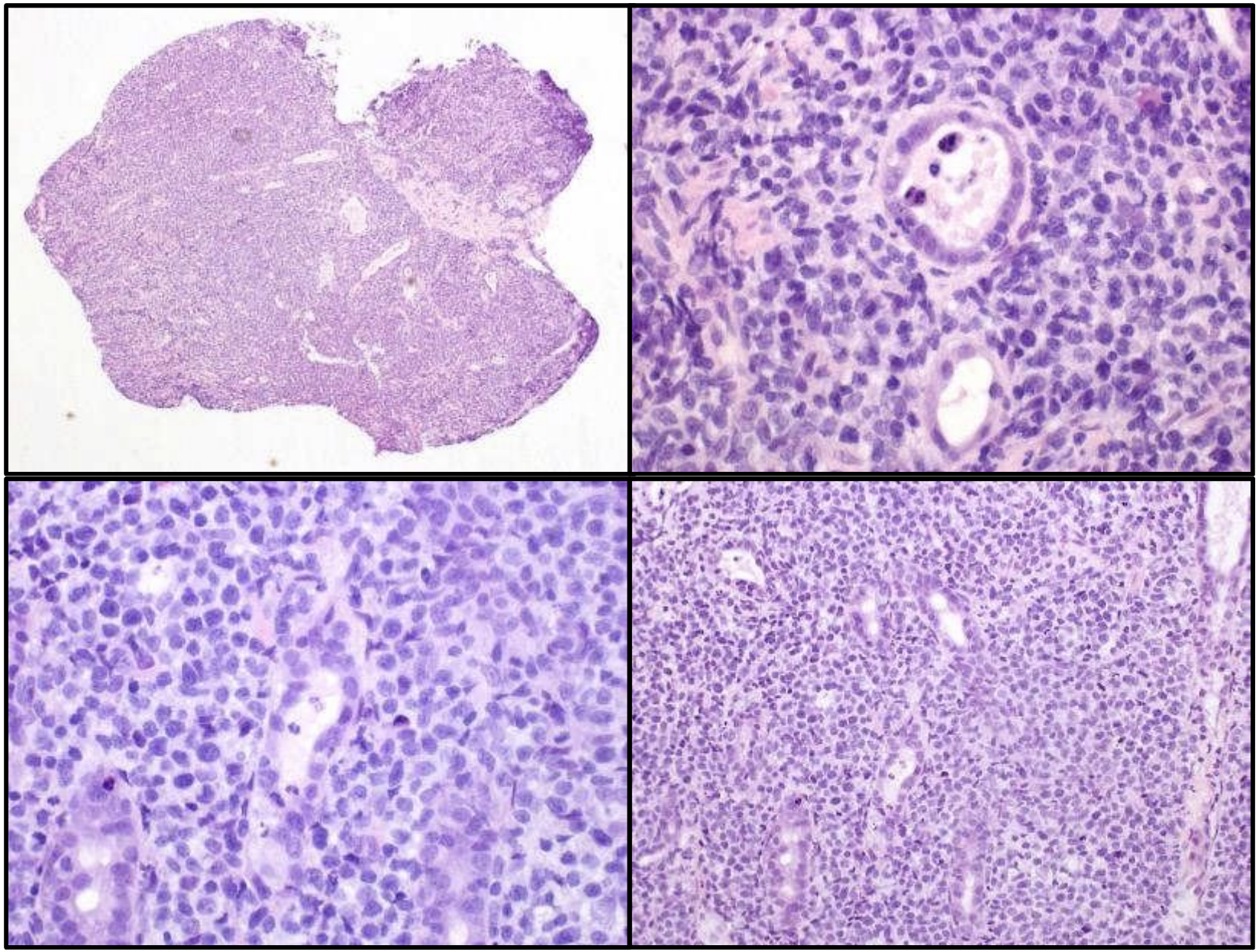


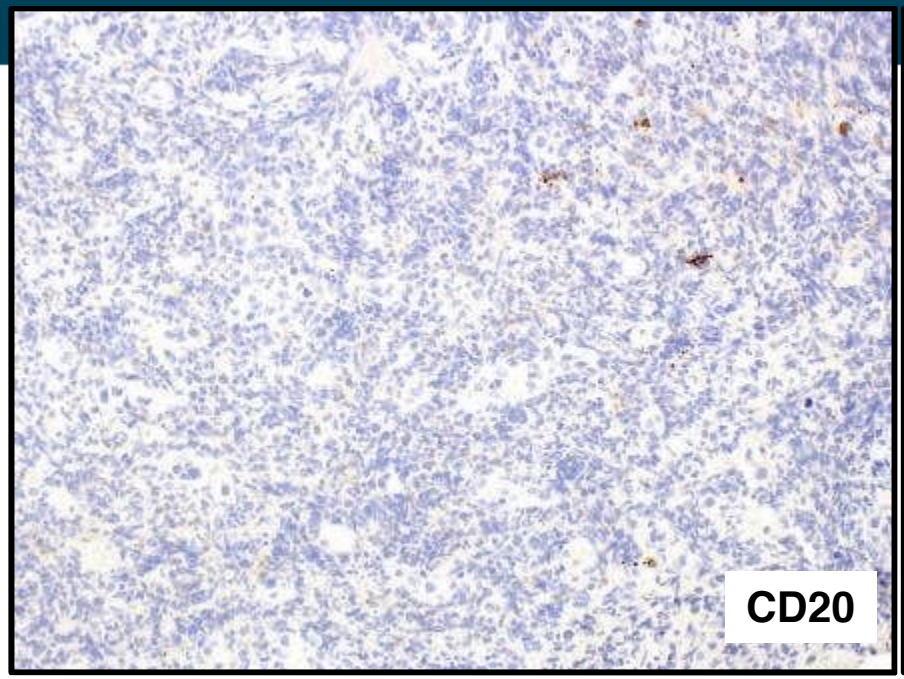
- Grade 1 in 60, Grade 2 in 3 cases
- Typical immunophenotype (bcl-2+, bcl-6+, CD10+, low Ki-67,..)
- t(14;18) by cytogenetics in 4/4 cases, no additional aberrations

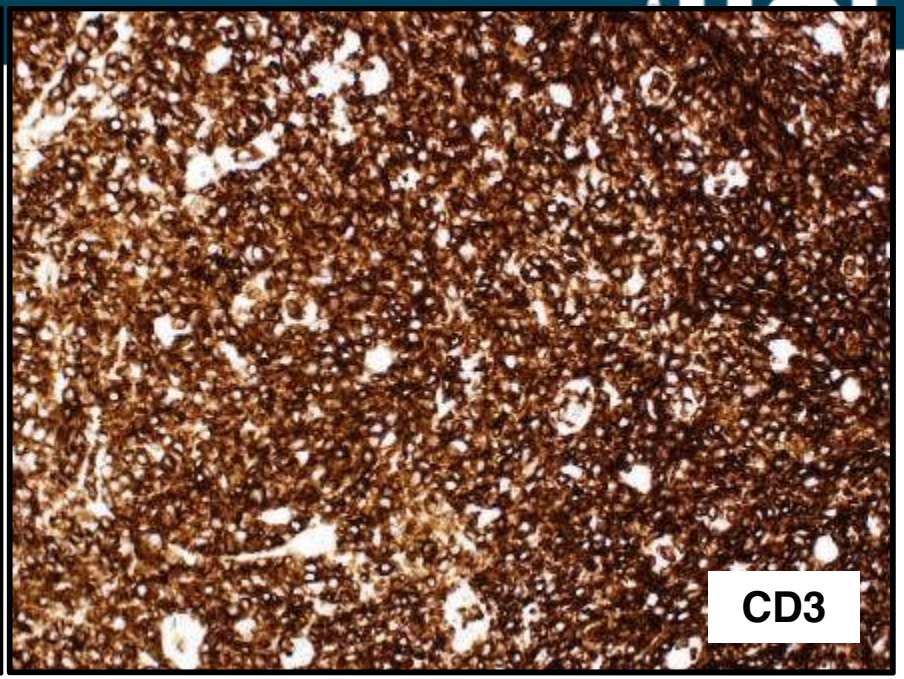
Duodenal-type Follicular lymphoma

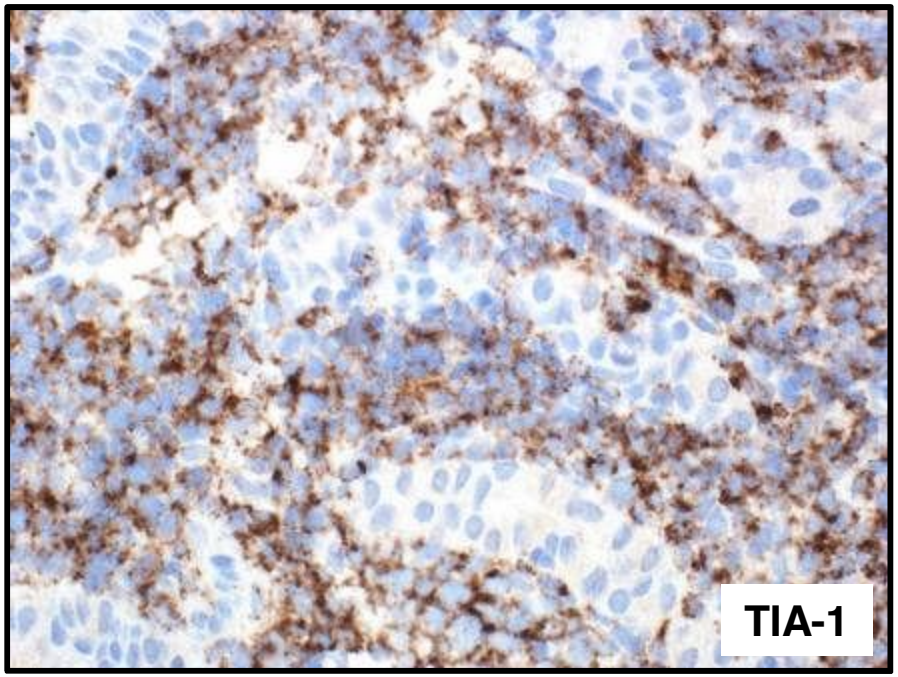
- localized overt low grade FL, is distinct from other GI tract FL
- Overlap with ISFN (in situ follicular neoplasm) and extranodal marginal zone lymphoma
- excellent outcome
- watch and wait strategy

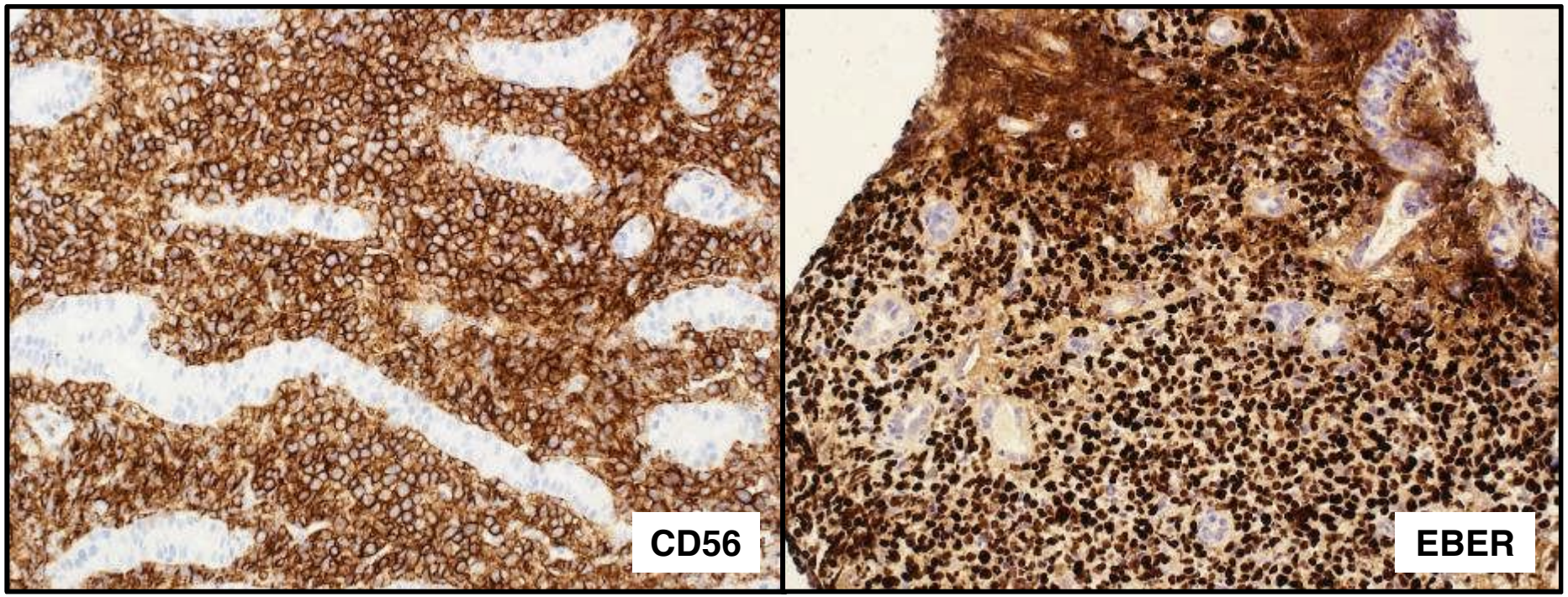





CD20


CD3


TIA-1


CD56
EBER

Extranodal NK/T cell lymphoma, nasal type

- Aerodigestive tract (nasal cavity, paranasal sinuses…)
- Extranasal involvement: GI tract, skin, testis
- Cytological spectrum and morphology very broad
- Highly aggressive, short survival, poor response to treatment.
- IHC: CD2(+), CD4 (-), CD8 (-), CD56 (+), cytotoxic markers (+), EBV (+)

	Classical EATL	EATL type II MEITL	NK	Indolent LPD
Morphology	Pleomorphic large cells	Monomorphic small cells	Monomorphic small cells	Monomorphic small cells
Phenotype	$CD3^+$ $CD4^-$ $CD8^-$	$CD3^+$ $CD8^+$ $CD56^+$	$CD3^{+/-}$, $CD4^-$, $CD8^-$, $CD56^+$	$CD3^+CD4^+$ or $CD8^+$
Genetics	TCR rearrangement	TCR rearrangement	TCR rearrangement	TCR rearrangement
Mucosa	Villous atrophy	Villous trophy	Villous atrophy in involved areas	Normal
IELs	Increased $CD4^-$ /$CD8^-$	Increased $CD8^+$	Increased in involved areas $CD4^-/CD8^-$	Normal
EBV	Neg	Neg	Positive	Neg

T-cell lymphomas compared with B-cell lymphomas:

– Frequent need for emergency operations.

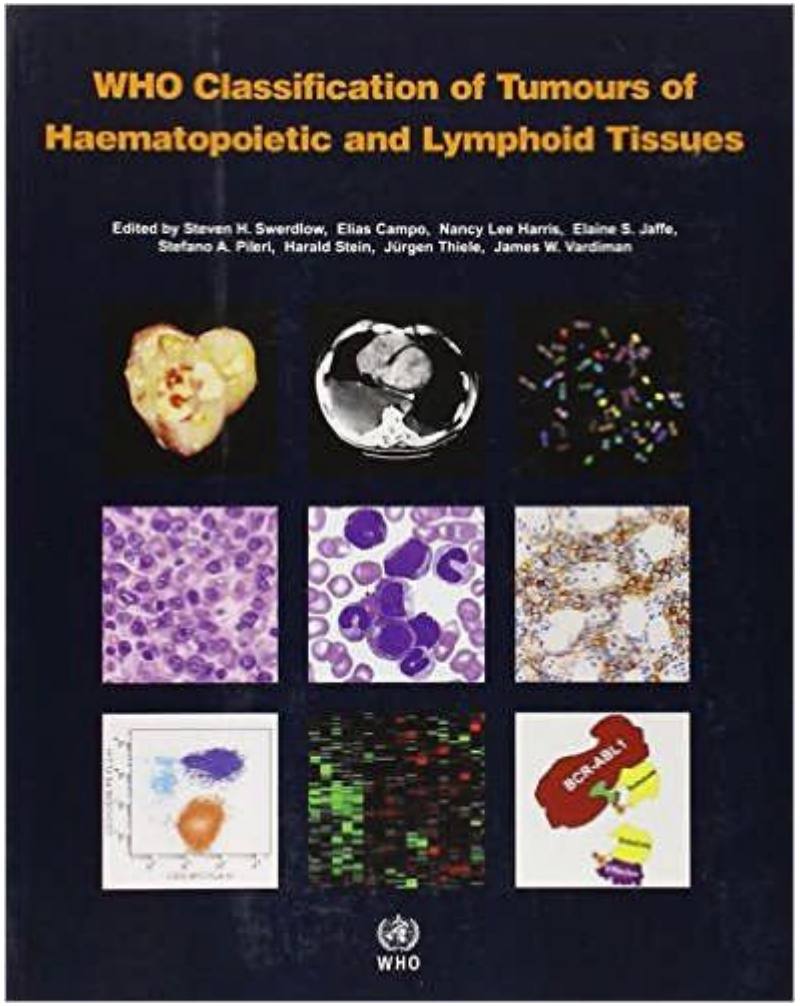
– Poorer survival

– Poorer response to chemotherapy

– Tumor progression and death commoner during chemotherapy

– Poorer general condition at presentation preclude any therapy in many

– More frequent and earlier relapses.



- 4th Edition is now >7 years old and out of date

- WHO will not permit a 5th edition until all volumes of the 4th are published

- Update to 4th edition has been allowed

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

The 2016 revision of the World Health Organization classification of lymphoid neoplasms

BLOOD, 19 MAY 2016 • VOLUME 127, NUMBER 20

MATURE B-CELL NEOPLASMS

- Chronic lymphocytic leukemia /small lymphocytic lymphoma
- Monoclonal B-cell lymphocytosis*
- B-cell prolymphocytic leukemia
- Splenic marginal zone lymphoma
- Hairy cell leukemia
- Splenic B-cell lymphoma/leukemia, unclassifiable
- Splenic diffuse red pulp small B-cell lymphoma
- Hairy cell leukemia-variant
- Lymphoplasmacytic lymphoma
- Waldenström macroglobulinemia
- Monoclonal gammopathy of undetermined significance (MGUS), IgM*
- Mu heavy chain disease
- Gamma heavy chain disease
- Alpha heavy chain disease
- Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*
- Plasma cell myeloma
- Solitary plasmacytoma of bone
- Extraosseous plasmacytoma
- Monoclonal immunoglobulin deposition diseases*
- Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Nodal marginal zone lymphoma
- Pediatric nodal marginal zone lymphoma
- Follicular lymphoma
  - In situ follicular neoplasia*
  - Duodenal-type follicular lymphoma*
- **Pediatric-type follicular lymphoma***
- **Large B-cell lymphoma with IRF4 rearrangement***
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
  - **In situ mantle cell neoplasia***
- Diffuse large B-cell lymphoma (DLBCL), NOS
- T cell/histiocyte-rich large B-cell lymphoma
- Primary DLBCL of the CNS
- Primary cutaneous DLBCL, leg type
- **EBV positive DLBCL, NOS***
- **EBV+ Mucocutaneous ulcer***
- DLBCL associated with chronic inflammation
- Lymphomatoid granulomatosis
- Primary mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- ALK positive large B-cell lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma
- **HHV8 positive DLBCL, NOS***
- Burkitt lymphoma
- Burkitt-like lymphoma with 11q aberration*
- **High grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements***
- **High grade B-cell lymphoma, NOS***
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

MATURE T-AND NK-NEOPLASMS

- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- Chronic lymphoproliferative disorder of NK cells
- Aggressive NK cell leukemia
- Systemic EBV+ T-cell Lymphoma of childhood*
- Hydroa vacciniforme-like lymphoproliferative disorder*
- Adult T-cell leukemia/lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma*
- Indolent T-cell lymphoproliferative disorder of the GI tract *
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis- like T-cell lymphoma
- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous CD30 positive T-cell lymphoproliferative disorders
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous gamma-delta T-cell lymphoma
- Primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T-cell lymphoma
- Primary cutaneous acral CD8+ T-cell lymphoma*

Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder*
Peripheral T-cell lymphoma, NOS
Angioimmunoblastic T-cell lymphoma
Follicular T-cell lymphoma*
Nodal peripheral T-cell lymphoma with TFH phenotype*
Anaplastic large cell lymphoma, ALK positive
Anaplastic large cell lymphoma, ALK negative *
Breast implant-associated anaplastic large cell lymphoma

UCL

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

The 2016 revision of the World Health Organization classification of lymphoid neoplasms

BLOOD, 19 MAY 2016 • VOLUME 127, NUMBER 20

- Formal separation of EATL Types I and II
- Introduction of new provisional entities for indolent T-cell LPD's in the GI tract (and Skin)
- Duodenal –type FL: localized overt low grade FL, is distinct from other GI tract FL
- New genetics in Mantle cell lymphoma:
  - Value of SOX11
  - Cyclin D1 negative MCL (Cyclin D2+)

RAPPAPORT CLASSIFICATION

Nodular
- Lymphocytic, poorly differentiated
- Mixed, lymphocytic and histiocytic
- Histiocytic

Diffuse
- Lymphocytic, well differentiated
- Lymphocytic, poorly differentiated
- Mixed, lymphocytic and histiocytic
- Histiocytic
- Undifferentiated
  - Burkitt's
  - Non-Burkitt's

KIEL CLASSIFICATION

B	T
Low grade	Low grade
ML, lymphocytic	ML, lymphocytic
ML, lymphoplasmacytic/cytoid	ML, small cerebriform cell- MF; Sezary's
ML, centroblastic/centrocytic	ML, lymphoepithelioid (Lennert's)
-follicular +/-diffuse	ML, angioimmunoblastic
-diffuse	ML, T zone
High grade	ML, pleomorphic-small cell
ML, centroblastic	High grade
ML, immunoblastic	ML, pleomorphic-medium;large cell
ML, large cell anaplastic	ML, immunoblastic
ML, Burkitt's	ML, large cell anaplastic
ML, lymphoblastic	ML, lymphoblastic
Rare types	Rare types

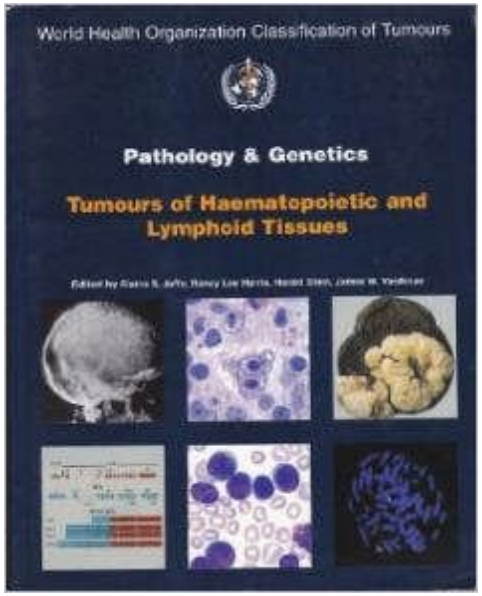
NEW WORKING FORMULATION for Clinical Use

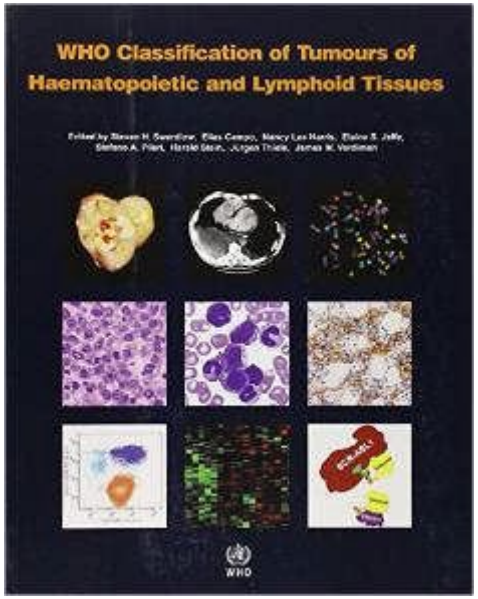
Low-Grade
- A. Small lymphocytic (lymphocytic; plasmacytoid)
- B. Follicular, predominantly small cleaved cell
- C. Follicular, mixed, small cleaved and large cleaved cell

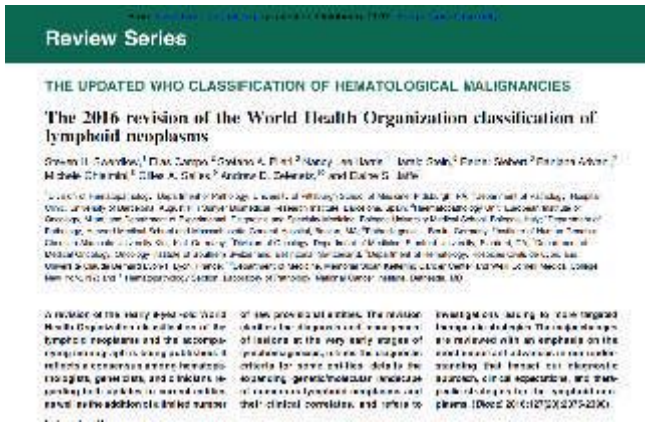
Intermediate-Grade
- D. Follicular, predominantly large cell, cleaved and/or non-cleaved
- E. Diffuse, small cleaved cell
- F. Diffuse, mixed, large and small cell
- G. Diffuse, large cell, cleaved or noncleaved

High-Grade
- H. Large cell, immunoblastic -(B- or T-cell type)
- I. Lymphoblastic
- J. Small noncleaved cell (Burkitt's and non-Burkitt's)

Miscellaneous







RAPPAPORT CLASSIFICATION

Nodular
Lym pho
Mixed, l
Histiocy
Diffuse
Lym pho
Lym pho
Mixed, l
Histiocy
Undiffer
Burkit
Non-B

KIEL CLASSIFICATION

B
Low grade

T
Low grade

NEW WORKING FORMULATION for Clinical Use

Low-Grade
A. Small lymphocytic (lymphocytic; plasmacytoid)
ed cell
large cleaved cell

leaved and/or non-cleaved

eaved

cell type)

non-Burkitt's)