

Autoimmune atrophic gastritis

Gastric immune injury • oxyntic atrophy • systemic consequences

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Diagnostic signature

- Corpus/fundus-predominant destruction of acid-producing oxyntic glands.
- Antral sparing, achlorhydria, hypergastrinemia, and endocrine proliferation.
- Intrinsic factor deficiency links gastric injury to vitamin B₁₂ deficiency.

Body + fundus

Oxyntic glands / parietal cells
Main autoimmune target

Antrum

G cells • typically relatively spared

Functional region map — schematic

Learning outcomes

- Explain the immune targets and why oxyntic atrophy develops.
- Connect acid and intrinsic factor loss to laboratory and clinical sequelae.
- Identify the characteristic morphology and distinguish H. Pylori gastritis.
- Recognize the two principal neoplastic associations.

Stomach regions have distinct gland populations

- Body and fundus contain well-developed oxyntic glands.
- Antral glands contain hormone-producing G cells.
- This functional compartmentalization explains the selective lesion pattern.

Body + fundus

Oxyntic glands / parietal cells
Main autoimmune target

Antrum

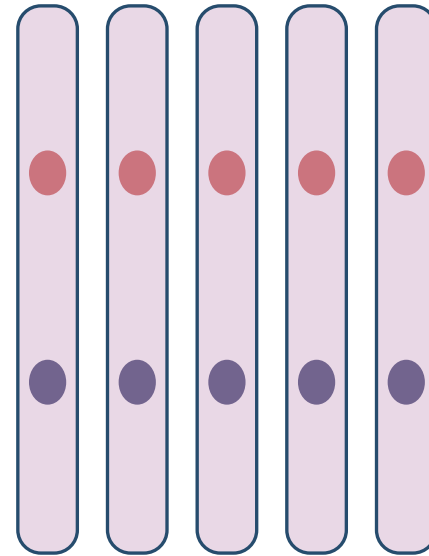
G cells • typically relatively spared

Functional region map — schematic

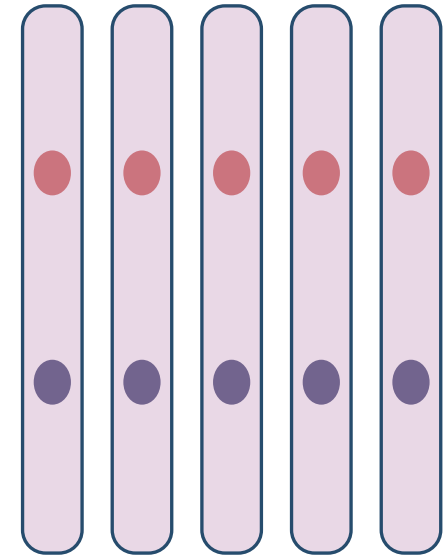
Oxyntic glands: Secretory specialization

- Parietal cells provide gastric acid and intrinsic factor.
- Chief cells produce pepsinogen (digestive enzyme precursor).
- Both cell populations are depleted as autoimmune oxyntic atrophy progresses.

Intact oxyntic mucosa



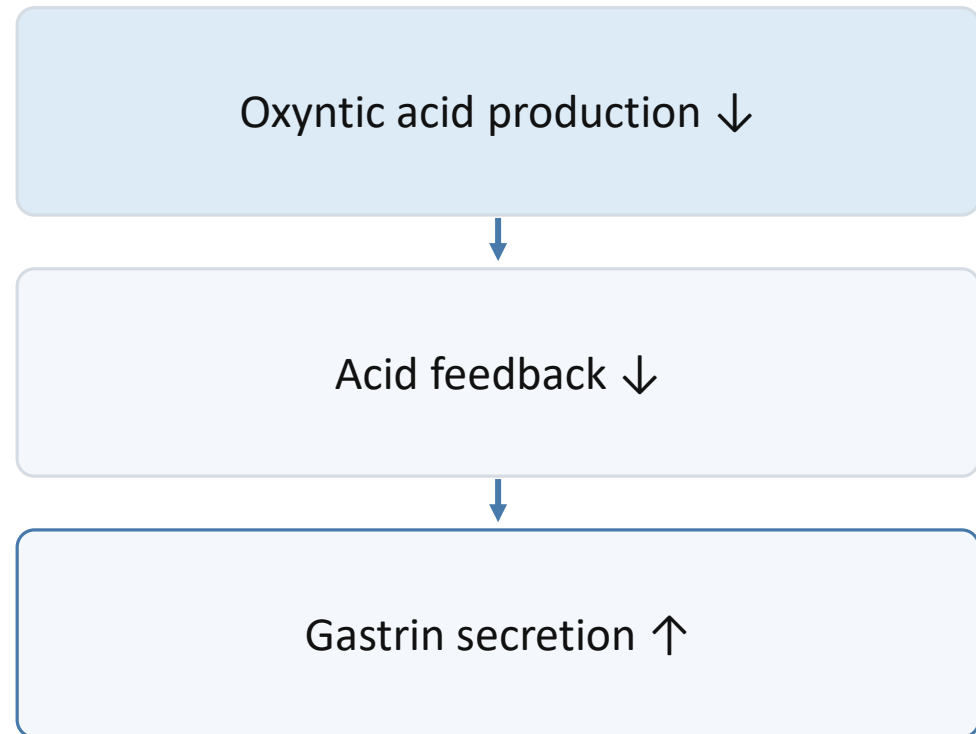
Atrophic oxyntic mucosa



Simplified gland architecture; Not an H&E image

Antral G cells respond to gastric acid loss

- Antral G cells secrete gastrin, stimulating parietal-cell acid production.
- Loss of acid removes an important physiological negative-feedback signal.
- Compensatory gastrin release persists despite low acid output.

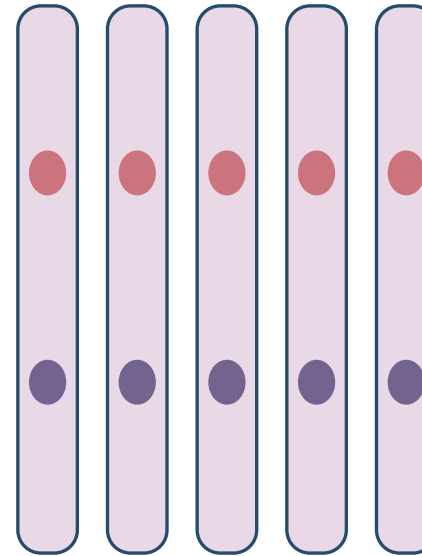


Mechanistic sequence — schematic

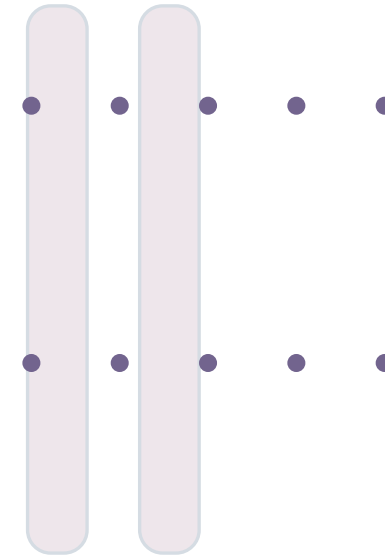
Disease definition: Immune-mediated oxyntic atrophy

- Autoimmune inflammation progressively damages gastric body and fundus.
- The defining structural endpoint is loss of parietal and chief cells.
- Functional and epithelial changes arise from the missing gland populations.

Intact oxyntic mucosa



Atrophic oxyntic mucosa



Simplified gland architecture; Not an H&E image

Classic topography separates two gastritides

- Autoimmune gastritis: Body/fundus predominant, antrum usually spared.
- H. Pylori gastritis: Commonly antral and superficially inflamed.
- Distribution is highly informative but should not be treated as an absolute exclusion rule.

Autoimmune

Body / fundus

Oxyntic loss

H. Pylori

Antrum often affected

Superficial inflammation

Characteristic patterns — not exclusive criteria

Frequency and typical diagnostic age

- Less than 10% of chronic gastritis cases estimate.
- Estimated prevalence: 2% among adults older than 60 years.
- Median age at clinical diagnosis: Approximately 60 years.

<10%

Chronic gastritis
cases

2%

Persons >60 years

60 years

Median age at
diagnosis

Demographic and autoimmune context

- Females are affected slightly more often than males.
- The disorder may coexist with autoimmune thyroid, pancreatic, or adrenal disease.
- Clinical presentation often follows a long subclinical course.

Hashimoto
Thyroiditis

Type 1
Diabetes mellitus

Addison
Disease

Family
Clustering

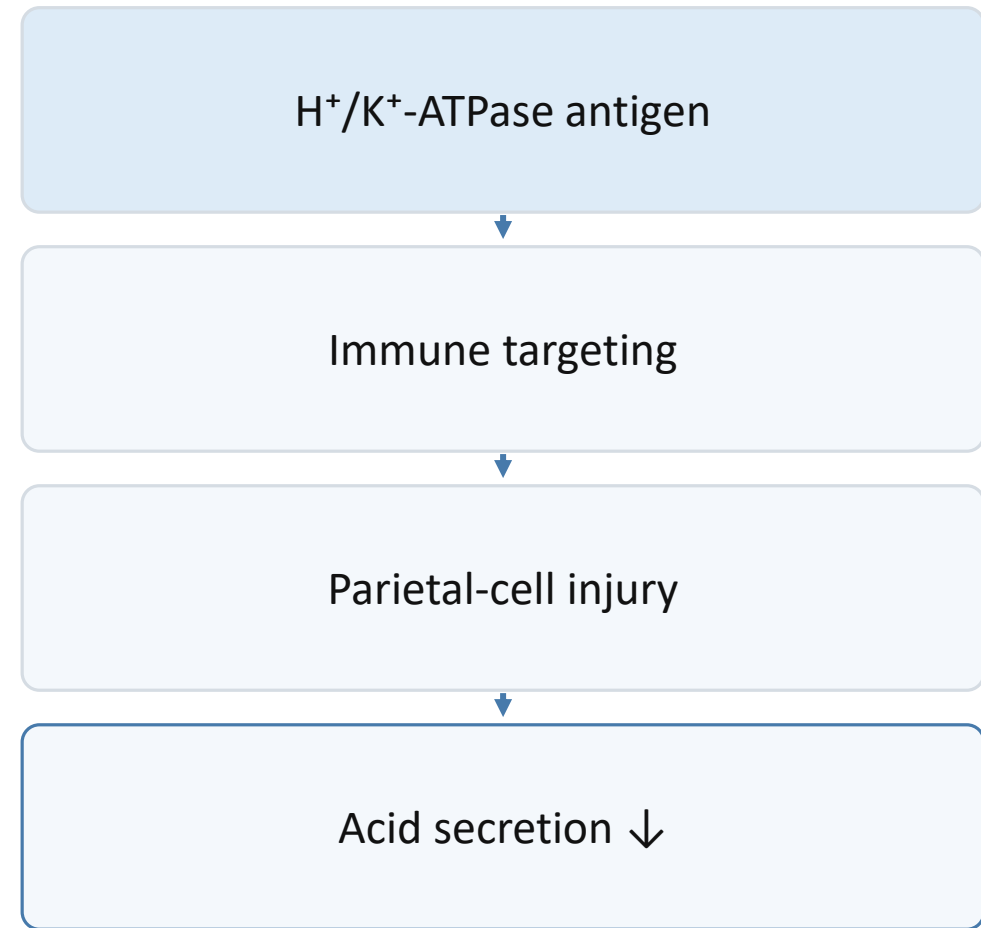
Associations; Not diagnostic criteria

Familial aggregation suggests predisposition

- Familial clustering has been observed.
- Concordance in some monozygotic twins supports inherited susceptibility.
- The textbook does not identify established responsible genetic variants.

Primary autoantigen: The gastric proton pump

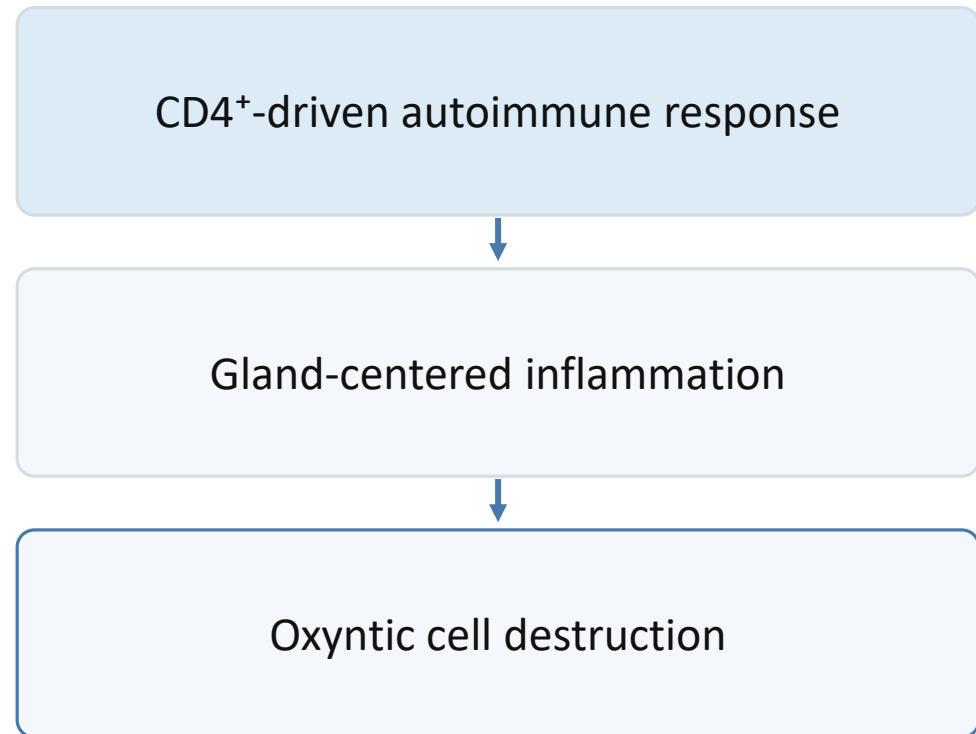
- The H^+/K^+ -ATPase of parietal cells is a major immune target.
- The membrane pump is required for hydrogen ion secretion.
- Loss of pump-bearing cells leads directly to impaired acidification.



Mechanistic sequence — schematic

CD4⁺ T cells participate in gland injury

- CD4⁺ T cells as principal agents of injury.
- The associated inflammation is centered deep around oxyntic glands.
- Persistent immune attack can culminate in marked glandular atrophy.



Mechanistic sequence — schematic

Anti-parietal cell antibodies: Diagnostic clue

- Antibodies recognize parietal-cell components, including H⁺/K⁺-ATPase.
- They may be found in serum and gastric secretions.
- Positive serology supports the diagnosis when matched to anatomy and morphology.

Anti-intrinsic factor antibodies: Parallel clue

- Autoantibodies to intrinsic factor can accompany anti-parietal cell antibodies.
- The antibodies may precede overt gastric atrophy and pernicious anemia.
- Absence of one antibody does not by itself settle the histologic diagnosis.

Target 1

Parietal-cell H^+/K^+ -ATPase

Oxyntic cell injury

Target 2

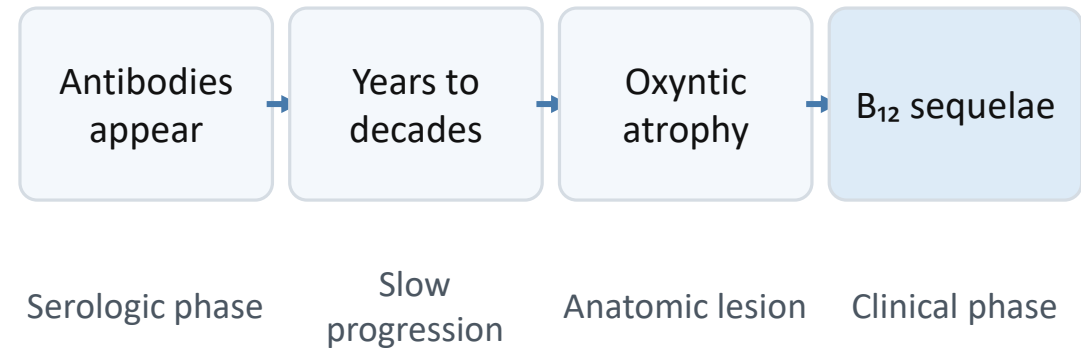
Intrinsic factor

B₁₂ deficiency context

Characteristic patterns — not exclusive criteria

Serology can precede tissue injury by decades

- Anti-parietal cell and anti-intrinsic factor antibodies may precede complications.
- Textbook interval: Approximately 2–3 decades before atrophy and pernicious anemia.
- A positive antibody result is not synonymous with established end-stage disease.

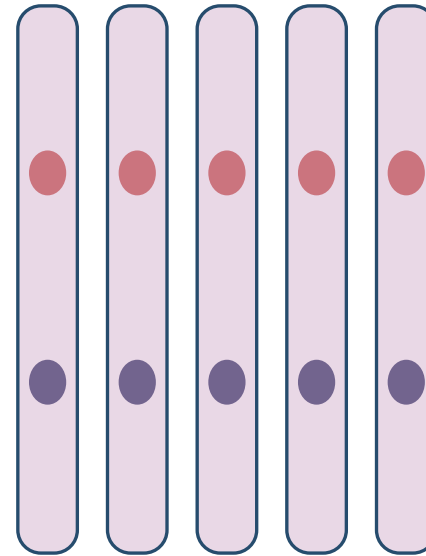


Possible lag: ~2–3 decades (textbook description)

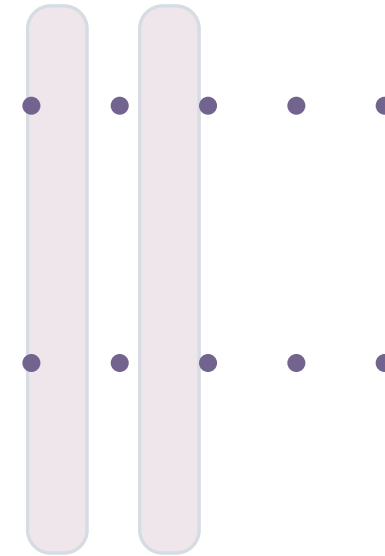
Loss of oxyntic glands integrates the disease

- Immune injury progressively removes parietal and chief cells.
- Inflammatory and replacement epithelial changes remodel the gastric mucosa.
- Structural atrophy generates the downstream endocrine and nutritional phenotype.

Intact oxyntic mucosa



Atrophic oxyntic mucosa



Simplified gland architecture; Not an H&E image

The distribution is anatomically selective

- Diffuse damage concentrates in acid-producing body and fundus mucosa.
- The antrum and cardia are typically relatively spared.
- Biopsy site identification is therefore part of histologic interpretation.

Body + fundus

Oxyntic glands / parietal cells
Main autoimmune target

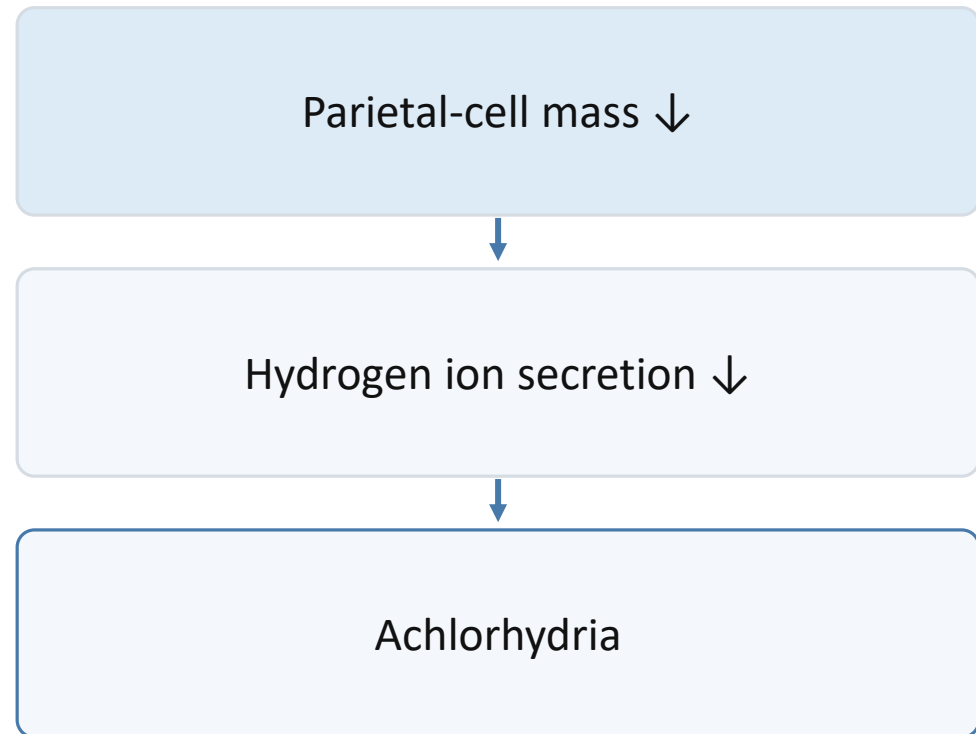
Antrum

G cells • typically relatively spared

Functional region map — schematic

Why achlorhydria occurs

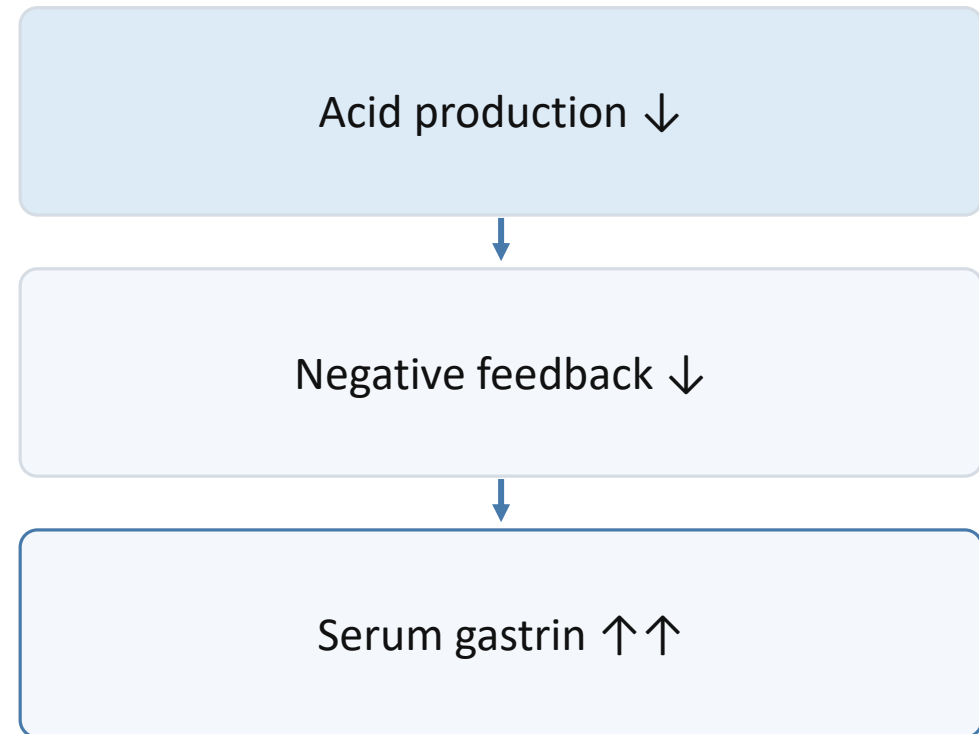
- Gastric acid secretion depends on surviving functional parietal cells.
- Diffuse depletion reduces acid production, often to achlorhydria.
- Acid output is low despite the compensatory rise in gastrin.



Mechanistic sequence — schematic

Low acid drives hypergastrinemia

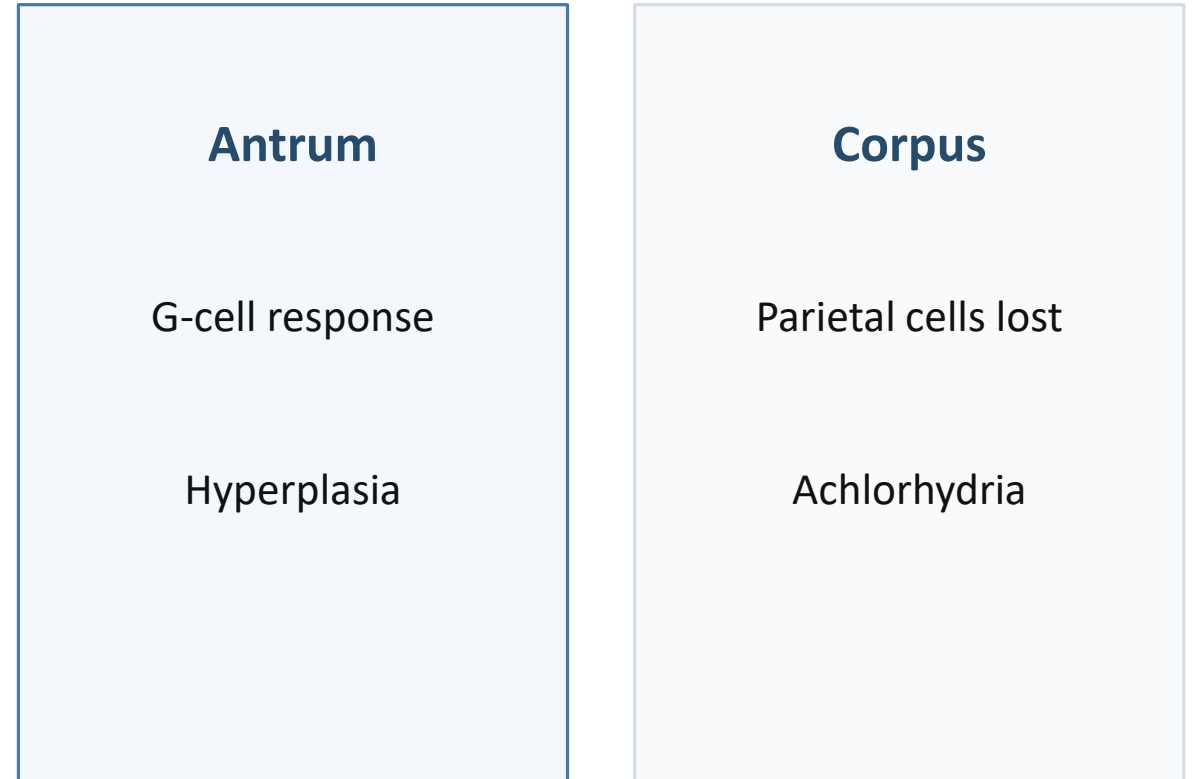
- Reduced luminal acid is sensed by the gastrin-regulatory system.
- Antral gastrin release increases after loss of acid inhibition.
- Marked hypergastrinemia is a characteristic biochemical feature.



Mechanistic sequence — schematic

Antral G-cell hyperplasia is compensatory

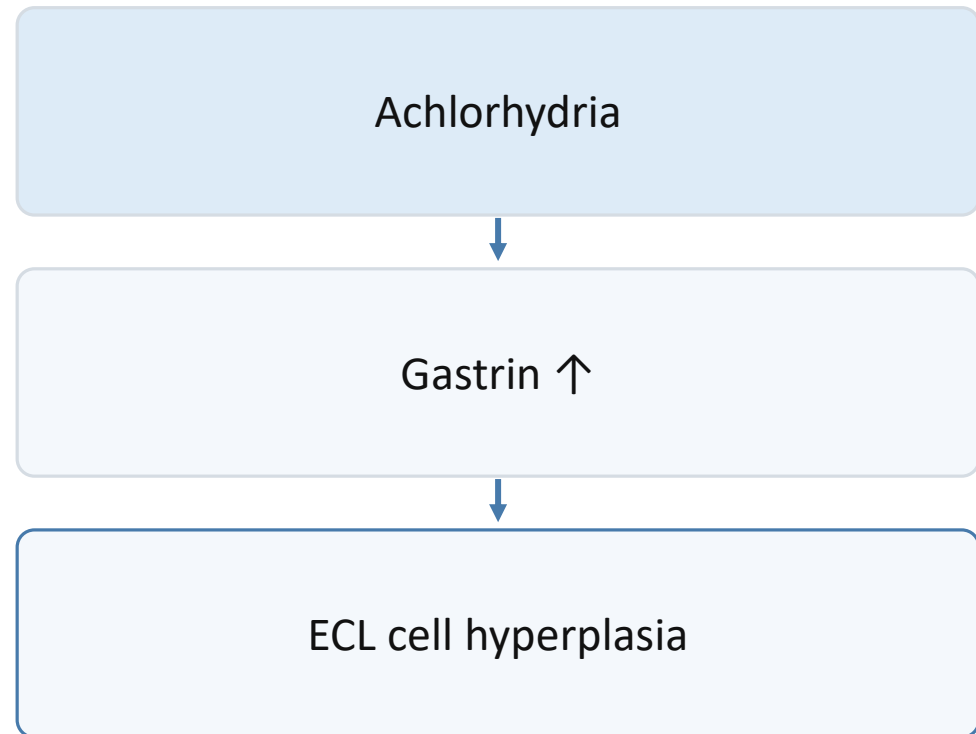
- G cells are located in the relatively preserved antrum.
- Persistent stimulation increases antral G-cell numbers.
- G-cell hyperplasia differs from the oxyntic gland destruction in the corpus.



Characteristic patterns — not exclusive criteria

Hypergastrinemia stimulates endocrine cells

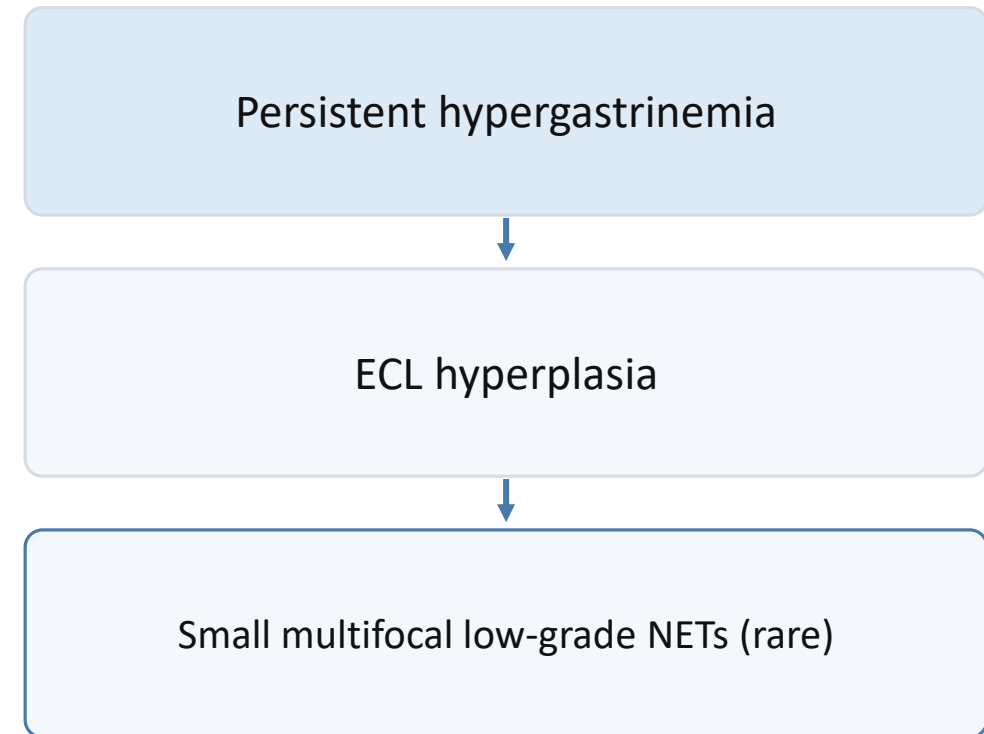
- Gastrin has trophic effects on gastric endocrine populations.
- Endocrine and enterochromaffin-like (ECL) cell hyperplasia is common.
- This is a proliferative consequence of impaired gastric acid production.



Mechanistic sequence — schematic

ECL hyperplasia creates a tumor pathway

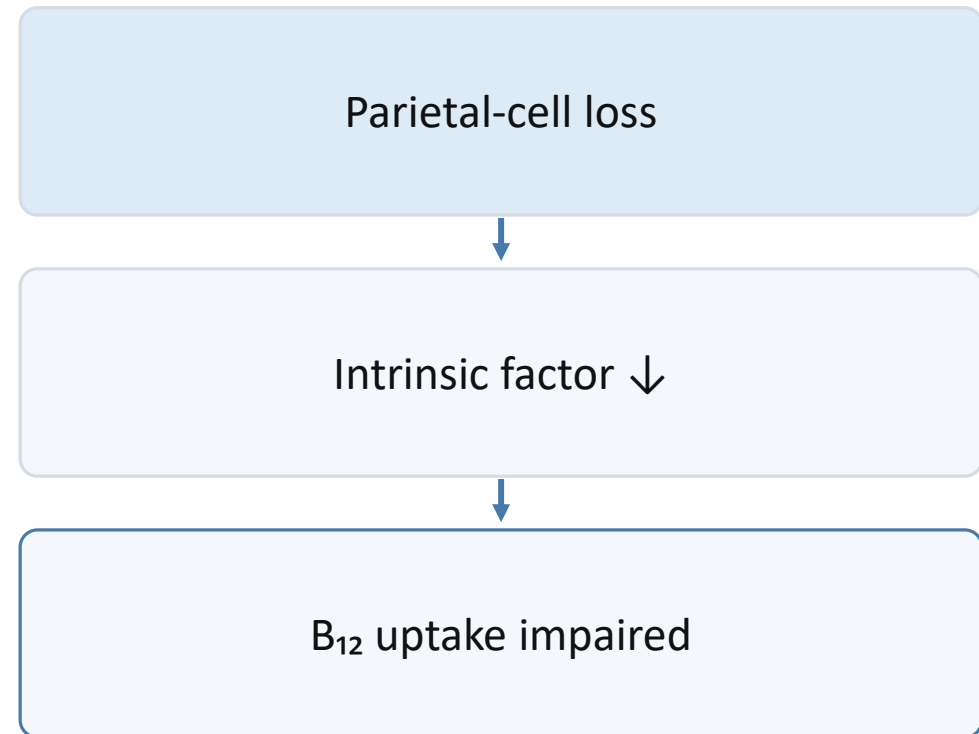
- Diffuse endocrine hyperplasia may be seen within the atrophic corpus.
- Occasionally, it progresses to multiple small, low-grade gastric NETs.
- These lesions are biologically distinct from metaplasia-associated adenocarcinoma.



Mechanistic sequence — schematic

Intrinsic factor is lost with parietal cells

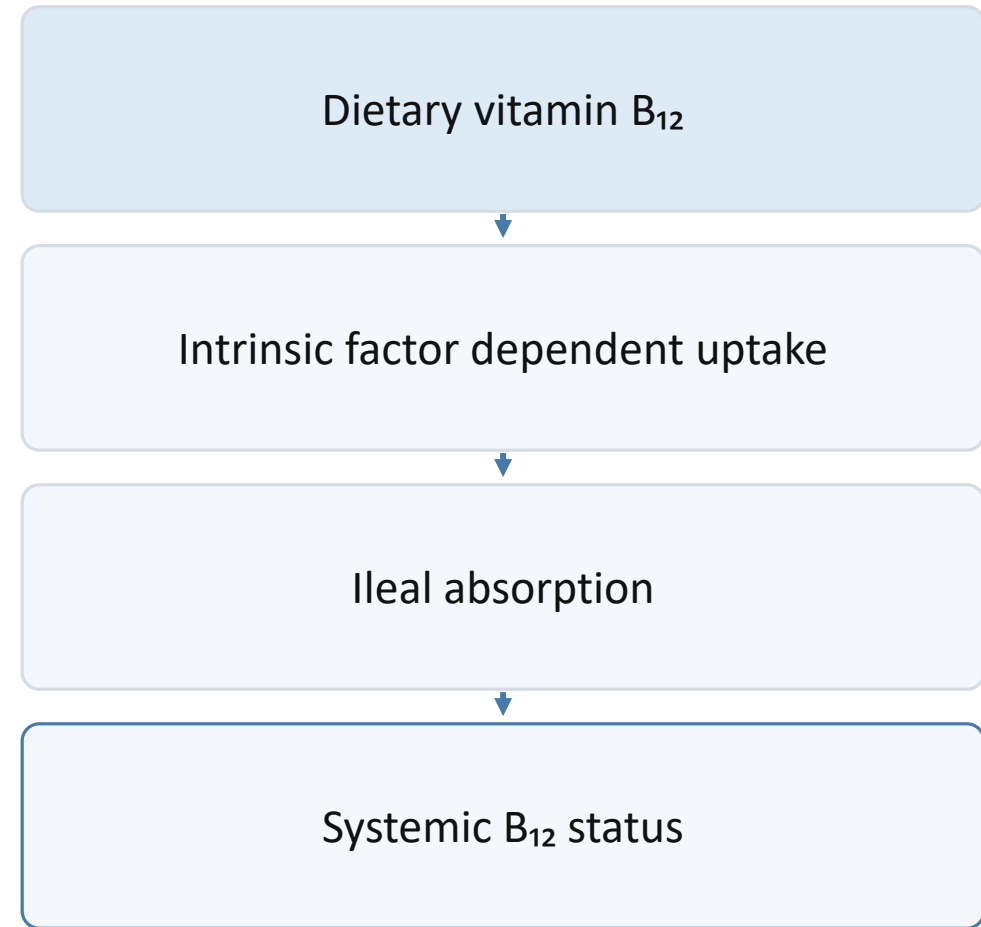
- Intrinsic factor is normally secreted by parietal cells.
- Oxyntic destruction compromises intrinsic factor availability.
- This produces a malabsorptive mechanism independent of dietary B₁₂ intake.



Mechanistic sequence — schematic

Vitamin B₁₂ requires intrinsic factor

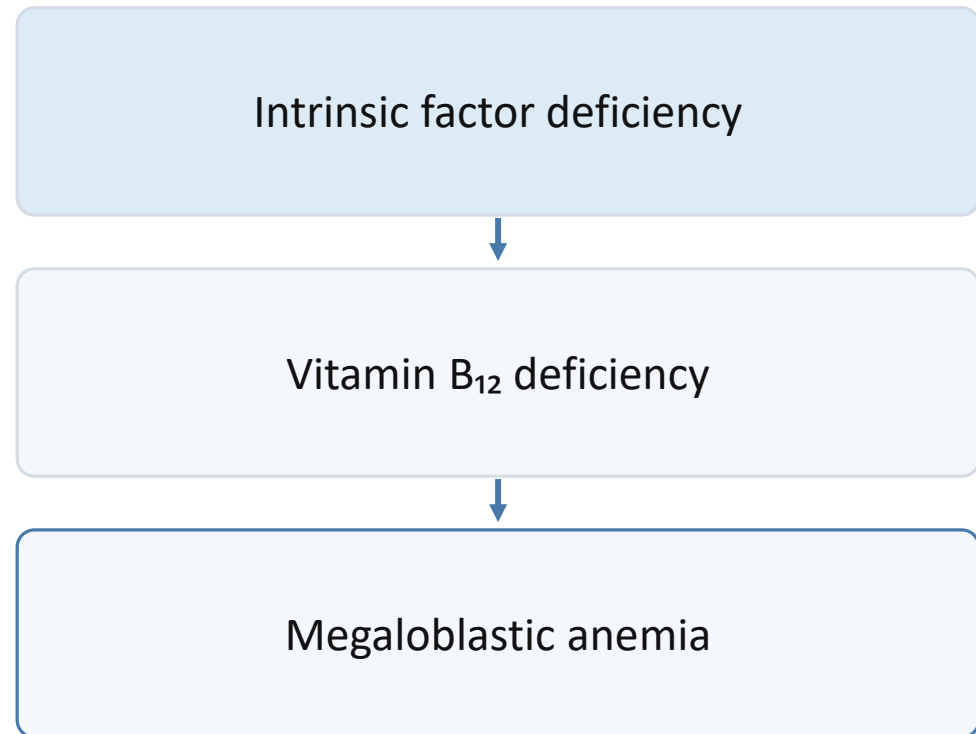
- Intrinsic factor enables vitamin B₁₂ absorption in the ileum.
- Deficiency of intrinsic factor interrupts that absorptive pathway.
- The resulting deficiency becomes clinically evident over time.



Mechanistic sequence — schematic

Pernicious anemia: The hematologic endpoint

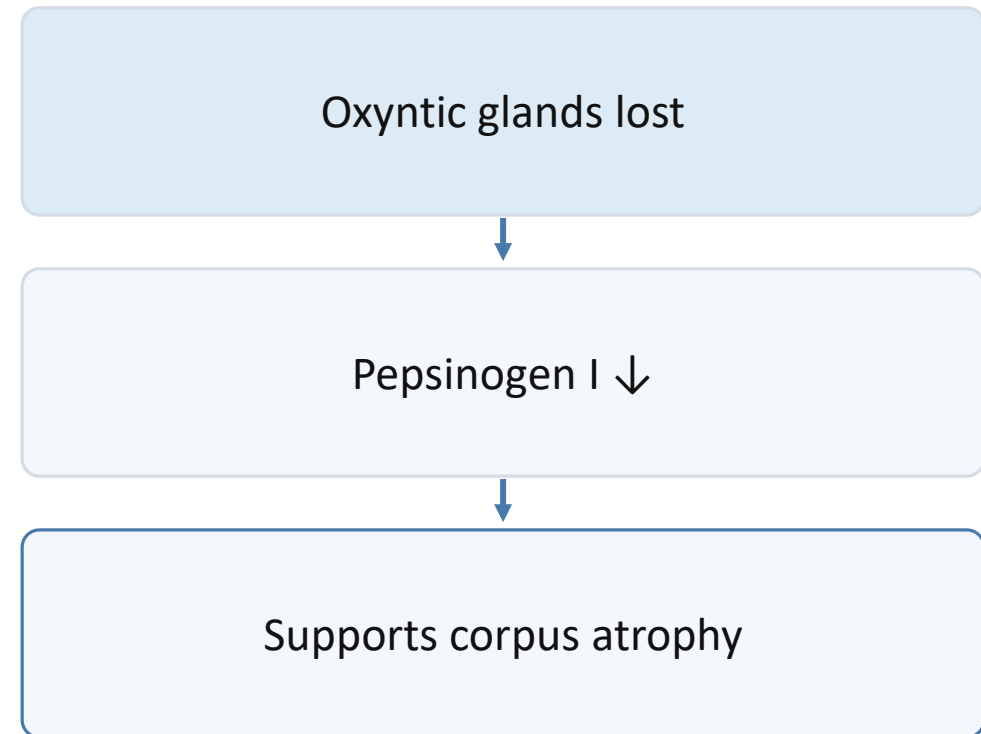
- Intrinsic factor deficiency produces vitamin B₁₂ malabsorption.
- Sustained deficiency leads to megaloblastic anemia.
- Pernicious anemia is a clinical complication, not a synonym for every early autoimmune lesion.



Mechanistic sequence — schematic

Serum pepsinogen I is reduced

- Oxyntic glands contribute to pepsinogen I production.
- Loss of oxyntic gland mass accompanies reduced serum pepsinogen I.
- This is a biochemical correlate of corpus glandular atrophy.



Mechanistic sequence — schematic

Functional biomarker pattern reflects cell loss

- Low acid secretion is a direct consequence of parietal-cell depletion.
- Elevated gastrin is a homeostatic response to low acid.
- Low pepsinogen I is a correlate of oxyntic gland loss.
- Autoantibodies support an autoimmune cause of the tissue damage.

Antibodies

Immune association

Gastrin ↑

Acid feedback loss

Pepsinogen I ↓

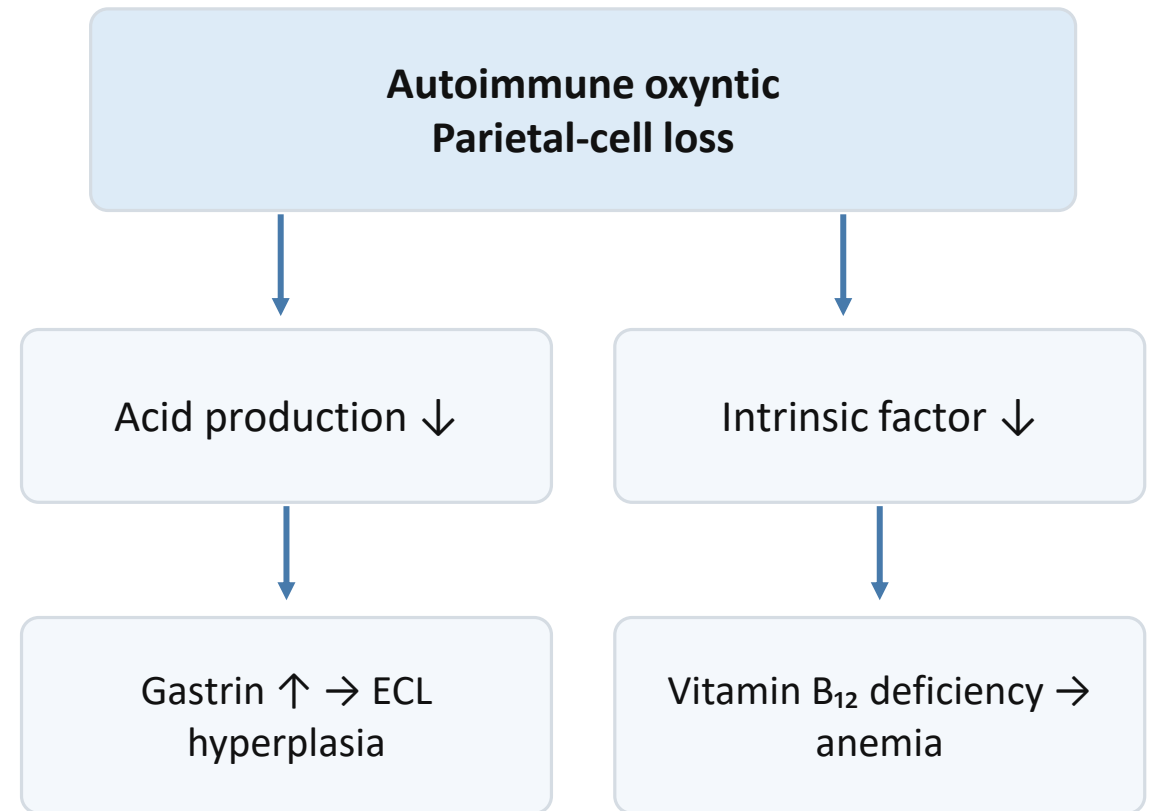
Oxyntic gland loss

Acid ↓

Parietal-cell loss

Two consequences of one destructive lesion

- Parietal-cell loss branches into acid deficiency and intrinsic factor deficiency.
- Acid deficiency drives gastrin and ECL proliferation.
- Intrinsic factor deficiency produces a vitamin B₁₂–dependent multisystem illness.



Two distinct consequences — schematic

Gross morphology: Advanced oxyntic thinning

- The corpus and fundic mucosa may become markedly thinned.
- Normal rugal folds are progressively reduced or lost.
- The antrum may appear comparatively preserved.

Normal rugal contours



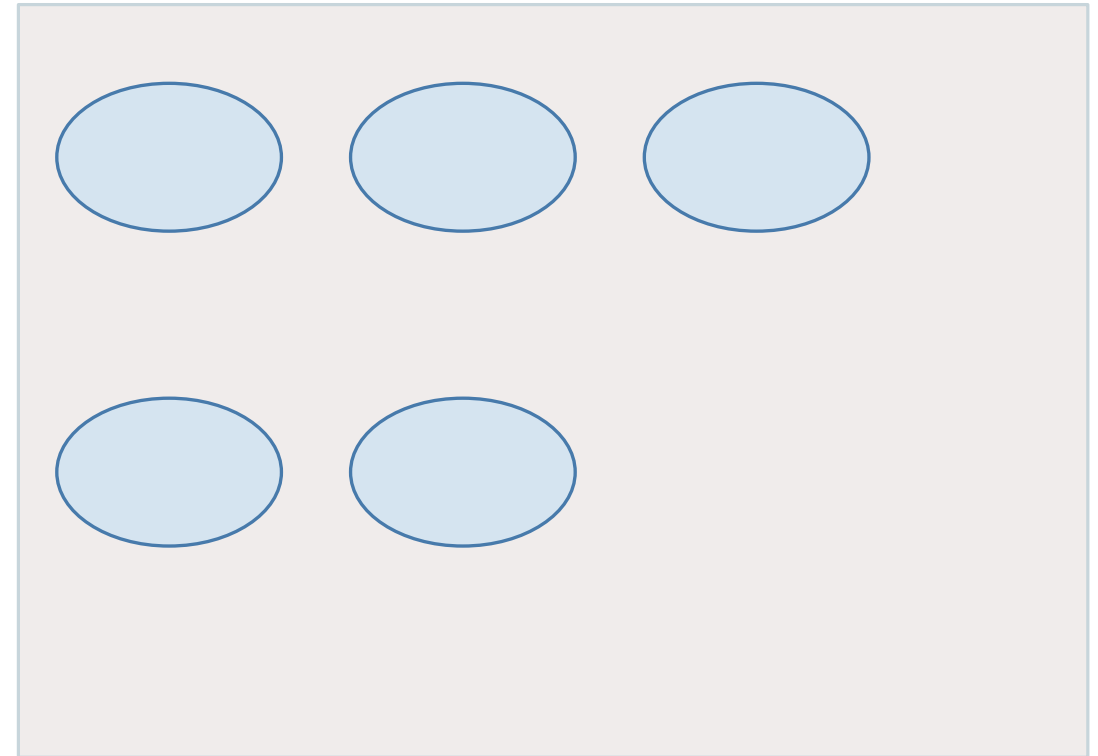
Atrophic corpus: Flatter folds



Conceptual surface contour; Not an endoscopic image

Incomplete atrophy may produce pseudopolyps

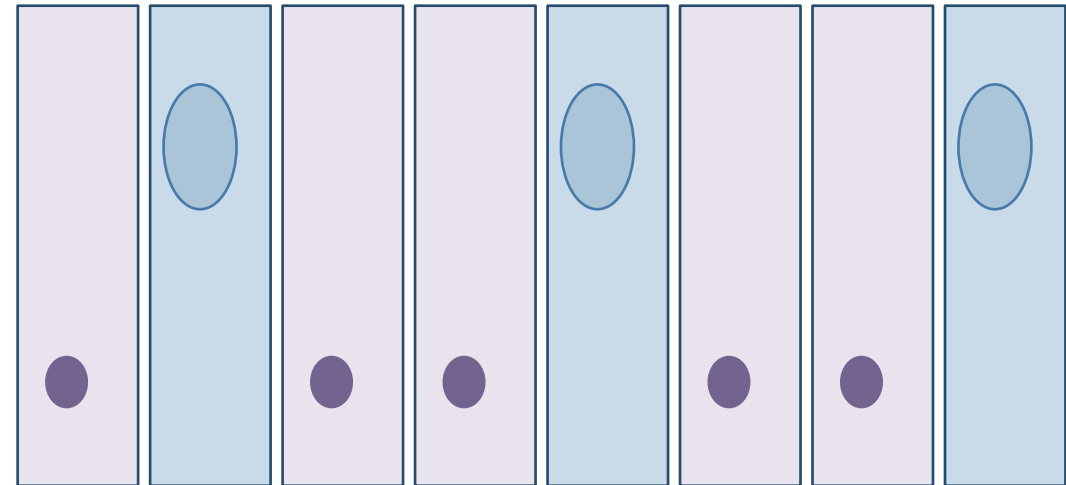
- Islands of surviving oxyntic mucosa may stand above atrophic surroundings.
- The resulting appearance can resemble numerous small polyps or nodules.
- Endoscopic elevation does not automatically imply a neoplasm.



Residual oxyntic islands surrounded by atrophy — schematic

Metaplastic foci can form small elevations

- Focal surface prominences may correspond to intestinal metaplasia.
- These foci replace normal gastric differentiation with intestinal-type cells.
- Gross appearances require correlation with targeted mucosal biopsy.

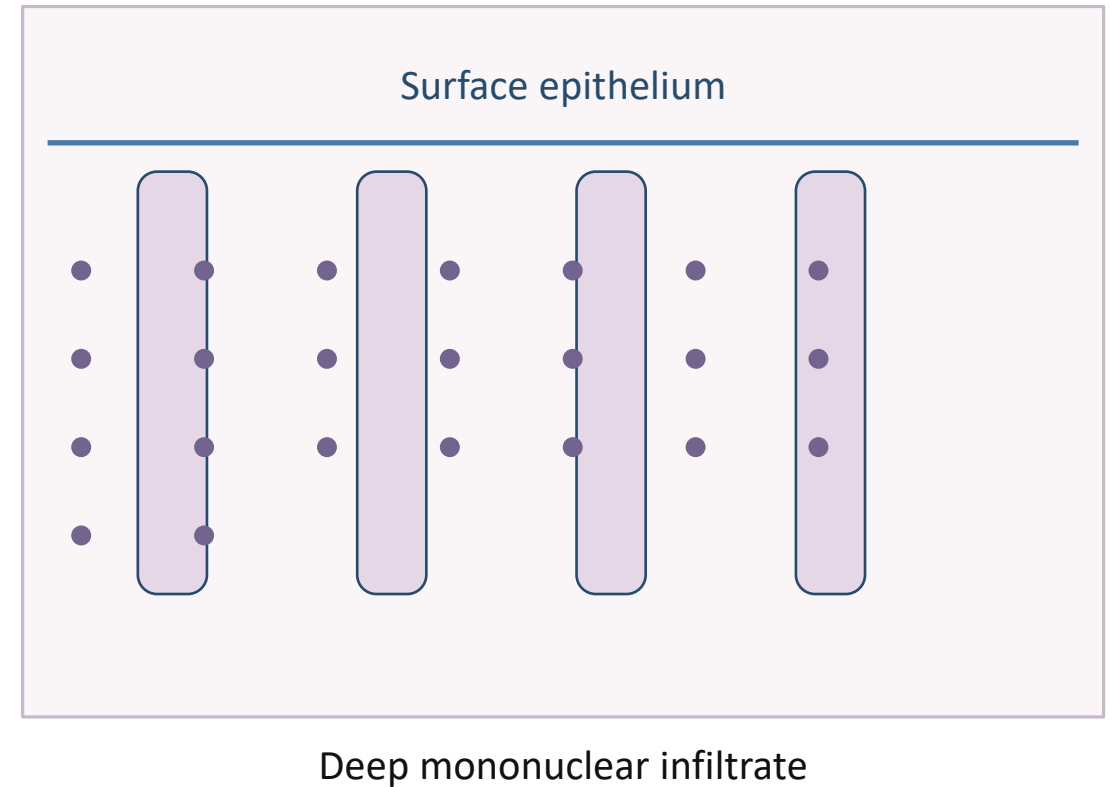


Goblet cell

Illustration of cell phenotype; Not a histologic specimen

The chronic infiltrate is mononuclear

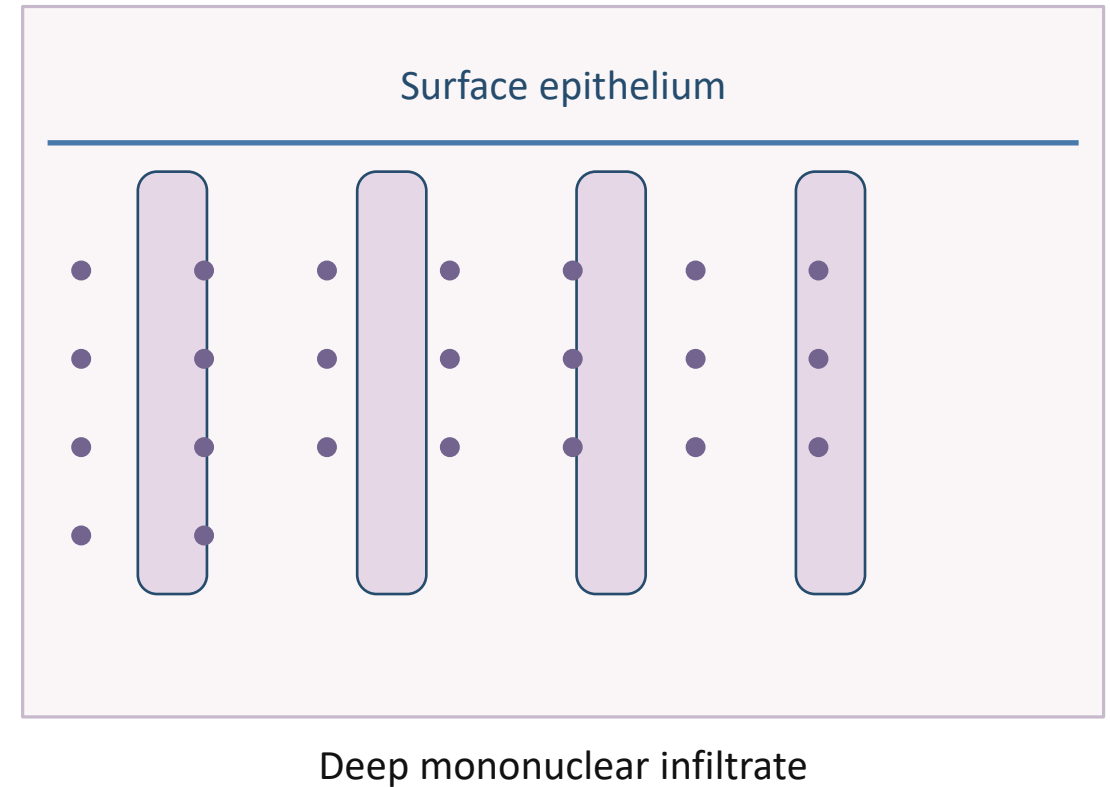
- Lymphocytes, macrophages, and plasma cells predominate.
- Lymphoid aggregates and follicles may accompany the infiltrate.
- Prominent neutrophilic activity is not characteristic of pure autoimmune gastritis.



Simplified mucosal architecture — schematic

Inflammation centers on deeper glands

- Autoimmune inflammatory injury is centered within deep oxyntic mucosa.
- Lymphocytes contact and damage the glandular compartment.
- This differs from the superficial emphasis of typical *H. Pylori* gastritis.



Simplified mucosal architecture — schematic

Superficial versus deep inflammation matters

- H. Pylori gastritis often shows superficial plasma-cell-rich inflammation.
- H. Pylori can show epithelial neutrophils and pit abscesses.
- Autoimmune gastritis favors deeper lymphocyte/macrophage-rich gland injury.

H. Pylori

Superficial lamina propria

Neutrophilic activity

Autoimmune

Deep oxyntic glands

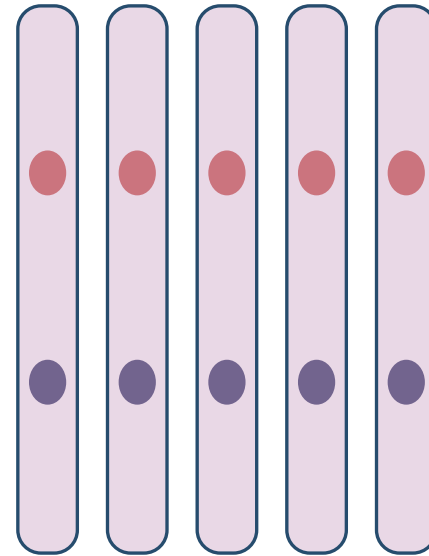
Mononuclear injury

Characteristic patterns — not exclusive criteria

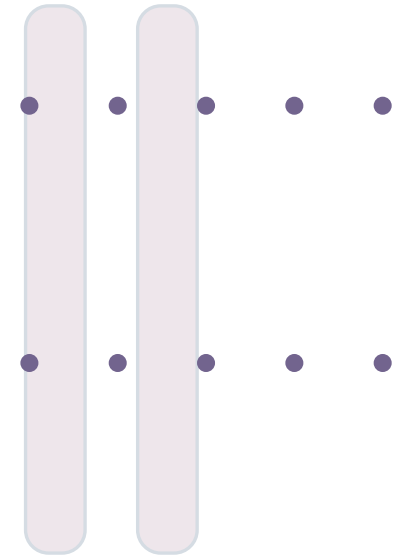
Histology: Parietal and chief cells disappear

- Oxyntic glands lose their characteristic parietal-cell component.
- Chief cell loss may be extensive as gland numbers decrease.
- Replacement epithelium and stromal inflammation alter normal gland architecture.

Intact oxyntic mucosa



Atrophic oxyntic mucosa

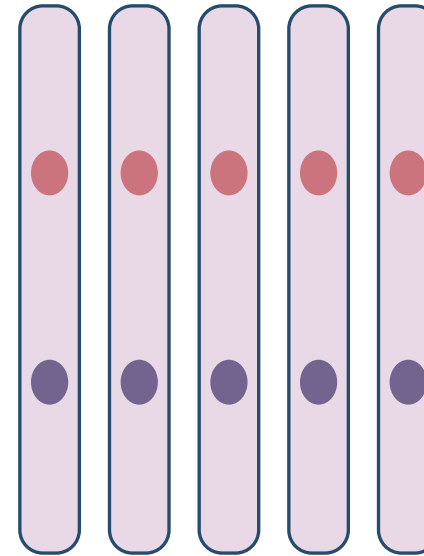


Simplified gland architecture; Not an H&E image

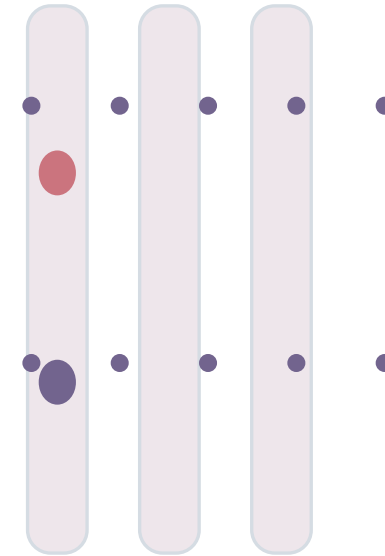
Partial involvement leaves uneven gland islands

- Residual oxyntic glands can persist within extensive atrophic mucosa.
- The architecture may be patchy before complete destruction.
- Tissue sampling can therefore influence how much atrophy is represented.

Intact oxyntic mucosa



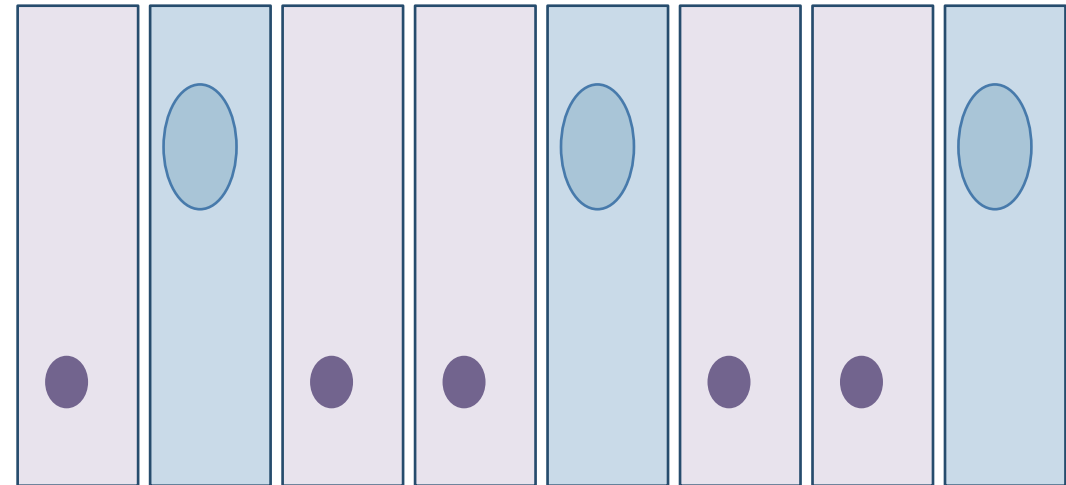
Residual gland islands



Simplified gland architecture; Not an H&E image

Intestinal metaplasia is recognizable by goblet cells

- The surface and gland epithelium may acquire intestinal differentiation.
- Goblet cells are the key morphologic clue.
- Metaplastic glands replace a portion of the former gastric mucosa.

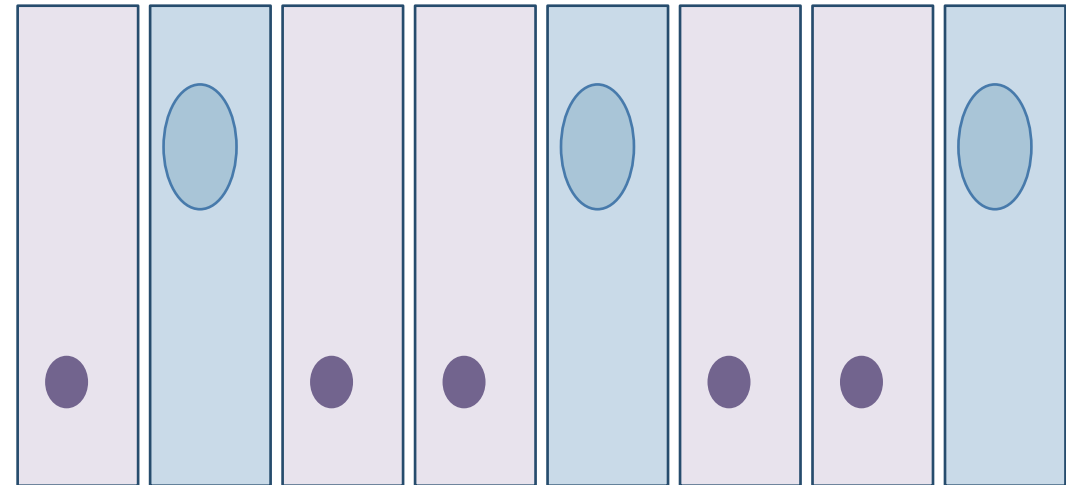


Goblet cell

Illustration of cell phenotype; Not a histologic specimen

Other intestinal-type cells may accompany metaplasia

- Metaplastic epithelium may also contain absorptive cells.
- Paneth cells can appear in some intestinalized gastric mucosa.
- The replacement cell phenotype documents altered epithelial differentiation.

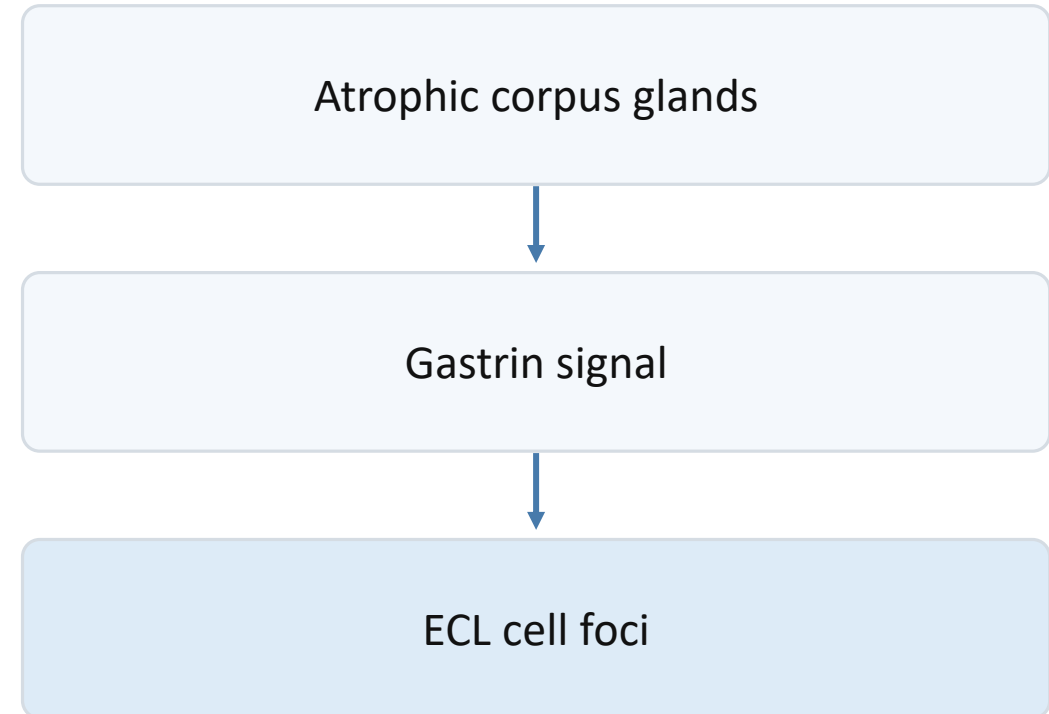


Goblet cell

Illustration of cell phenotype; Not a histologic specimen

Endocrine proliferation is a separate histologic clue

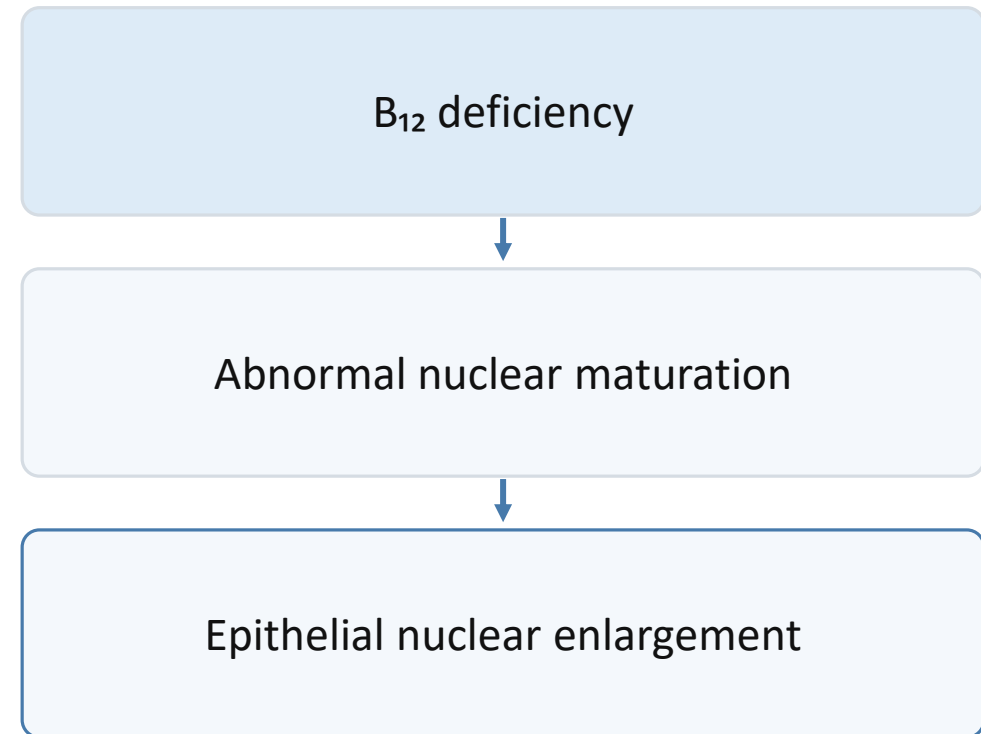
- Hyperplasia of endocrine and ECL cells commonly accompanies atrophy.
- This finding reflects sustained gastrin stimulation.
- It should not be conflated with the presence of an established NET.



Schematic endocrine response, not IHC

Severe B₁₂ deficiency affects the epithelium

- Deficiency can cause enlarged epithelial nuclei (megaloblastic change).
- This is a systemic nutritional consequence expressed in a rapidly dividing mucosa.
- It is not the primary mechanism of parietal-cell destruction.



Mechanistic sequence — schematic

A characteristic biopsy constellation

- Body/fundus: Prominent oxyntic gland loss with deep chronic inflammation.



Corpus-predominant gland loss

- Associated intestinal metaplasia and endocrine-cell hyperplasia.



Deep chronic infiltrate

- Antrum relatively preserved; Neutrophils usually not prominent.



Intestinal metaplasia



ECL hyperplasia

Correct site labeling strengthens interpretation

- Interpret body/fundus biopsy findings in light of native oxyntic glands.
- Compare antral findings rather than assuming diffuse pan-gastric injury.
- Location, gland phenotype, and inflammation must be read together.

Body + fundus

Oxyntic glands / parietal cells
Main autoimmune target

Antrum

G cells • typically relatively spared

Functional region map — schematic

Serology supports—not replaces—morphology

- Anti-parietal cell and anti-intrinsic factor antibodies support an autoimmune process.
- Antibodies may be detected long before histologic atrophy or anemia.
- A concordant corpus-predominant pattern provides the necessary tissue context.

Serology

Etiologic support

Can precede lesions

Biopsy

Anatomic pattern

Demonstrates atrophy

Characteristic patterns — not exclusive criteria

Antibody frequencies: Avoid overinterpretation

- Anti-pump/intrinsic factor antibodies in up to 80% of patients.
- This is a grouped statement; It does not establish equal performance for both assays.
- Negative serology does not erase a characteristic injury pattern.

Up to 80%

Reported antibody
presence

2–3 decades

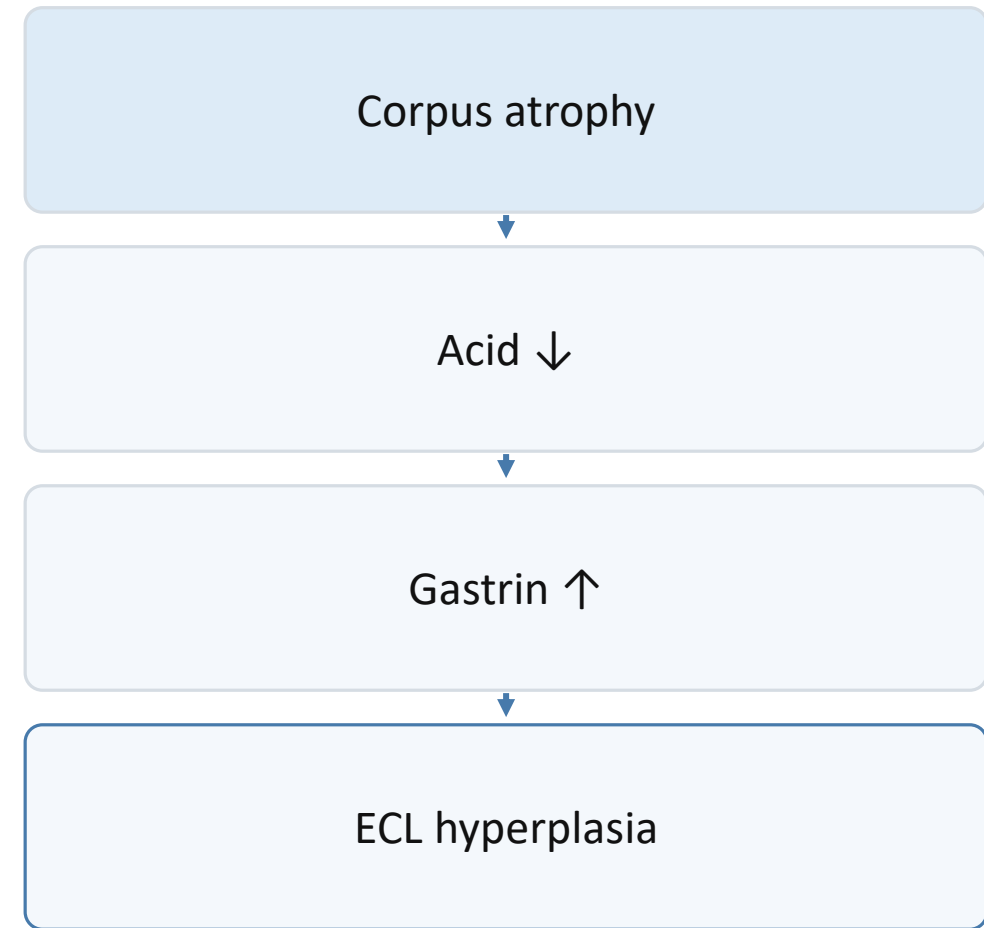
Possible preclinical
lead time

**No fixed
cutoff**

Source gives no
diagnostic threshold

Hypergastrinemia has a mechanistic explanation

- The stomach can produce high gastrin while still secreting little acid.
- Loss of parietal-cell mass is the limiting lesion.
- ECL hyperplasia is a tissue correlate of the endocrine response.



Mechanistic sequence — schematic

Reduced pepsinogen I points toward oxyntic loss

- Chief-cell depletion accompanies loss of body/fundic glands.
- Lower pepsinogen I reflects reduced secretory gland mass.
- The marker is characteristic, not a standalone diagnostic test.

The major manifestations reflect B₁₂ deficiency

- The clinical syndrome can involve bone marrow, oral mucosa, intestine, and nervous system.
- Symptoms need not be confined to epigastric discomfort.
- The gastric autoimmune process explains the systemic findings.

Bone marrow
Megaloblastosis

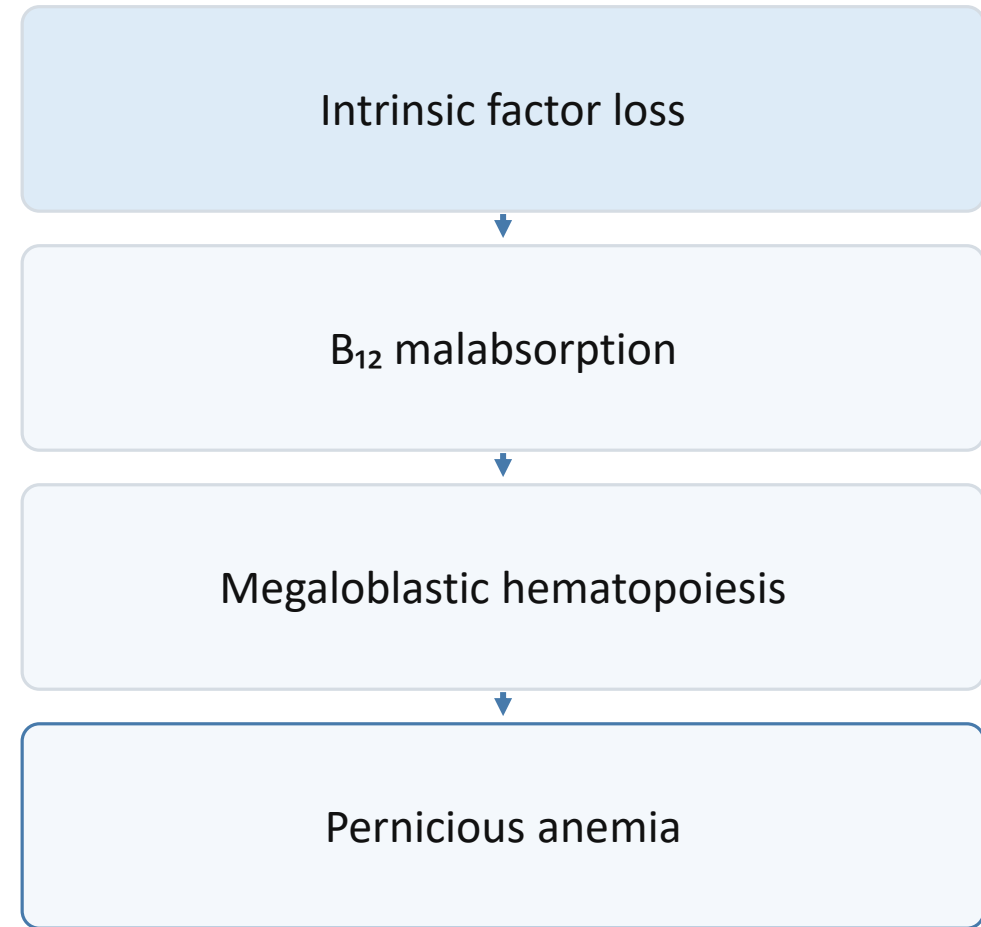
Oral mucosa
Atrophic glossitis

Intestine
Malabsorptive diarrhea

Spinal cord
Subacute combined
degeneration

Megaloblastic anemia results from deficient B₁₂

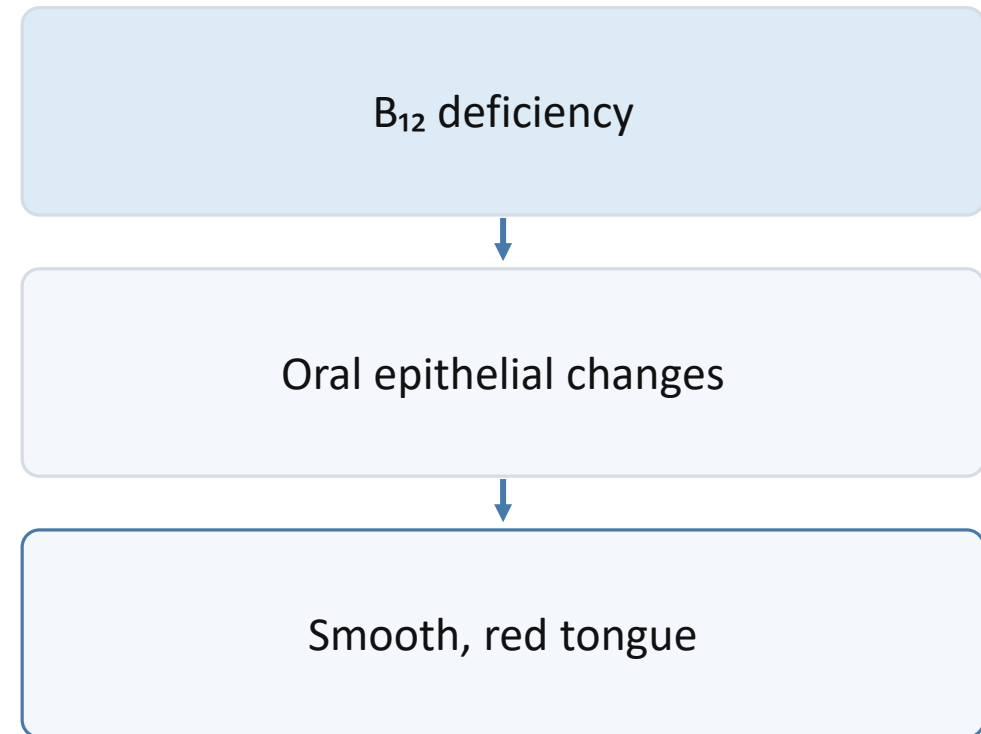
- Intrinsic factor loss impairs B₁₂ absorption in the terminal ileum.
- Hematopoietic precursors develop megaloblastic maturation abnormalities.
- Anemia can become a presenting feature of previously unrecognized gastric disease.



Mechanistic sequence — schematic

Atrophic glossitis is a mucosal signal

- Deficient B₁₂ can result in a smooth, beefy-red tongue.
- The loss of papillary texture is termed atrophic glossitis.
- This supports the clinical link between stomach pathology and epithelial turnover.



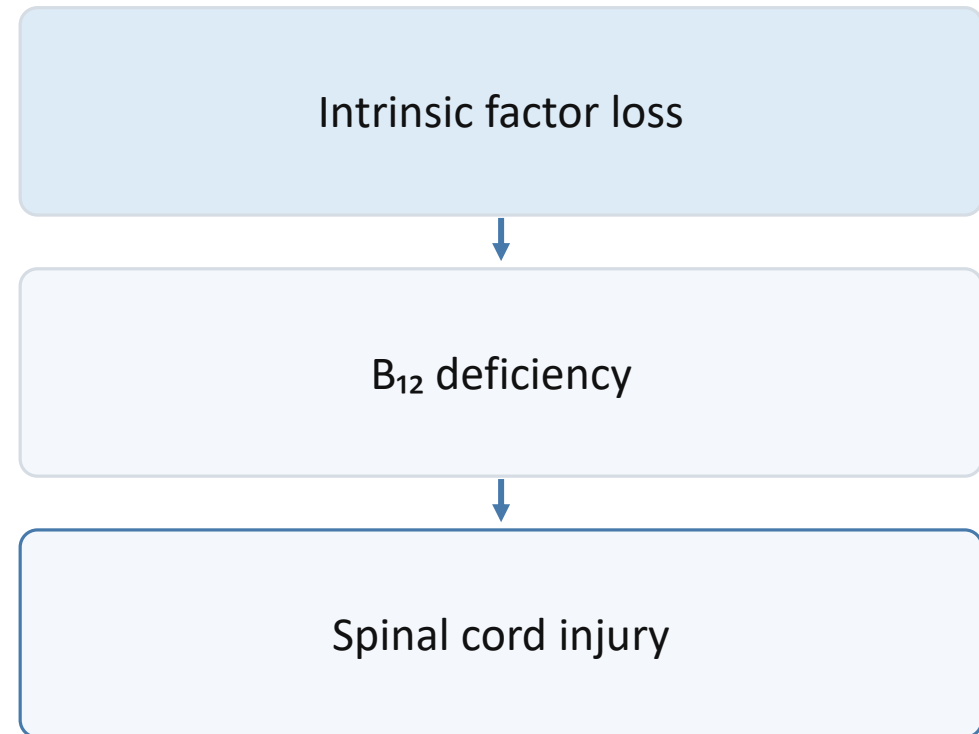
Mechanistic sequence — schematic

Intestinal symptoms can accompany deficiency

- Malabsorptive diarrhea among clinical manifestations.
- Epithelial megaloblastosis helps link cellular dysfunction and symptoms.
- The presence or absence of diarrhea does not define the gastric histologic pattern.

Neurologic consequences require recognition

- Vitamin B₁₂ deficiency can involve the central nervous system.
- Subacute combined degeneration of the spinal cord is a major example.
- A clinical assessment limited to hemoglobin can miss neurologic involvement.



Mechanistic sequence — schematic

Associated autoimmune disorders are a clue

- Hashimoto thyroiditis is a frequent named association.
- Type 1 diabetes mellitus and Addison disease are also documented.
- A multisystem autoimmune history increases the relevance of the gastric pattern.

Hashimoto
Thyroiditis

Type 1
Diabetes mellitus

Addison
Disease

Family
Clustering

Associations; Not diagnostic criteria

Comparison: Injury site and cell infiltrate

- Topography and depth of inflammation provide the first discriminators.
- The table summarizes the characteristic textbook patterns, not absolute rules.

Feature	H. pylori-associated	Autoimmune
Predominant site	Antrum	Body / fundus
Inflammatory pattern	Neutrophils; superficial plasma cells	Lymphocytes, macrophages; deep injury
Acid output	Increased to slightly decreased	Decreased
Gastrin	Normal to increased	Increased to markedly increased

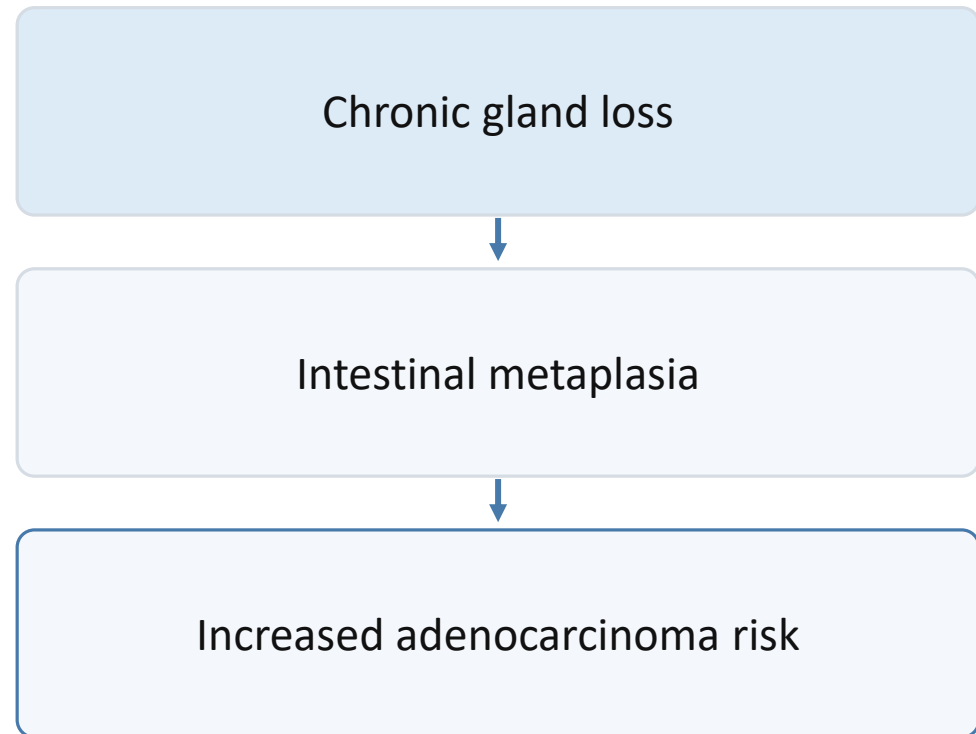
Comparison: Markers and clinical sequelae

- Etiologic markers and end-organ outcomes help refine a morphologic differential.
- Both chronic inflammatory conditions may carry gastric cancer risk.

Feature	H. pylori-associated	Autoimmune
Serology	Anti-H. pylori	Anti-parietal cell / anti-IF
Other lesion	Inflammatory / hyperplastic polyps	ECL / endocrine hyperplasia
Characteristic sequel	Peptic ulcer; MALT lymphoma	Atrophy; pernicious anemia; NET
Autoimmunity	Not a defining association	Thyroiditis, type 1 diabetes, etc.

Cancer risk follows chronic atrophy and metaplasia

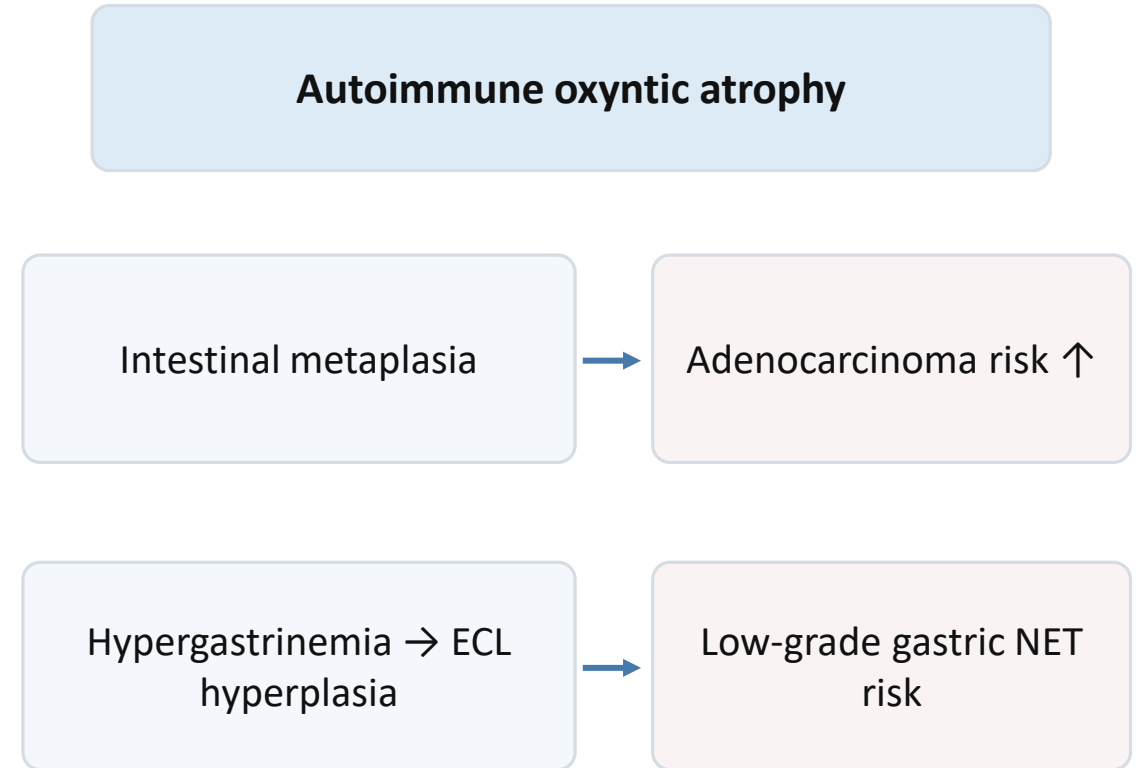
- Chronic oxyntic atrophy is frequently associated with intestinal metaplasia.
- Intestinal metaplasia is strongly associated with gastric adenocarcinoma risk.
- Particularly high risk in autoimmune metaplastic atrophy.



Mechanistic sequence — schematic

Adenocarcinoma and NET arise by distinct routes

- Epithelial intestinal metaplasia is associated with adenocarcinoma risk.
- Gastrin-driven ECL cell proliferation can lead to low-grade NETs.
- Both consequences occur in the same autoimmune atrophic setting.



Associated pathways; Neither outcome is inevitable

Avoid a diagnostic shortcut

- Antibody positivity alone does not establish the extent of gastric atrophy.



Corpus-predominant gland loss

- Marked gastrin elevation must be interpreted alongside acid-secretory context.



Deep chronic infiltrate

- A biopsy showing goblet cells must still be localized within the stomach.



Intestinal metaplasia



ECL hyperplasia

Teaching case: Anemia with autoimmune history

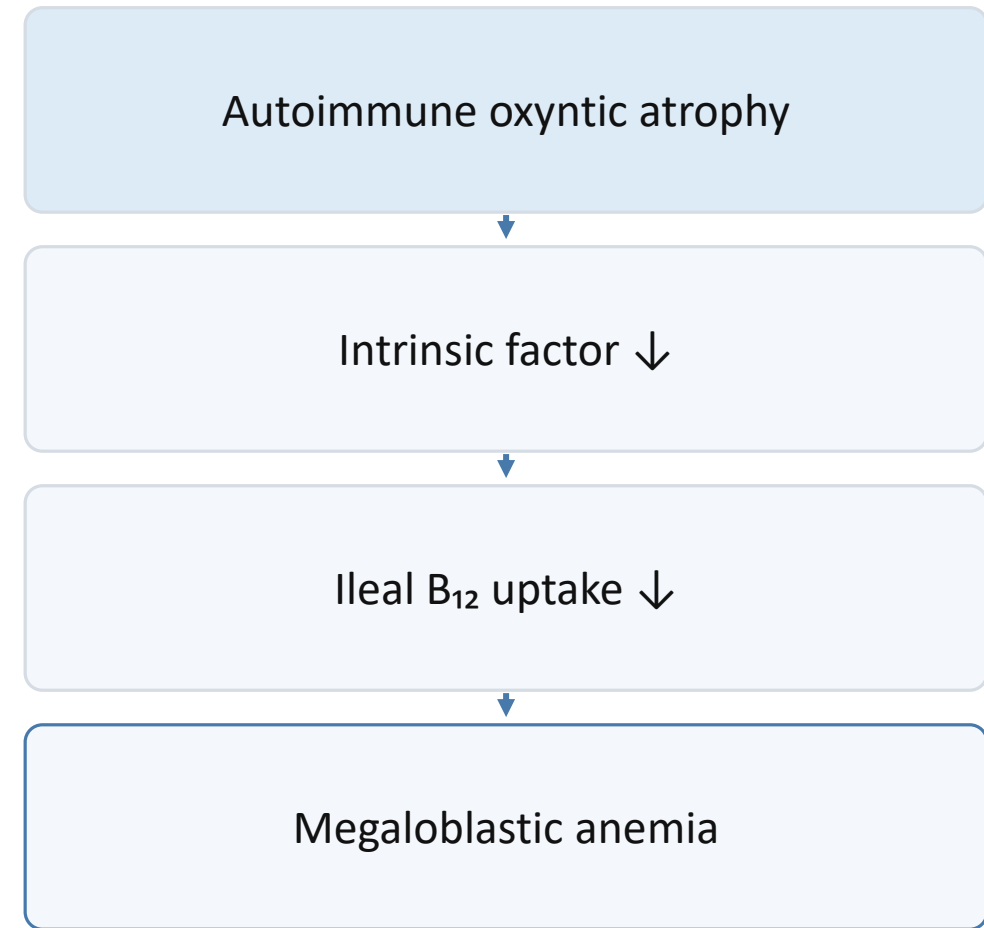
- Hypothetical patient: 61-year-old woman with fatigue and a history of Hashimoto thyroiditis.
- Laboratory evaluation reveals vitamin B₁₂ deficiency and parietal-cell antibodies.
- Biopsies show body-predominant oxyntic gland loss with relative antral preservation.
- Question: Identify the unifying gastric process and explain the anemia.

Hypothetical teaching case

Correlate anatomy + serology + function

Case interpretation: Two linked deficiencies

- The anatomic distribution and autoantibodies support autoimmune atrophic gastritis.
- Parietal-cell loss leads to intrinsic factor deficiency.
- Ileal B₁₂ malabsorption explains the pernicious-anemia phenotype.



Mechanistic sequence — schematic

Teaching case: Hypergastrinemia without acid

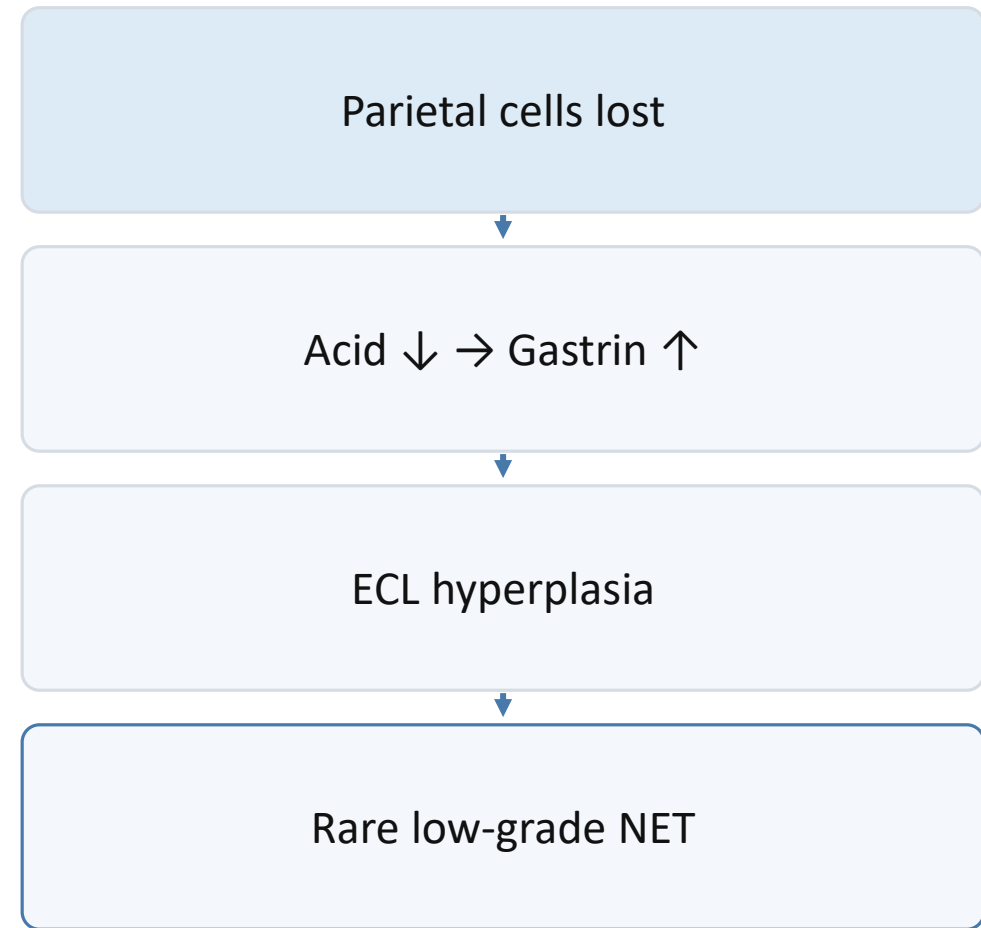
- Hypothetical patient: Body/fundus atrophy, little gastric acid secretion, markedly elevated gastrin.
- Biopsy demonstrates endocrine-cell hyperplasia in the atrophic corpus.
- Question: Why does gastrin rise when gastric acid remains low?

Hypothetical teaching case

Correlate anatomy + serology + function

Case interpretation: Feedback cannot restore glands

- Loss of acid suppresses the normal inhibitory feedback on gastrin release.
- G cells increase gastrin secretion, but the target parietal-cell mass is depleted.
- Gastrin continues to stimulate ECL cells, creating a NET-predisposing milieu.



Mechanistic sequence — schematic

Histopathology synthesis

- Identify the oxyntic site and the deep, gland-centered chronic infiltrate.



Corpus-predominant gland loss

- Evaluate the degree of parietal/chief cell loss and intestinal metaplasia.



Deep chronic infiltrate

- Recognize endocrine hyperplasia, usually preserved antrum, and the clinical B₁₂ context.



Intestinal metaplasia

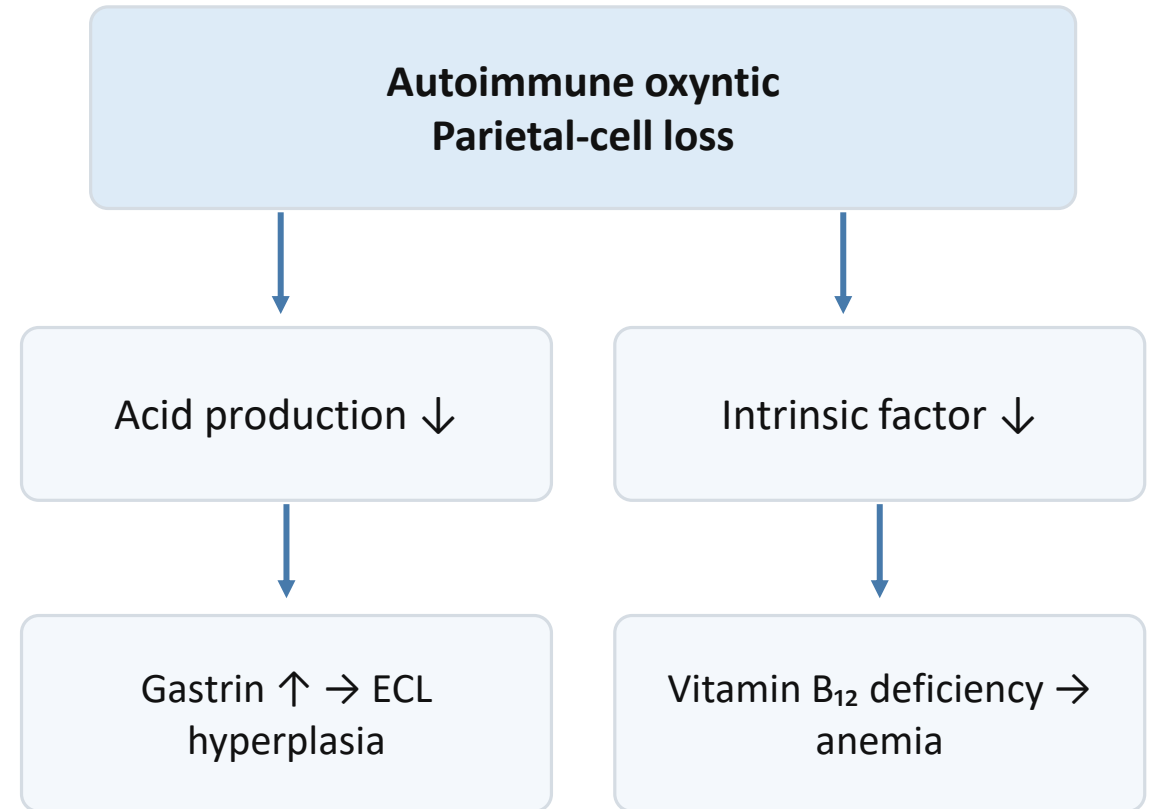
- Contrast with superficial, often neutrophilic H. Pylori gastritis.



ECL hyperplasia

Key clinicopathologic causal chain

- CD4⁺ T cells and anti-parietal cell immunity → oxyntic gland injury.
- Parietal-cell loss → achlorhydria → hypergastrinemia → ECL proliferation.
- Intrinsic factor loss → vitamin B₁₂ deficiency → pernicious anemia / neurologic risk.
- Atrophy plus metaplasia → increased gastric adenocarcinoma risk.



Two distinct consequences — schematic

Primary reference and source boundaries

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026).
- Chapter 17: The Gastrointestinal Tract—autoimmune atrophic gastritis.
- Adjacent source context: stomach anatomy, *H. pylori* gastritis, and mucosal metaplasia.
- Morphology diagrams are original schematics, not tissue photomicrographs.