

Gastrointestinal lymphoma

Gastric MALT lymphoma: pathogenesis, morphology and diagnosis

A clinicopathologic lecture

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning outcomes

- Explain why chronic *Helicobacter* gastritis can generate gastric MALT lymphoma
- Trace antigen-dependent and antigen-independent NF- κ B signaling
- Recognize the defining morphology and immunophenotype
- Integrate molecular findings with clinical response and diagnostic pitfalls

Why the gastrointestinal tract matters

Extranodal setting

The GI tract is the commonest location for extranodal lymphomas.

Gastric emphasis

The stomach is a particularly important GI site for primary lymphomas.

Main entity

Indolent extranodal marginal zone B-cell lymphoma predominates among gastric lymphomas.

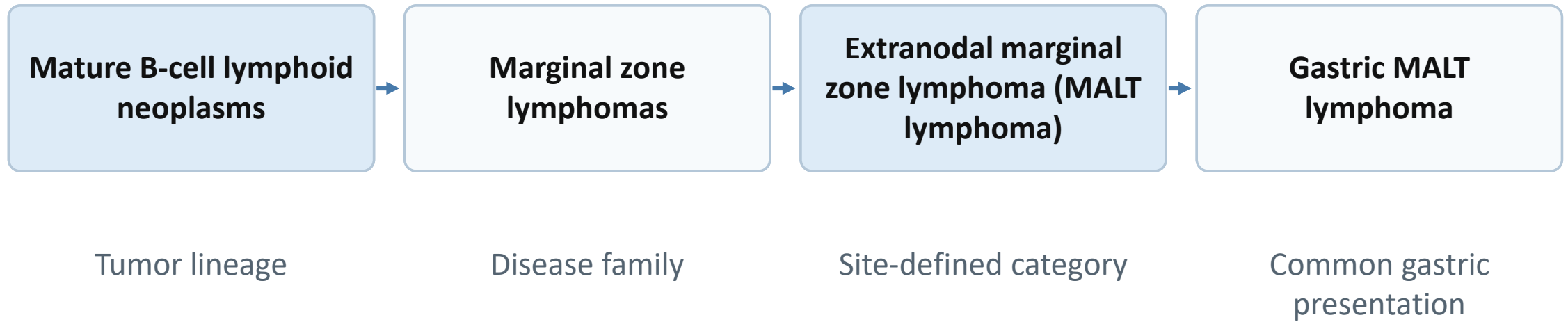
Primary gastric lymphoma: The scale of the problem

- Primary lymphomas account for nearly 5% of gastric malignancies.
- Gastric MALT lymphoma is the characteristic indolent B-cell entity.
- Its inflammatory pathogenesis separates it from most gastric epithelial cancers.

Conceptual distinction

Lymphoid malignancy ≠
epithelial malignancy

Gastric lymphoma belongs to a broader family



Marginal zone lymphoma: Three anatomic settings

Extranodal

Mucosal and other extranodal tissues; The stomach is a classical example.

Nodal

Marginal zone lymphoma occurring primarily in lymph nodes.

Splenic

Marginal zone lymphoma centered on the spleen.

Why MALT is an unusual name in the stomach

- Organized mucosa-associated lymphoid tissue is not normally present in the healthy stomach.
- Chronic gastritis can induce acquired lymphoid aggregates in gastric mucosa.
- These acquired immune structures provide the setting for lymphomatous evolution.

Surface epithelium

Lamina propria

Muscularis mucosae

Submucosa

Muscularis propria

Schematic gastric wall layers

Normal intestinal MALT versus acquired gastric MALT

Small intestine

Peyer patches provide preexisting organized mucosal lymphoid tissue.

Stomach

Lacks normal organized MALT; Lymphoid aggregates emerge during chronic gastritis.

Chronic immune stimulation is the recurring context

Stomach

Helicobacter-associated
chronic gastritis

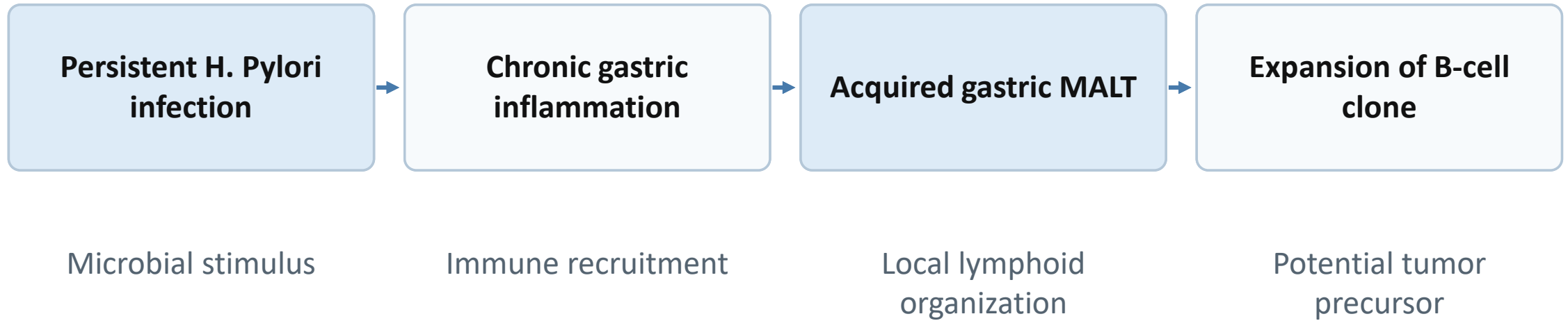
Salivary gland

Chronic autoimmune
inflammation in Sjögren
syndrome

Thyroid

Chronic autoimmune
inflammation in Hashimoto
thyroiditis

The central sequence: Gastritis to lymphoma



How H. Pylori persists in gastric mucosa

Motility

Flagella allow movement through gastric mucus.

Chemical protection

Urease produces ammonia and supports local survival.

Adherence and injury

Adhesins and toxins facilitate epithelial interaction and inflammation.

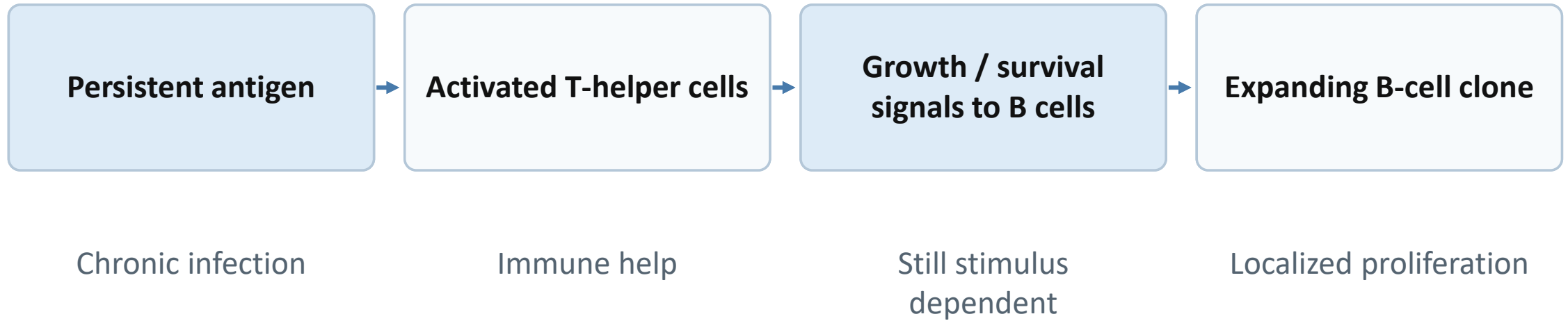
H. Pylori acts chiefly through the inflammatory niche

- Chronic bacterial colonization sustains local immune-cell recruitment.
- Antigen-dependent stimulation can maintain the emerging B-cell clone.
- The pathological link to lymphoma is immune stimulation, not simple conversion of a gastric epithelial cell into a B-cell.

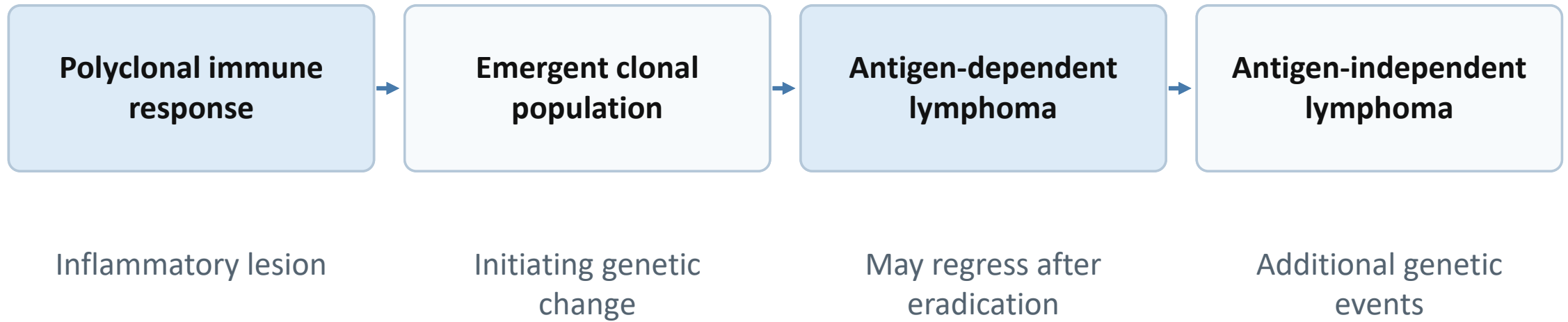
Causal logic

Bacterial antigen →
lymphoid response →
clonal selection

An early phase may remain antigen dependent



Reactive hyperplasia and lymphoma form a continuum



Polyclonality does not equal lymphoma

Reactive immune proliferation

Multiple B-cell clones respond to a continuing immune stimulus.

Emerging neoplastic clone

A favored clone acquires survival advantages; Clonal dominance may be demonstrable.

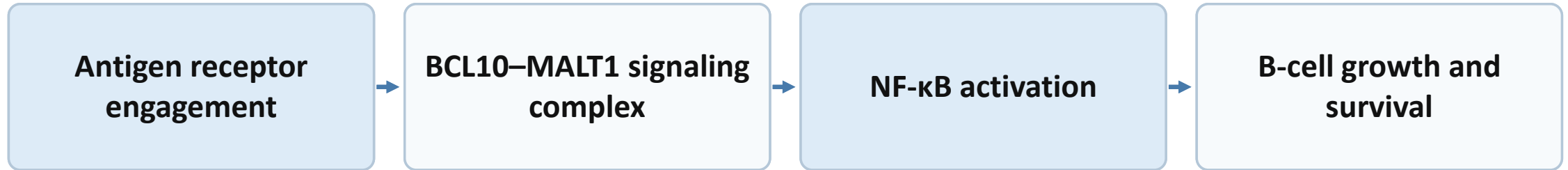
What makes early gastric MALT lymphoma exceptional?

- Often remains confined to its extranodal site for a prolonged period.
- May respond to elimination of the underlying H. Pylori stimulus.
- Can acquire lesions that remove the need for persistent antigen.

Clinical meaning

Biology can determine response to pathogen eradication.

BCL10 and MALT1 form a signaling hub



Editable pathway schematic: Physiological receptor input → NF-κB-dependent transcription

NF- κ B is a survival program, not a histologic pattern

- NF- κ B is a transcription factor involved in B-cell activation.
- Physiological antigen receptor signaling can activate this pathway.
- Abnormal constitutive activation allows neoplastic cells to survive with reduced antigen dependence.

Mechanistic pivot

Regulated signaling →
persistent signaling

Two routes to NF- κ B activation

Antigen-driven route

H. Pylori-related inflammation supplies a continuing upstream signal.

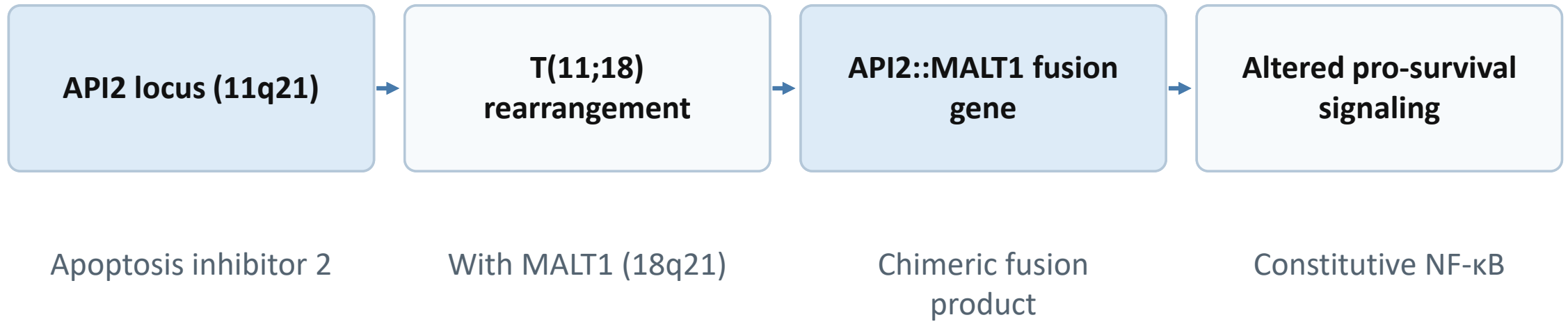
Genetically autonomous route

MALT1/BCL10-related alterations maintain signaling despite withdrawal of antigen.

Four recurrent gastric MALT lymphoma translocations

Rearrangement	Principal target	Consequent change
t(11;18)(q21;q21)	API2::MALT1	Fusion protein
t(1;14)(p22;q32)	BCL10 / IGH	Increased BCL10
t(14;18)(q32;q21)	IGH / MALT1	Increased MALT1
t(3;14)(p13;q32)	FOXP1 / IGH	Increased FOXP1

T(11;18): The API2::MALT1 fusion



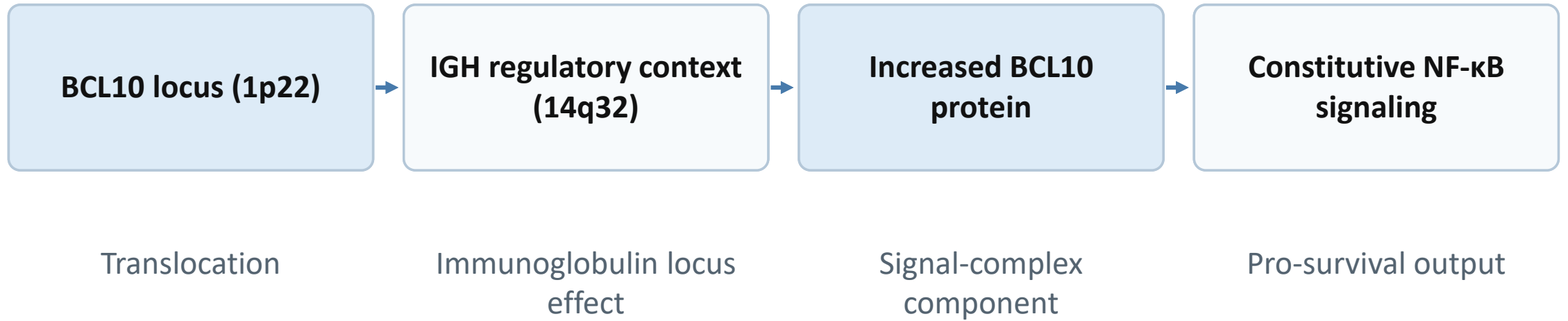
Why the API2::MALT1 product matters

- This rearrangement fuses material from the API2 and MALT1 genes.
- The chimeric protein supports constitutive NF- κ B activation.
- Tumors harboring this alteration generally resist regression after H. Pylori clearance.

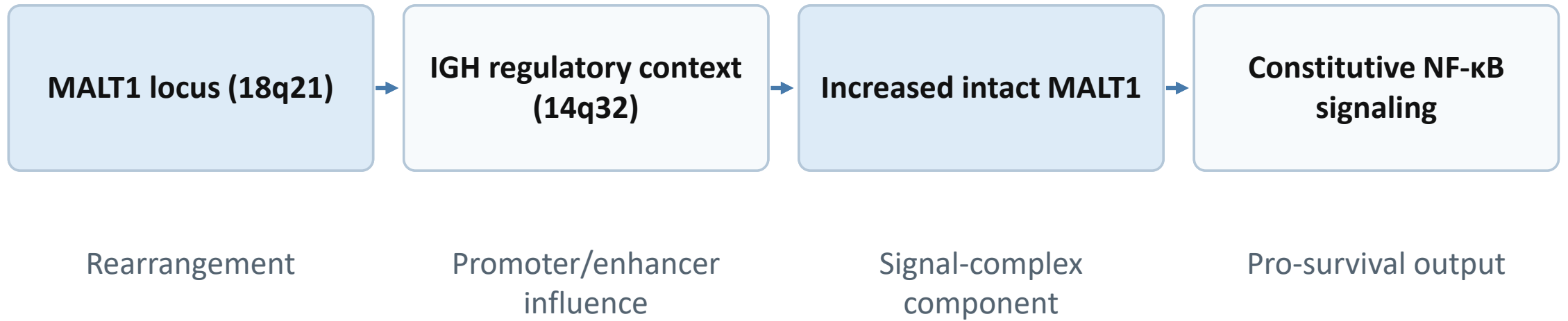
Mechanism to management

Oncogenic signaling becomes less reliant on bacterial antigen.

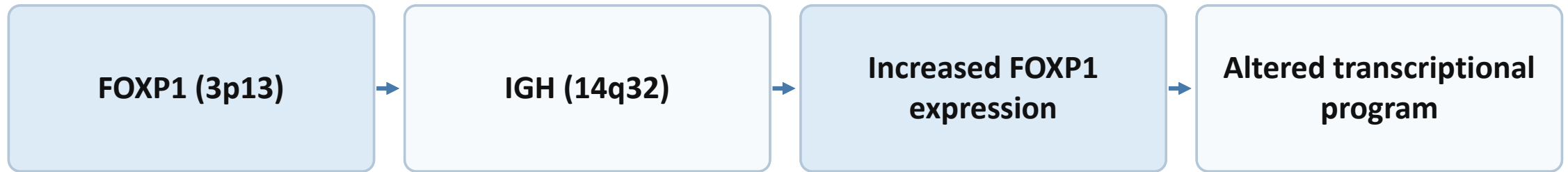
T(1;14): Increased BCL10 expression



T(14;18) in gastric MALT lymphoma



T(3;14) involves FOXP1



Translocation partner

Immunoglobulin locus

Transcription factor

Do not equate with
BCL10–MALT1 fusion

Genetic alterations converge on growth advantage

API2::MALT1

Fusion protein; Constitutive survival signaling

BCL10 or MALT1 upregulation

Increased signal-complex activity → NF-κB

FOXP1 upregulation

Transcription-factor overexpression; Biologically distinct alteration

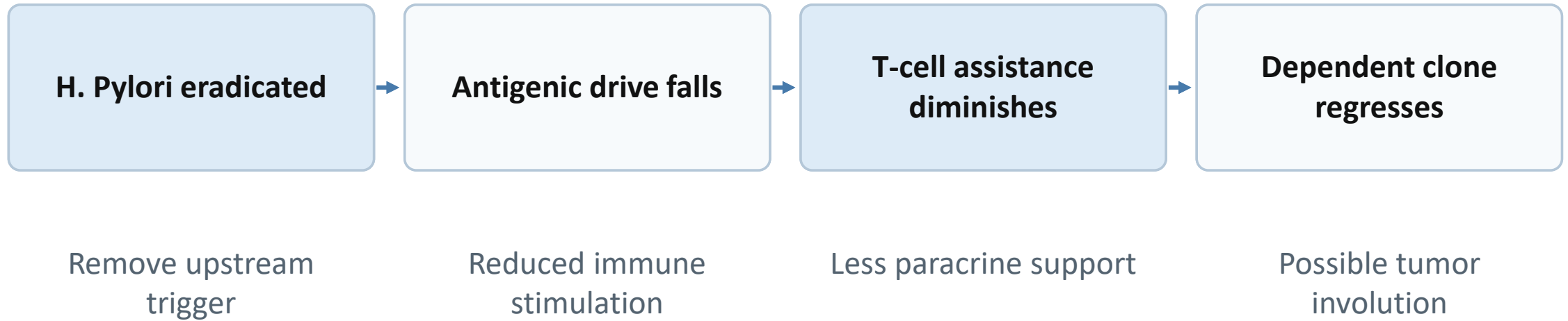
Not every gastric MALT lymphoma is fusion driven

- Some tumors lack the listed chromosomal translocations.
- In these tumors, antigen-dependent activation of NF- κ B may remain essential.
- The molecular state helps explain heterogeneous response to H. Pylori eradication.

Caution

Absence of a translocation does not itself prove eradication response.

Why eradication can cause lymphoma regression



Why eradication can fail

Biologic independence

MALT1- or BCL10-related rearrangements allow self-sustaining survival signals.

Extent of disease

Deep muscular invasion and involved lymph nodes also correlate with resistance.

Depth of infiltration changes response expectations

- Mucosal-limited disease is conceptually distinct from deep wall infiltration.
- Invasion into or through the muscularis propria correlates with reduced eradication responsiveness.
- Lymph-node involvement is another adverse response correlate.

Surface epithelium

Lamina propria

Muscularis mucosae

Submucosa

Muscularis propria

Schematic gastric wall layers

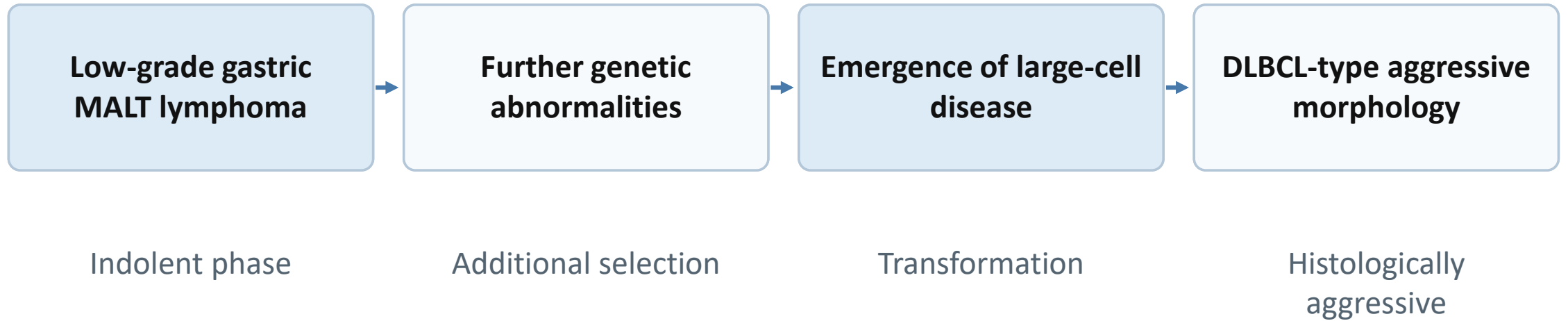
MALT lymphoma often remains localized

- Extranodal marginal zone lymphomas may remain local for prolonged periods.
- Systemic dissemination tends to occur later than in aggressive lymphomas.
- Localized behavior should not be confused with absence of malignant potential.

Natural history

Indolent ≠ biologically inert

Clonal evolution can change tumor behavior



TP53 and CDKN2A can be affected in transformation

- Progression with additional genetic changes.
- Inactivation of genes encoding p53 and p16 is cited as an example.
- These events illustrate loss of tumor-suppressive control during clonal evolution.

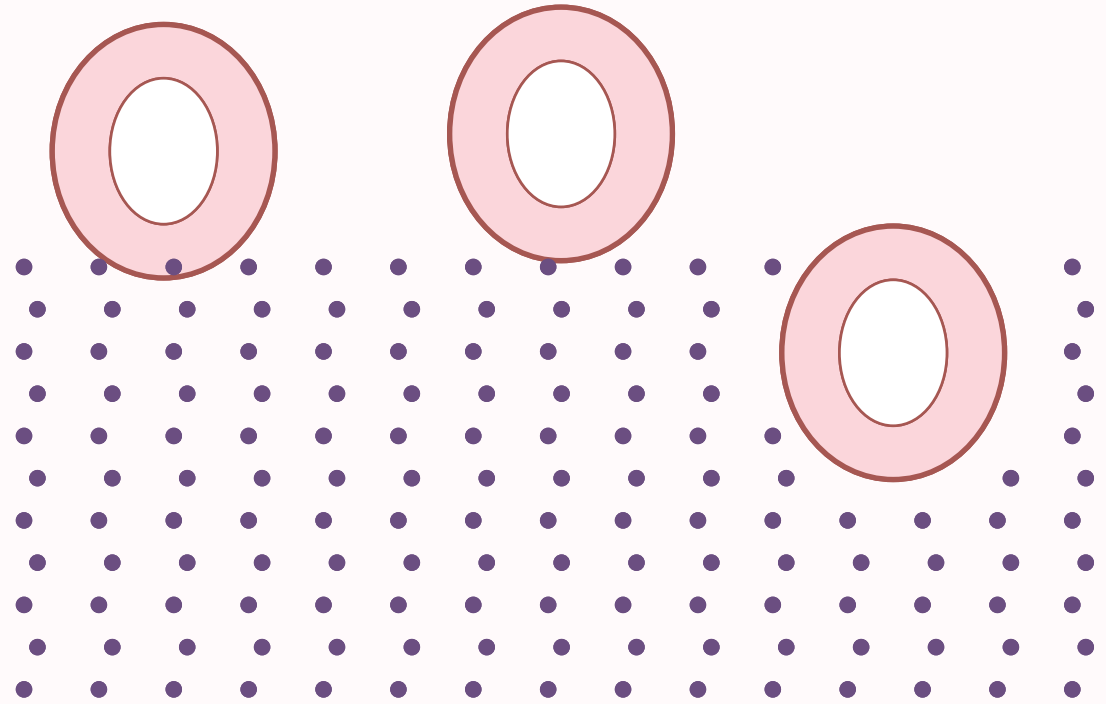
Interpretation

This is an association in the described progression model.

MALT lymphoma: Low-power tissue pattern

- Dense lymphoid expansion occupies the lamina propria.
- Gastric glands persist within, and may be disrupted by, the infiltrate.
- Architecture must be assessed together with cytology and immunophenotype.

Schematic — not a tissue specimen

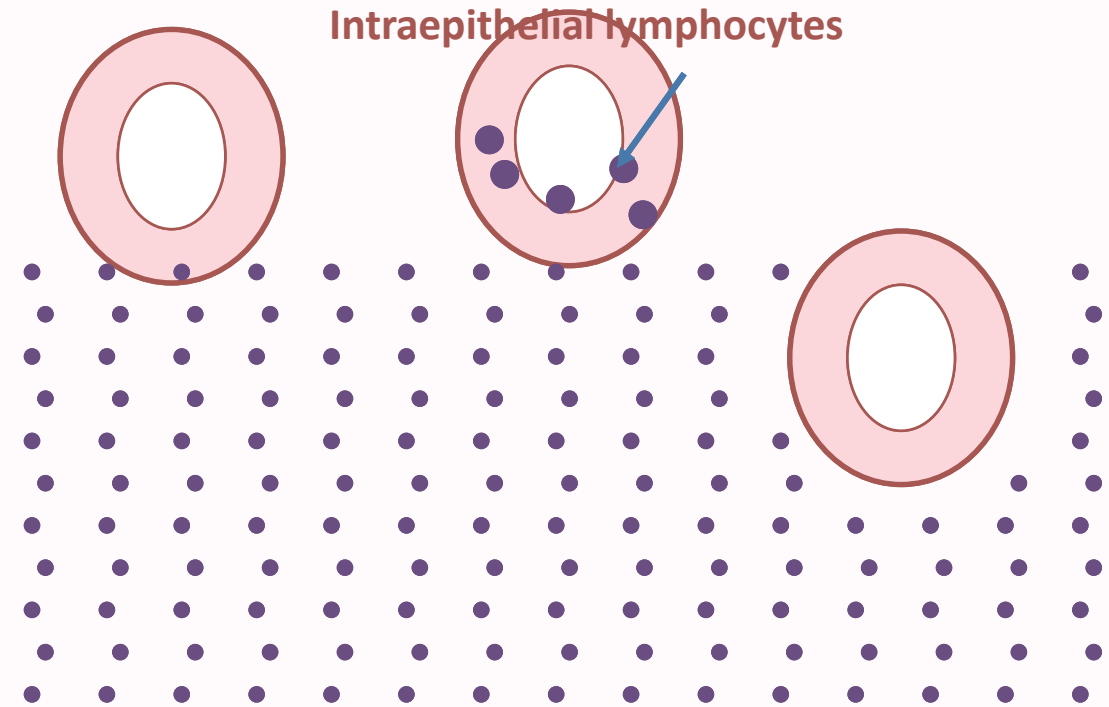


Lamina propria expansion

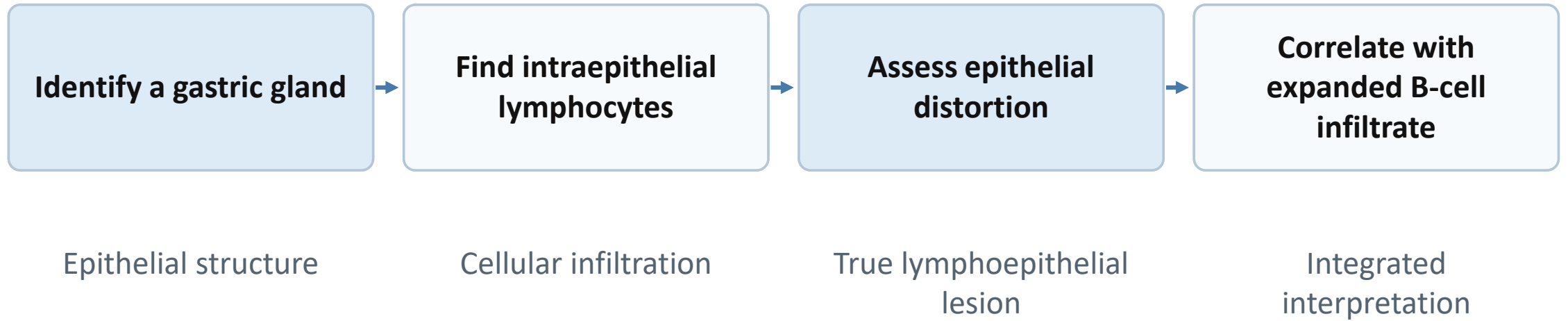
Lymphoepithelial lesions are the key clue

- Neoplastic lymphocytes infiltrate glandular epithelium.
- The affected gland becomes distorted or disrupted.
- Recognize the lesion in context: It is not sufficient alone to establish the entire diagnosis.

Schematic — not a tissue specimen



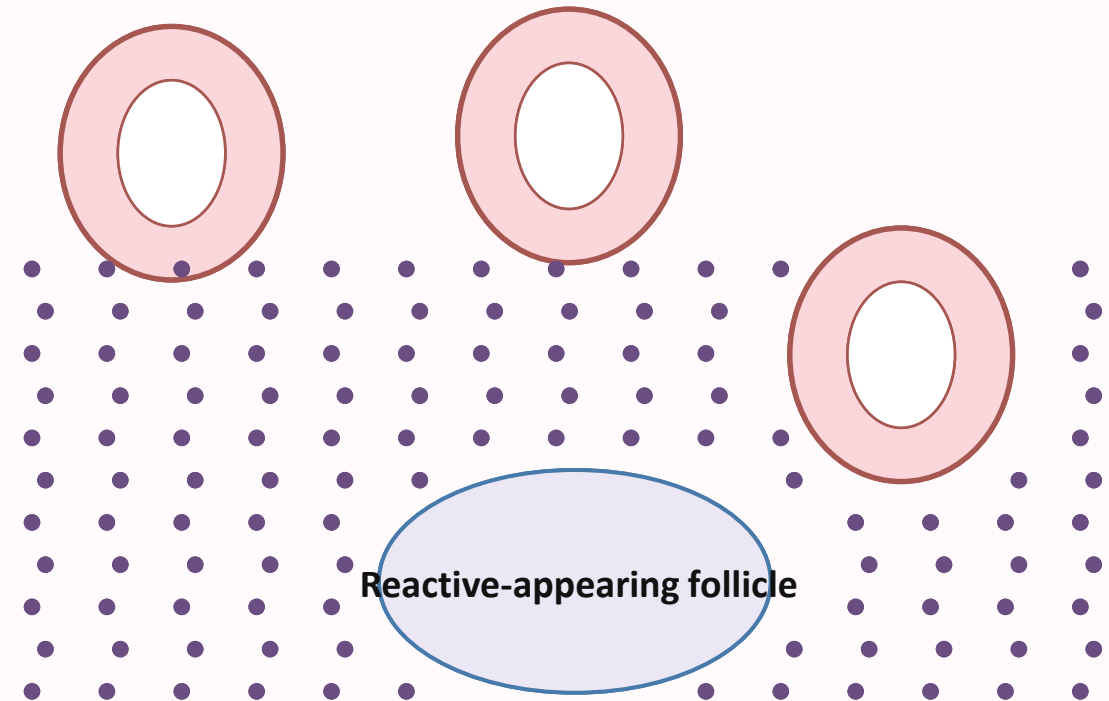
A lymphoepithelial lesion: Read it in steps



Reactive follicles may coexist with tumor

- B-cell follicles with reactive-appearing centers may be present.
- A reactive-looking follicle does not exclude adjacent lymphoma.
- Assess the surrounding marginal-zone infiltrate and epithelial lesions.

Schematic — not a tissue specimen



Plasmacytic differentiation is not rare

Frequency

Approximately 40% of gastric MALT lymphomas show plasmacytic differentiation.

Morphologic implication

The infiltrate may contain cells resembling plasma cells.

Diagnostic implication

Light-chain restriction can support clonality when appropriate.

GI lymphoma can appear in different growth patterns

Mucosal involvement

Dense expansion of the gastric lamina propria

Small nodules

Some intestinal lymphomas form discrete nodular deposits

Diffuse wall involvement

Other GI lymphomas infiltrate the bowel wall broadly

Immunophenotyping establishes B-cell lineage

Marker	Robbins pattern	What it supports
CD19	Positive	Mature B-cell lineage
CD20	Positive	Mature B-cell lineage
CD5	Usually negative	Helps exclude common CD5+ B-cell mimics
CD10	Usually negative	Helps exclude germinal-center B-cell mimics
CD43	Positive in $\approx$ 25%	Aberrant coexpression may be informative

CD19 and CD20: Lineage, not unique identity

- Gastric MALT lymphomas express mature B-cell markers CD19 and CD20.
- These markers confirm B-cell identity but are shared by several other B-cell lymphomas.
- Morphology and an exclusionary immunophenotypic pattern remain essential.

Diagnostic reasoning

Lineage marker ≠
lymphoma subtype

CD5– / CD10–: A useful exclusionary pattern

Typical gastric MALT lymphoma

CD5– and CD10– with preserved mature B-cell marker expression.

Why it matters

A different marker pattern should prompt reconsideration of alternate B-cell neoplasms.

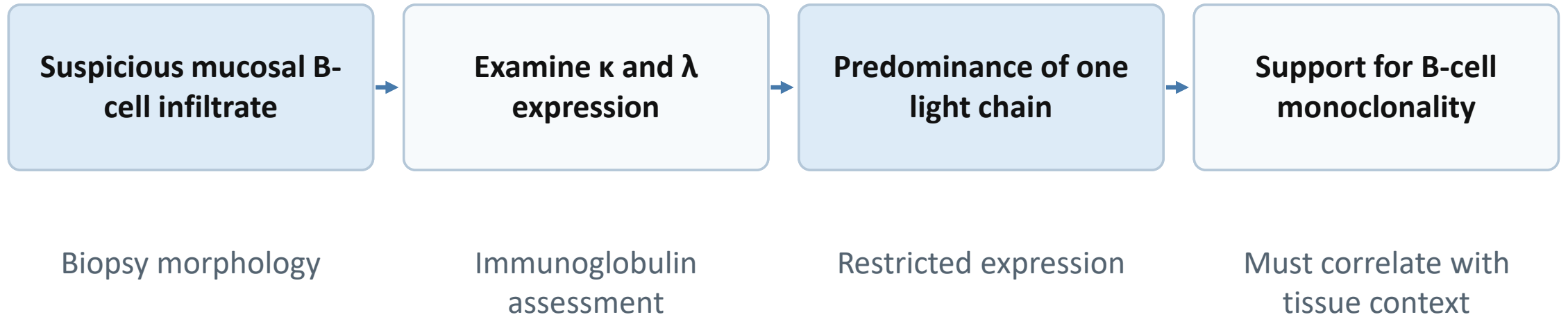
CD43 coexpression is a diagnostic clue

- About one quarter of gastric MALT lymphomas express CD43.
- Aberrant CD43 expression can help establish a neoplastic B-cell population.
- Its absence cannot exclude MALT lymphoma because most cases lack this finding.

Common error

Do not treat a minority-feature marker as mandatory.

Light-chain restriction supports a clonal population



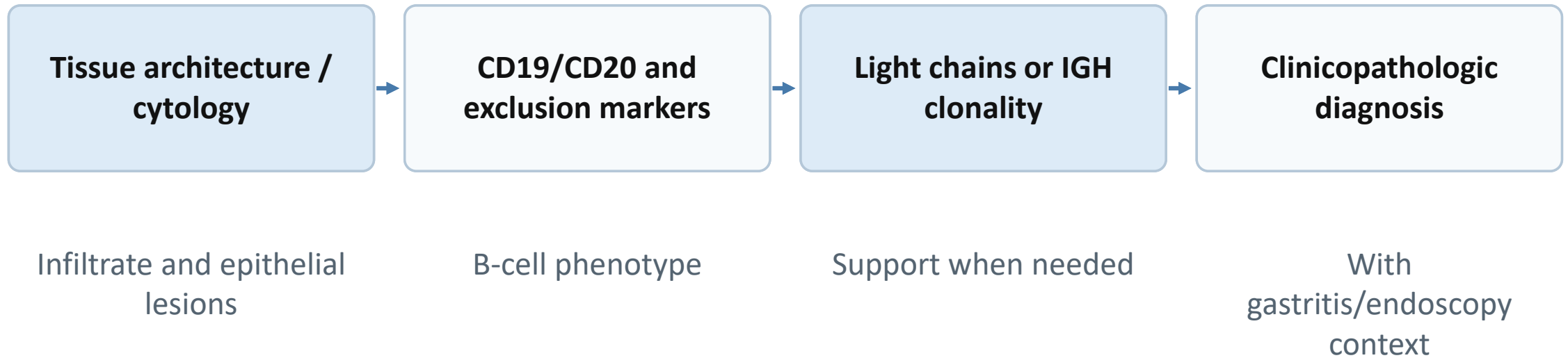
Clonal IGH rearrangement testing

- Molecular analysis can detect clonal immunoglobulin heavy-chain gene rearrangement.
- This is especially useful when lymphoepithelial lesions are absent.
- A molecular clonal result contributes evidence; It does not replace morphologic interpretation.

Integration rule

Histology + phenotype +
clonality > any isolated
test

Diagnosis is an evidence-integration problem



The major mimic is chronic H. Pylori gastritis

Chronic gastritis

Can induce mucosal lymphoid aggregates and similar symptoms.

MALT lymphoma

Clonal B-cell proliferation with characteristic infiltrative morphology and phenotype.

Small biopsies are a particular challenge

- Gastritis and lymphoma may coexist in the same gastric mucosa.
- Both can share dyspeptic symptoms and similar endoscopic appearances.
- Sampling may miss the most diagnostic lymphoepithelial lesions or deeper infiltration.

Practical implication

A limited negative feature may reflect sampling rather than absent disease.

Morphology must be read with the stomach in mind

Background

Is there active or chronic Helicobacter-associated gastritis?

Architecture

Does the infiltrate expand the lamina propria and invade glands?

Clonality

Does the B-cell population show restricted light chains or clonal IGH?

Dyspepsia and epigastric pain predominate

- The most frequent clinical complaints are dyspepsia and epigastric discomfort.
- These symptoms are nonspecific and overlap with H. Pylori gastritis.
- The clinical presentation alone cannot establish lymphoma.

Clinicopathologic point

A common symptom can conceal a lymphoid neoplasm.

Gastrointestinal bleeding may occur

Hematemesis

Upper GI bleeding can present with vomiting of blood.

Melena

Digested blood may produce black, tarry stools.

Underlying lesion

Lymphomatous mucosal involvement may contribute to bleeding symptoms.

Constitutional features may accompany gastric disease

- Weight loss is among the constitutional manifestations described.
- The symptom pattern can include local gastric and systemic manifestations.
- Clinical severity should not be inferred from symptoms alone without staging or pathology.

Symptom synthesis

Local discomfort ±
bleeding ± weight loss

Endoscopic appearances overlap with gastritis

Endoscopy

Surface appearances may not reliably distinguish H. Pylori gastritis from MALT lymphoma.

Histopathology

Biopsy reveals infiltrative pattern, B-cell phenotype and sometimes clonality.

Anatomic involvement extends beyond the stomach

Stomach

Characteristic site of MALT lymphoma

Small bowel

Peyer patches are preexisting MALT; Other GI lymphomas also arise

Colon / bowel wall

May show nodular or diffuse infiltration depending on lymphoma subtype

Post-transplant B-cell proliferations involve the bowel

- The bowel is a frequent site for EBV-positive B-cell proliferations following transplantation.
- Transplant-related T-cell dysfunction impairs immune control of EBV-infected B cells.
- Intestinal predilection to local effects of orally absorbed immunosuppressants.

Separate mechanism

EBV-associated immune deficiency ≠ H. Pylori-driven gastric MALT lymphoma

Immunosuppression changes the differential

Chronic Helicobacter inflammation

Typical context for indolent gastric MALT lymphoma.

Post-transplant T-cell dysfunction

Raises the possibility of EBV-positive B-cell lymphoproliferation.

Not every GI B-cell lymphoma is MALT lymphoma

Entity	Characteristic GI connection
Gastric MALT lymphoma	Indolent, often H. pylori linked
Diffuse large B-cell lymphoma	Aggressive nodal or extranodal masses; may follow transformation
Mantle cell lymphoma	Can produce lymphomatoid polyposis
Sporadic Burkitt lymphoma	Often presents near ileocecum / peritoneum

Large B-cell transformation changes morphology

Indolent MALT lymphoma

Small B-cell–rich infiltrates and lymphoepithelial lesions.

DLBCL-type transformation

A population of large, rapidly proliferating malignant B cells.

Mantle cell lymphoma: Lymphomatoid polyposis

- Mantle cell lymphoma may involve mucosal sites in the small bowel or colon.
- Multiple polypoid deposits are termed lymphomatoid polyposis.
- Its typical CD5 expression and cyclin D1 overexpression differ from the usual gastric MALT profile.

Differential focus

Polypoid distribution and phenotype redirect diagnosis.

Burkitt lymphoma: Another GI-predominant pattern

- Sporadic Burkitt lymphoma often appears as an ileocecal or peritoneal mass.
- It has MYC rearrangement—associated rapid proliferation.
- The morphologic and biological course differs substantially from indolent gastric MALT lymphoma.

Differential focus

Aggressive growth + ileocecal mass ≠ typical gastric MALT.

Comparison: Indolent versus aggressive GI lymphoma

Feature	Gastric MALT	DLBCL / Burkitt
Characteristic tempo	Often indolent	Often aggressive
Microanatomy	Lamina propria; glands	Mass-forming / diffuse tumor
Molecular focus	MALT1 / BCL10 pathways	Other subtype-specific drivers
Antibiotic regression	Can occur in H. pylori–dependent cases	Not a defining biological feature

Case 1: Dyspepsia with a dense B-cell infiltrate

- A patient with persistent dyspepsia has gastric mucosal biopsies.
- Histology shows lamina propria expansion and lymphocytes infiltrating gastric glands.
- The infiltrate is CD20-positive, CD5-negative and CD10-negative.

What diagnosis is most strongly supported, and what evidence is still useful?

Case 1: Integrate rather than overcall

The pattern strongly suggests gastric extranodal marginal zone (MALT) lymphoma.

Confirm the lymphoepithelial pattern and assess the *Helicobacter* background.

Light-chain restriction or IGH clonality may add support, particularly in equivocal samples.

Case 2: Failure to regress after eradication

- Gastric MALT lymphoma is identified in a Helicobacter-associated setting.
- After H. Pylori eradication, lymphoma persists.
- Molecular studies find t(11;18)(q21;q21).

Which pathway explains why withdrawal of antigen may be insufficient?

Case 2: Antigen independence explains persistence

T(11;18) generates the API2::MALT1 fusion.

The rearrangement supports constitutive NF- κ B survival signaling.

Such tumors are generally unresponsive to H. Pylori clearance alone.

Case 3: New large-cell morphology

- A previously indolent gastric MALT lymphoma develops an enlarging mass.
- Histology shows a newly dominant population of large malignant lymphoid cells.
- The clinical course appears more aggressive than before.

Which biological event should be considered?

Case 3: Consider histologic transformation

Progression to diffuse large B-cell lymphoma–type morphology is a recognized event.

Additional genetic changes, including loss of p53 or p16 function, may accompany transformation.

The new large-cell component must be evaluated as aggressive lymphoma.

Pathogenesis at a glance

- H. Pylori → sustained mucosal immune response → acquired gastric MALT.
- Clonal marginal-zone B-cell expansion can remain antigen dependent.
- MALT1/BCL10 pathway alterations can provide constitutive NF- κ B survival signaling.
- Additional evolution may produce large B-cell transformation.

Diagnosis at a glance

- Recognize a dense lamina propria B-cell infiltrate with lymphoepithelial lesions.
- Check CD19/CD20 positivity and typical CD5/CD10 negativity.
- Use CD43 coexpression, light-chain restriction or IGH clonality as supporting evidence.
- Interpret with H. Pylori status, depth and clinical context.

Principal source and scope

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026).
- Chapter 17: The Gastrointestinal Tract — Lymphoma, pp. 706–707.
- Chapter 13: Marginal Zone Lymphomas, pp. 548–549.
- Related context: *Helicobacter pylori* gastritis, DLBCL, mantle cell and Burkitt lymphomas.