

Ménétrier Disease

Hypertrophic gastropathy • morphology, mechanisms, and clinical consequences

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Learning objectives

- Recognize the distinctive gross and microscopic features of Ménétrier disease.
- Connect TGF- α /EGFR signaling to foveolar hyperplasia and gastric protein loss.
- Differentiate this disorder from other gastric fold enlargements and apply the clinicopathologic pattern.

The stomach has region-specific mucosa

- Fundus and body contain well-developed oxyntic glands.
- The antrum and cardia emphasize mucin-secreting epithelium and smaller glands.
- Disease location helps identify the dominant cellular response.

Fundus

Oxyntic glands

Body

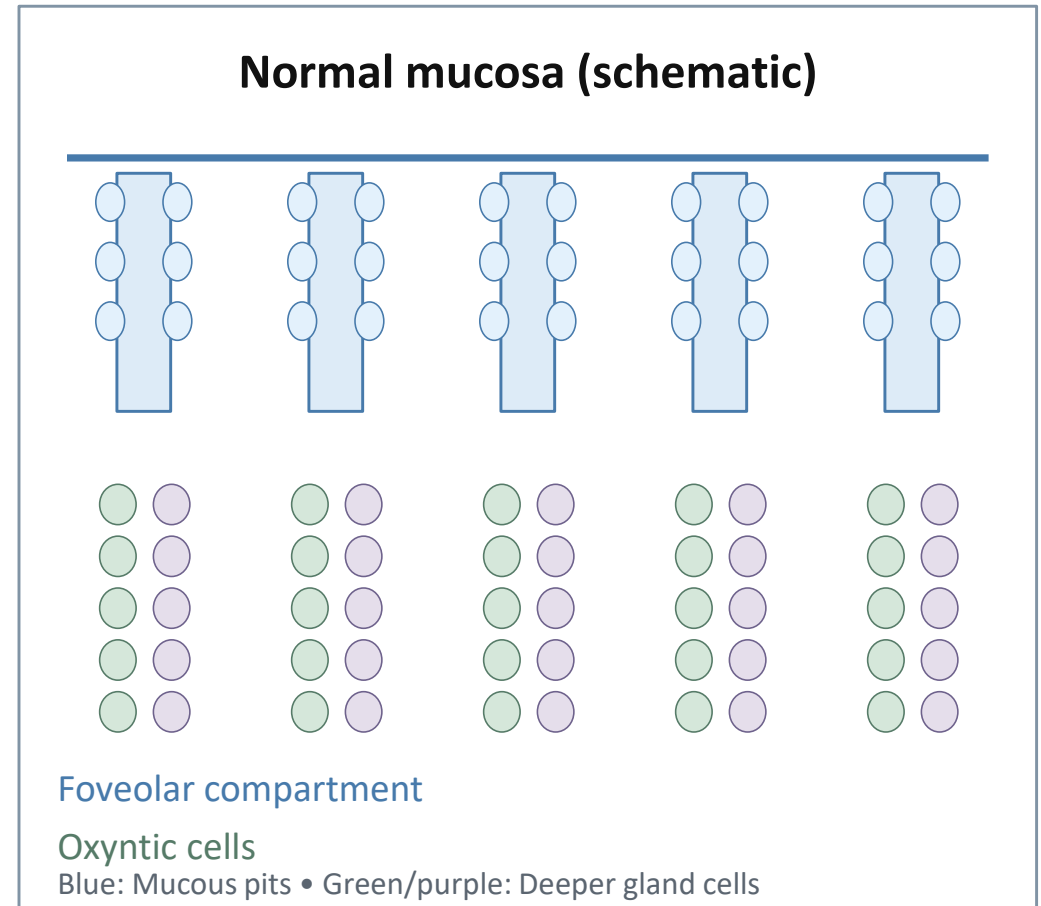
Oxyntic glands

Antrum

Mucin-secreting /
endocrine

Normal oxyntic mucosa: A functional baseline

- Surface and foveolar mucous epithelium lines the lumen and pits.
- The deeper body/fundus glands contain acid-secreting parietal cells and enzyme-secreting chief cells.
- Both compartments must be considered when reading hypertrophic mucosa.

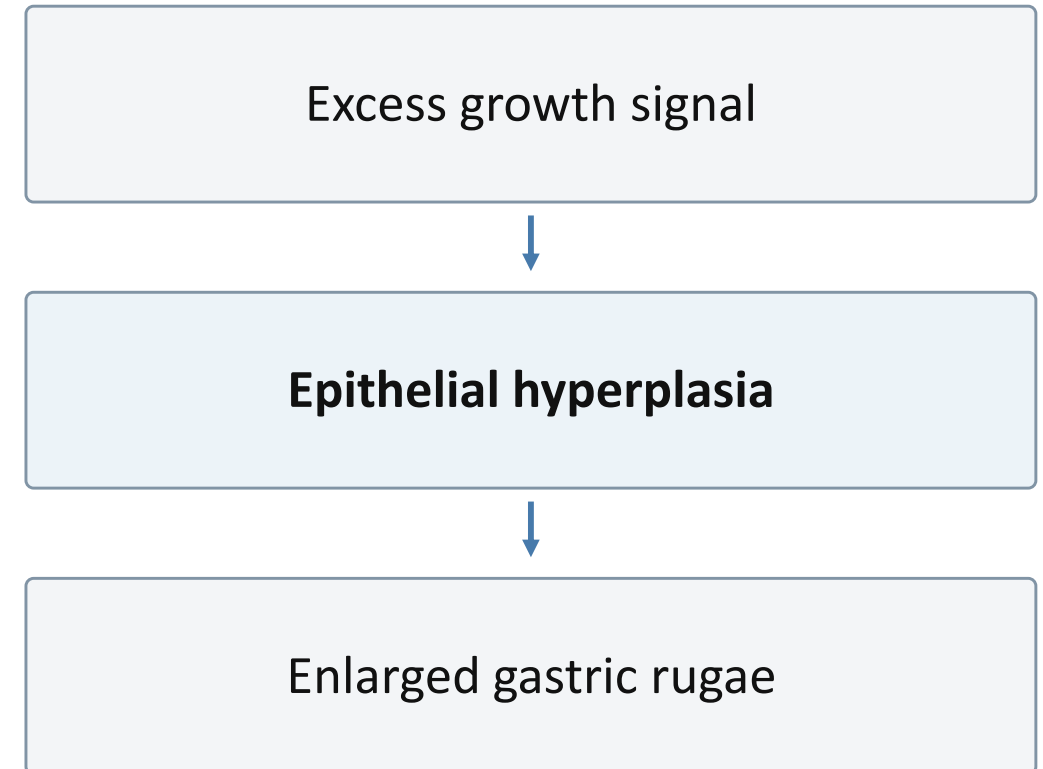


Gastropathy differs from gastritis

- Gastropathy emphasizes epithelial or mucosal injury/change without prominent inflammatory infiltration.
- Gastritis refers to an inflammatory process in the gastric mucosa.
- A markedly thickened fold is not necessarily an inflammatory lesion.

What is a hypertrophic gastropathy?

- Uncommon gastric disorders can cause giant, cerebriform rugal folds.
- In the Robbins parent section, epithelial hyperplasia is the fundamental basis of fold enlargement.
- Excess growth-factor signaling provides a mechanistic link.



Two archetypal hypertrophic gastropathies

- Ménétrier disease: Predominantly mucous/foveolar epithelial hyperplasia.
- Zollinger–Ellison syndrome: Predominantly parietal-cell hyperplasia with acid-driven ulceration.
- The same gross descriptor—large folds—can reflect different cellular processes.

Ménétrier disease

Foveolar mucous cells

Protein loss

Zollinger–Ellison

Parietal cells

Peptic ulcers

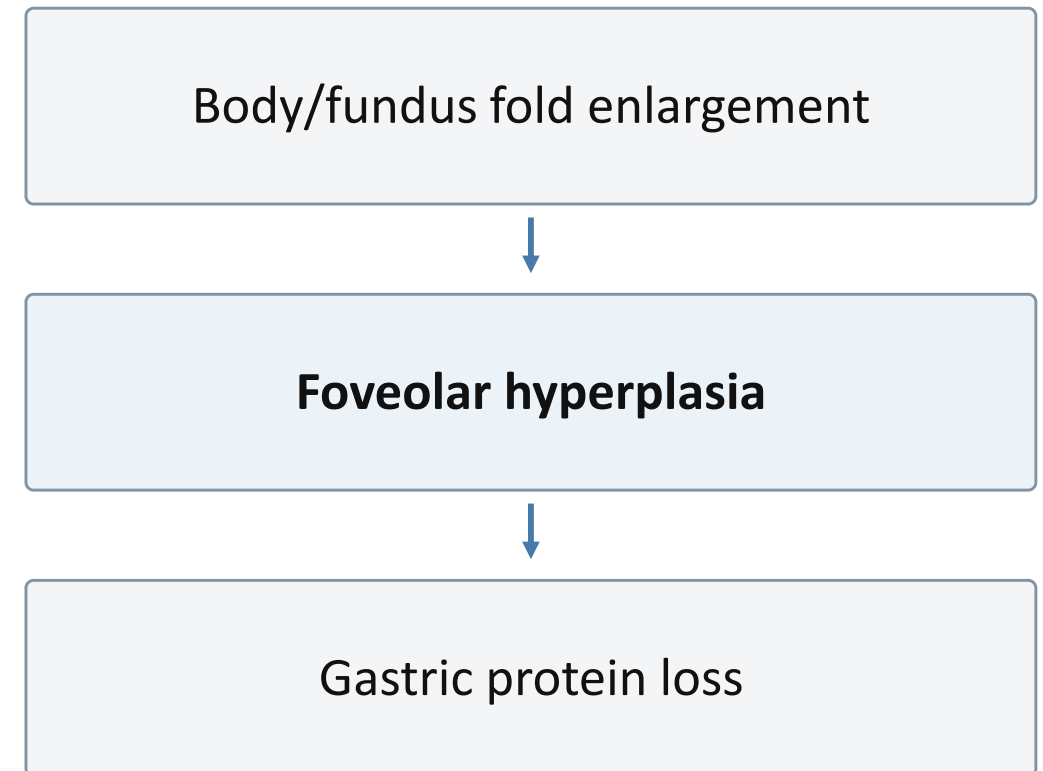
Schematic • contrasting patterns

Core definition of Ménétrier disease

- Rare hypertrophic gastropathy with diffuse foveolar hyperplasia.
- Typically centered in the gastric body and fundus.
- A protein-losing gastric mucosa produces clinically significant hypoproteinemia.

The defining clinicopathologic pattern

- The anatomic, epithelial, and biochemical abnormalities belong to one process.
- Neither enlarged folds alone nor hypoalbuminemia alone identifies the disease.
- Integrate morphology with protein loss and exclusion of mimics.



Body and fundus are the principal sites

- Irregularly enlarged rugae localize mainly to the body and fundus.
- The antrum is generally spared rather than obligatorily normal in every patient.
- Distribution directs endoscopic assessment and histologic sampling.

Fundus

Enlarged rugae

Body

Enlarged rugae

Antrum

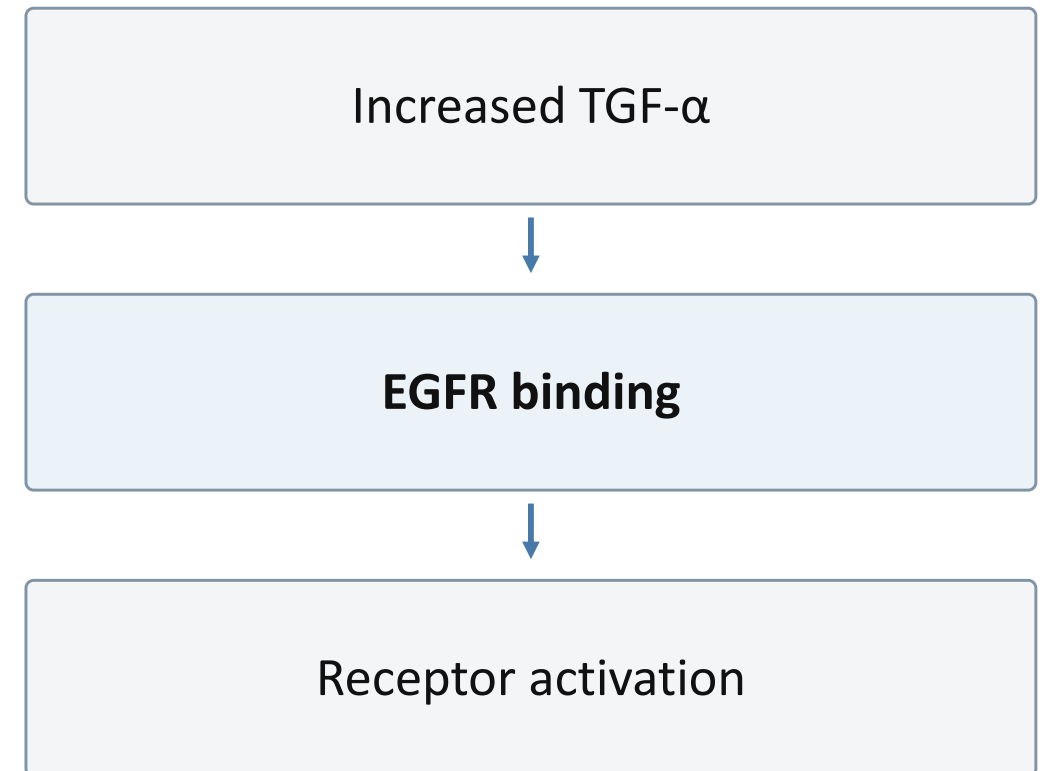
Generally spared

What makes the disease clinically consequential?

- Protein can be lost directly across the abnormal gastric mucosa.
- Albumin depletion manifests as low circulating protein and peripheral edema.
- Adults have an increased association with gastric adenocarcinoma.

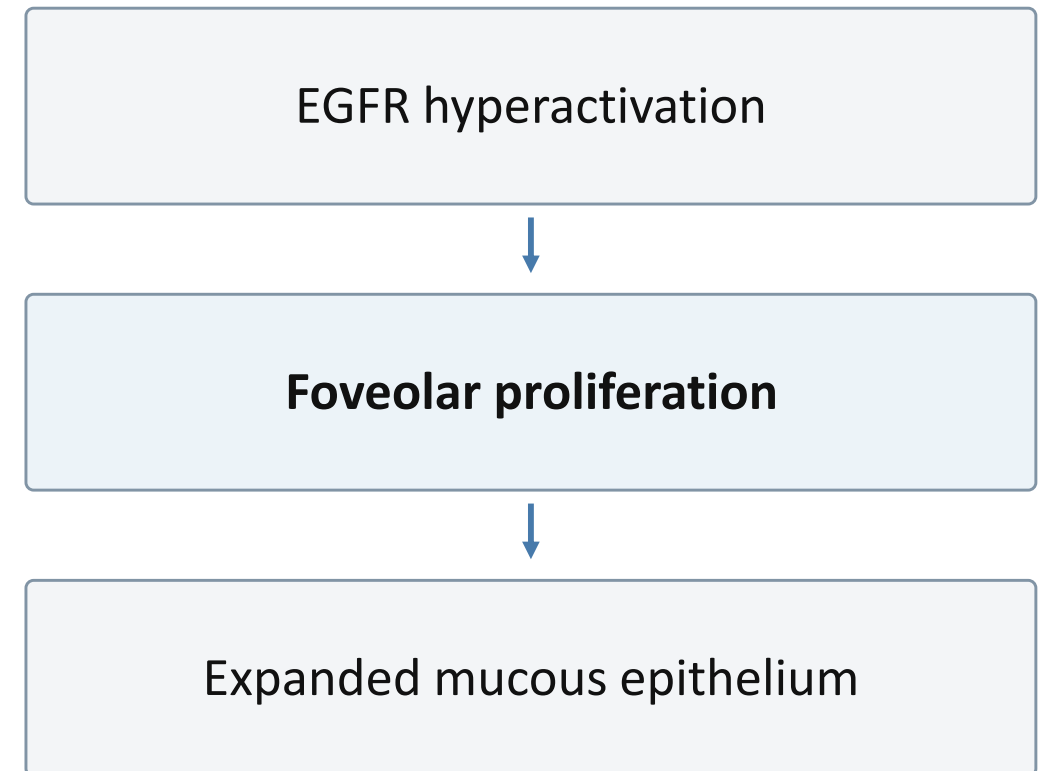
TGF- α is the proximal growth-factor signal

- The disorder to excessive transforming growth factor- α secretion.
- TGF- α acts as a ligand for the epidermal growth factor receptor.
- This ligand–receptor relationship is central to the pathogenesis.



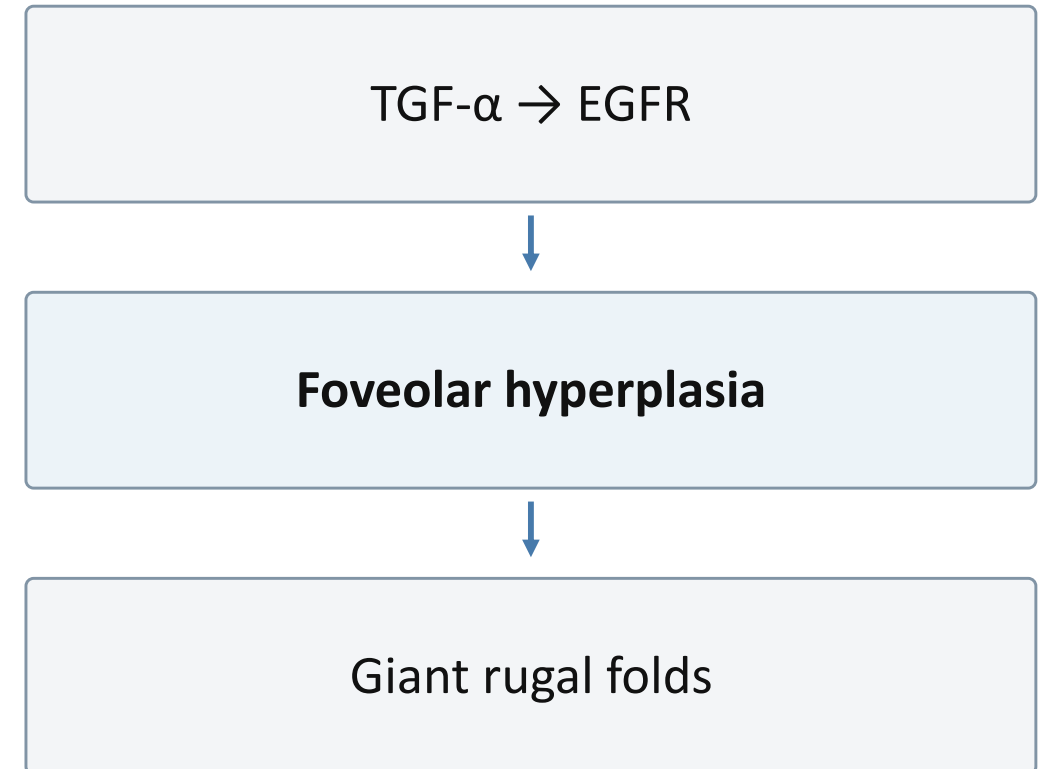
EGFR hyperactivation expands foveolar epithelium

- Hyperactivation of EGFR occurs on gastric epithelial cells.
- Proliferation becomes disproportionately directed toward the foveolar mucous compartment.
- The resulting mucosal expansion remodels the gland architecture.



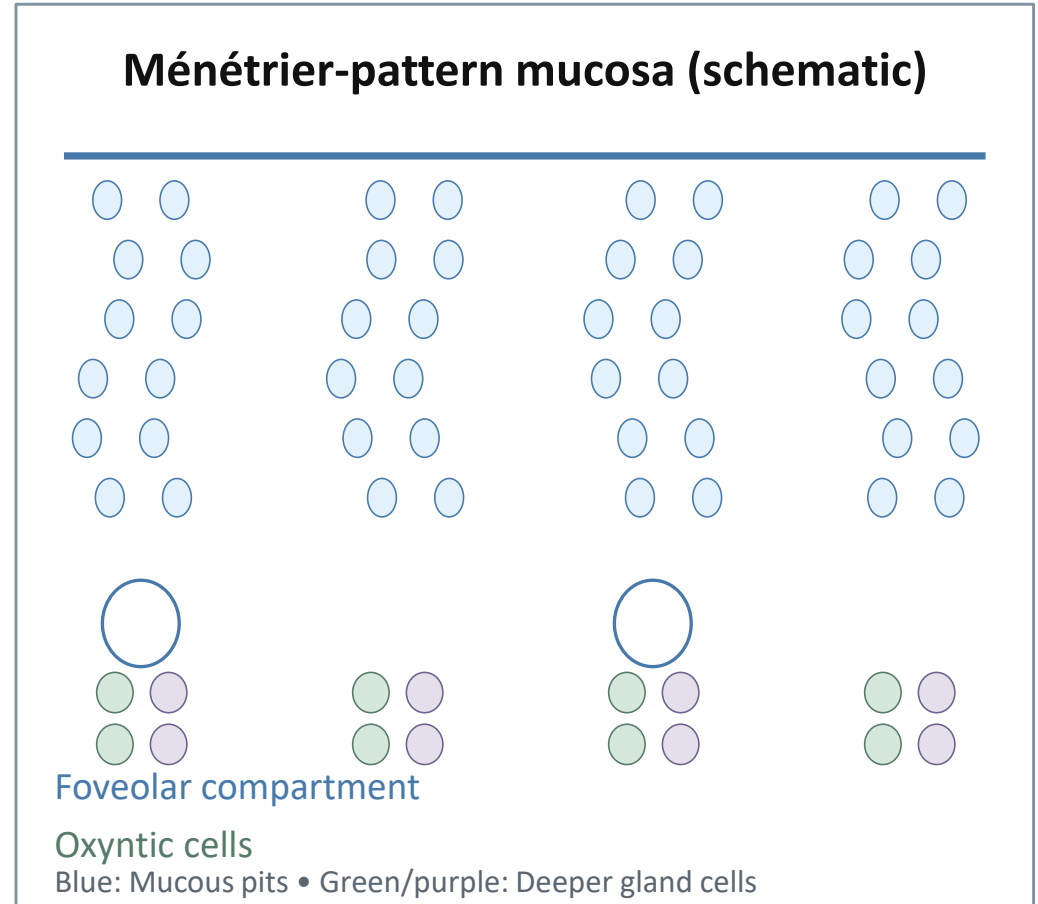
Molecular signaling becomes gross morphology

- The molecular signal is reflected in increased epithelial mass.
- Expanded mucous-cell epithelium produces thickened and irregular mucosal folds.
- This links a cell-level event to the endoscopic finding of enlarged rugae.



Foveolar expansion alters the gland balance

- Hyperplasia affects the surface/pit mucous-cell lineage.
- Atrophic or hypoplastic oxyntic glands can coexist with surface expansion.
- Fold size therefore does not imply an increase in all secretory cell types.



Hyperplasia and atrophy can coexist

- A hypertrophic surface compartment can mask the loss of deeper functional glands.
- In Ménétrier disease, foveolar epithelial expansion contrasts with reduced chief/parietal cells.
- Report both changes rather than equating thicker mucosa with more oxyntic tissue.

Surface/pit compartment

Foveolar hyperplasia

Expansion

Oxyntic compartment

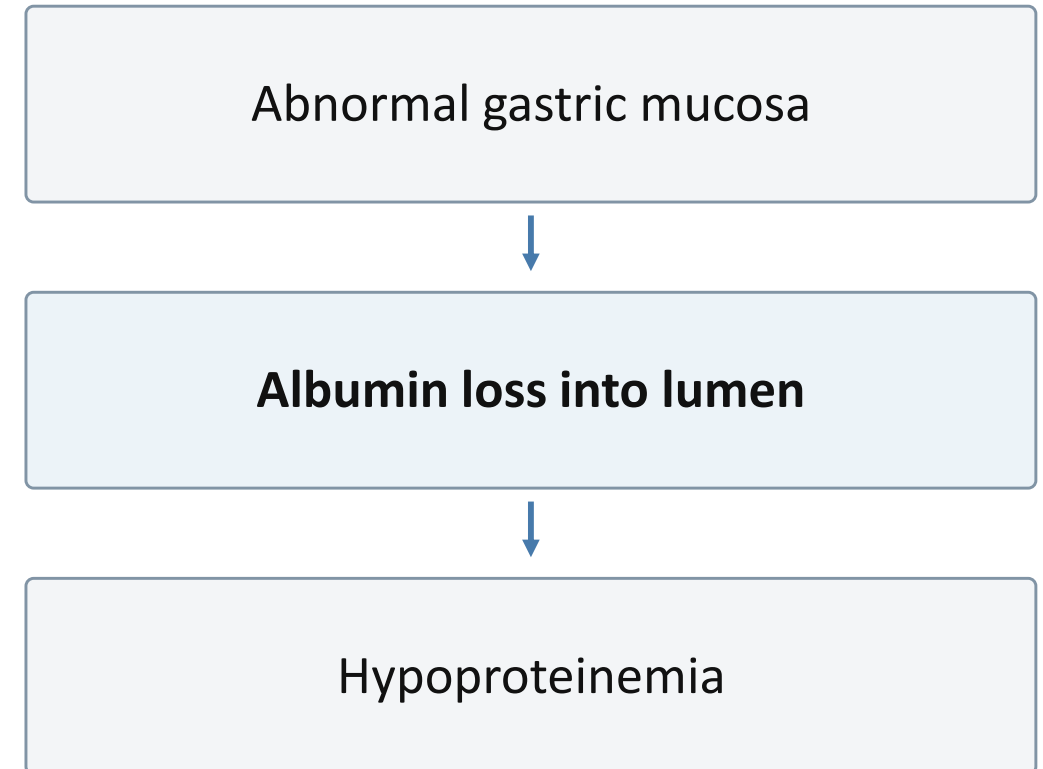
Chief/parietal hypoplasia

Reduction

Schematic • contrasting patterns

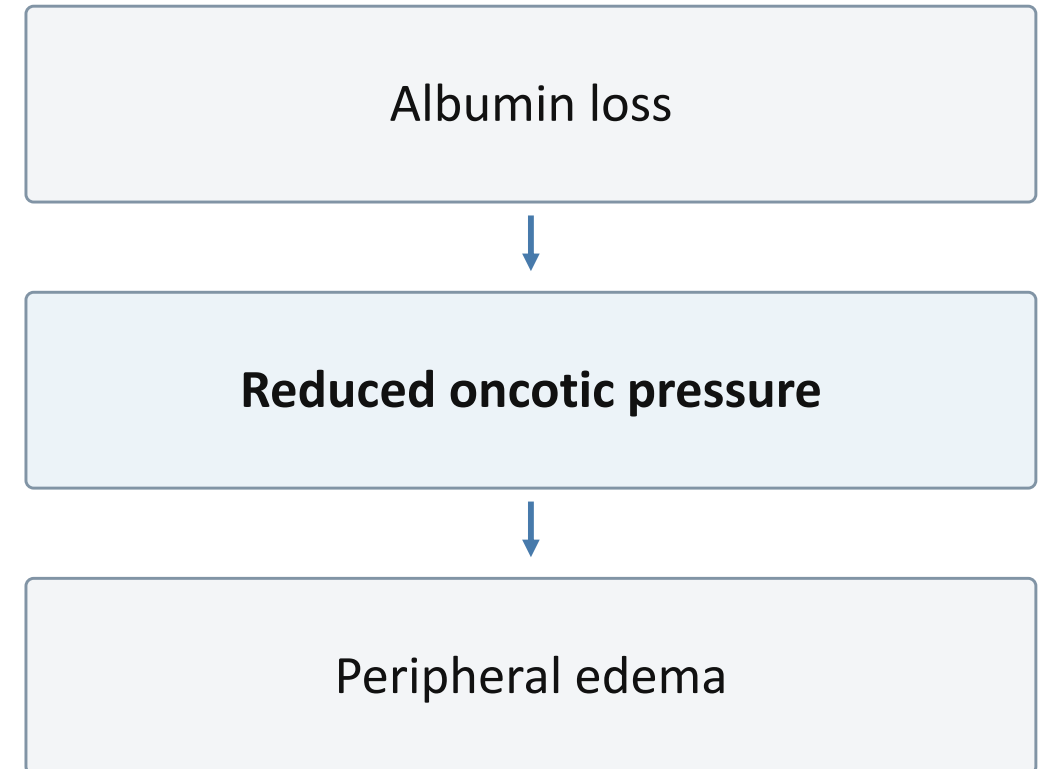
The protein-losing phenotype

- Robbins documents albumin loss across the gastric mucosa.
- This gastric leak can be large enough to produce systemic hypoproteinemia.
- Clinical edema is a systemic consequence of a mucosal lesion.



Why does peripheral edema occur?

- Albumin depletion lowers the plasma colloid osmotic contribution to intravascular fluid retention.
- Fluid movement toward interstitial tissues contributes to peripheral swelling.
- This is a pathophysiologic interpretation of the protein-loss finding.



Magnitude of protein loss: Interpret correctly

- Albumin loss may approach 10 g/day.
- This is a reported potential magnitude, not a diagnostic threshold or typical value for every patient.
- The key diagnostic concept is enteric protein loss from the stomach.

Infection associations require nuance

- Some cases are associated with viral infection or *Helicobacter pylori*.
- The adult disorder is linked to growth-factor signaling; A single infectious cause is not established for all adults.
- Pediatric disease frequently follows CMV or other infections.

Adult presentations

No universal infectious trigger

May be persistent

Pediatric presentations

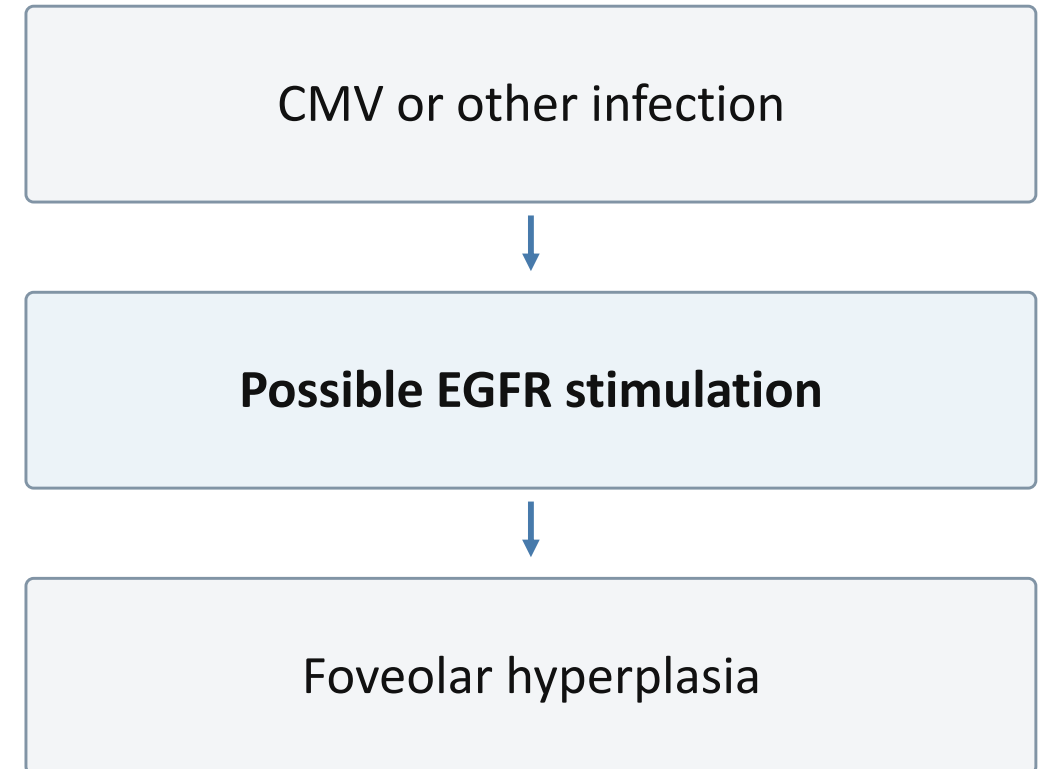
Often postinfectious

Often self-limited

Schematic • contrasting patterns

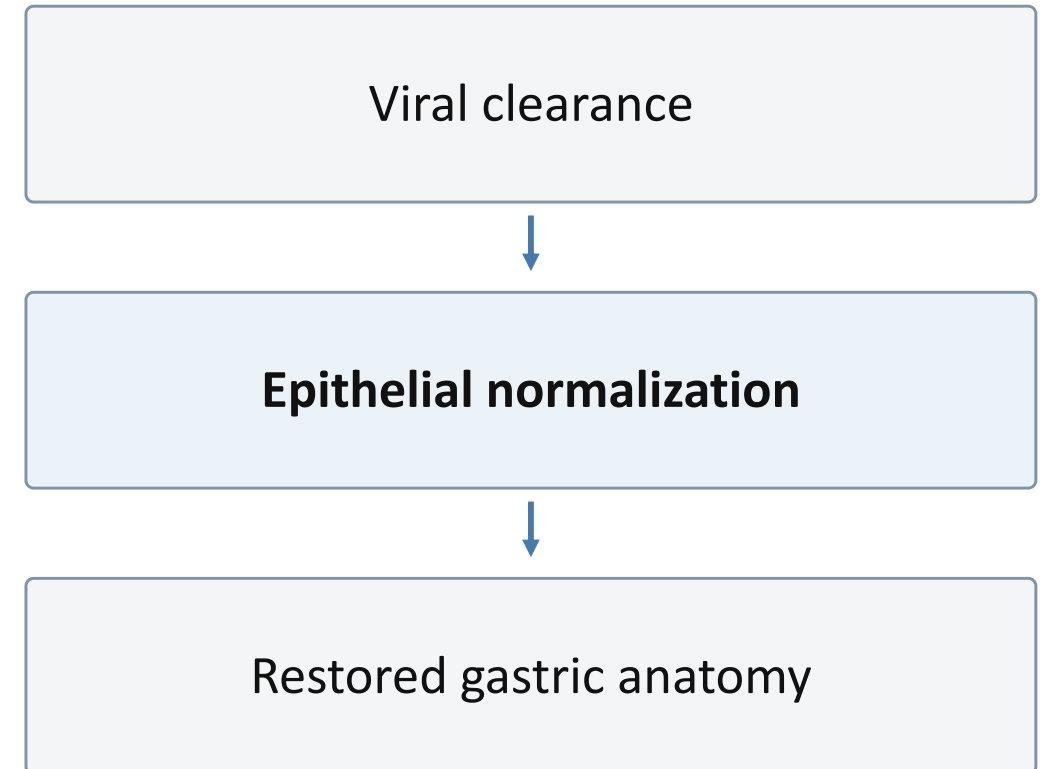
Proposed pediatric CMV–EGFR link

- The text suggests that CMV-induced EGFR activation can help drive pediatric disease.
- This is presented as a potential mechanism, not as a universally demonstrated pathway.
- Viral clearance can coincide with reversal of mucosal proliferation.



Regression links mechanism to reversibility

- The pediatric form often resolves when the associated viral illness clears.
- Epithelial proliferation may normalize.
- Gastric anatomy can be restored without the same chronic course expected in many adults.



Systemic TGF- α effects extend beyond the stomach

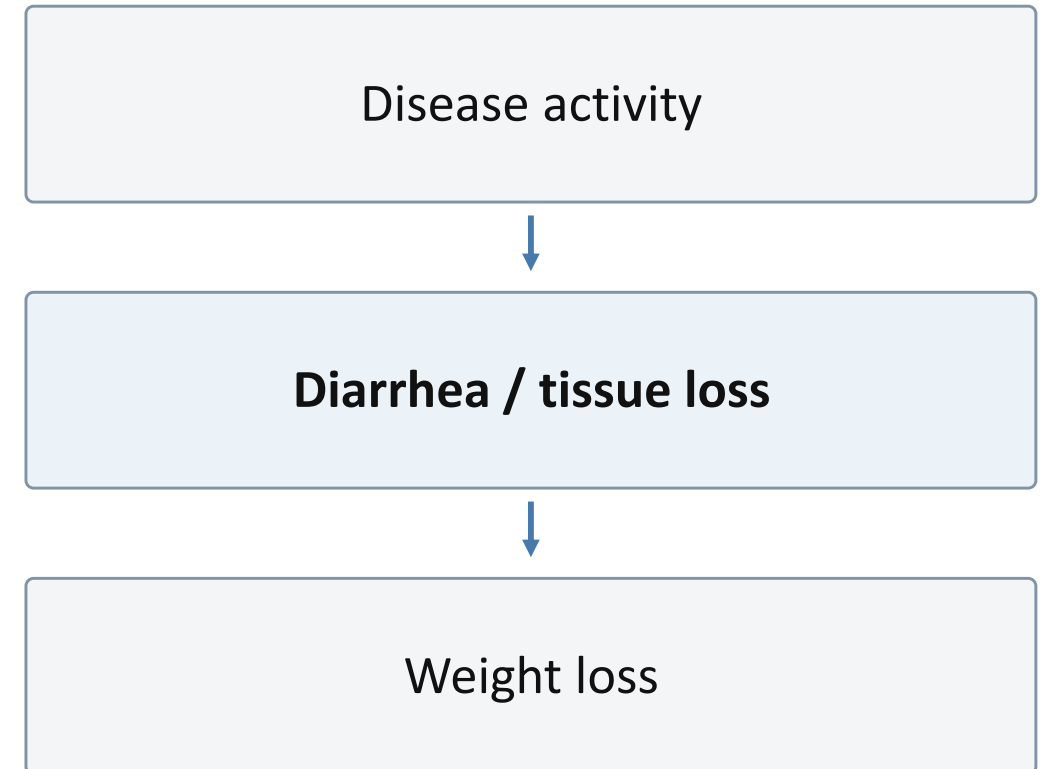
- The source describes possible hyperplasia of the liver, pancreas, and other GI segments.
- Muscle and adipose tissue loss may accompany systemic involvement.
- Psoriasis can also be seen as an associated manifestation.

Hypoproteinemia is the biochemical anchor

- Diffuse gastric mucosal albumin loss can lower circulating protein concentrations.
- Biochemical findings should be interpreted with the gastric morphology.
- The systemic consequences may overshadow the primary mucosal abnormality.

Weight loss has multiple pathologic connections

- Weight loss is a common clinical manifestation in the source.
- Diarrhea and systemic muscle/adipose loss may coexist.
- Avoid attributing weight loss to malignancy without diagnostic evidence.



Diarrhea belongs to the clinical spectrum

- Diarrhea as a frequent secondary symptom.
- The clinical picture combines enteric symptoms with an altered gastric mucosa.
- Diarrhea does not by itself differentiate Ménétrier disease from Zollinger–Ellison syndrome.

Edema connects symptoms to a mechanism

- Peripheral edema is common in the source description.
- Albumin loss from the stomach provides the causal bridge between mucosal pathology and swelling.
- The physical finding can be clinically more conspicuous than the gastric lesion.

Localized lesion; Systemic presentation

- The dominant morphologic lesion involves gastric body/fundus mucosa.
- Its systemic expressions include hypoproteinemia, edema, diarrhea, and weight loss.
- The disease illustrates how mucosal epithelium can produce generalized physiologic effects.

Local stomach change

Enlarged folds

Foveolar hyperplasia

Systemic effects

Low proteins / edema

Weight loss / diarrhea

Schematic • contrasting patterns

Adult presentations merit neoplastic awareness

- Adult Ménétrier disease is associated with increased gastric adenocarcinoma risk.
- An association is not proof that every lesion is dysplastic or will progress.
- Suspicious focal abnormalities need separate pathologic consideration.

The pediatric course is often distinct

- Childhood disease is commonly associated with CMV or other preceding infections.
- It is often self-limited, unlike many adult cases.
- The possibility of spontaneous mucosal recovery changes the clinical context.

Adult and pediatric phenotype at a glance

- Both presentations share the foveolar hyperplasia / protein-losing core.
- Adults are particularly relevant to adenocarcinoma risk discussions.
- Children more often display a reversible, infection-linked course.

Adult disease

Malignancy
association

Persistence can occur

Pediatric disease

CMV/postinfectious
association

Often reversible

Schematic • contrasting patterns

Gross morphology: Distribution matters

- The rugal folds become irregularly enlarged.
- The body/fundus predominance is characteristic; Antral sparing is common.
- Anatomic distribution helps separate a diffuse fold disorder from a focal polyp.

Fundus

Enlarged rugae

Body

Enlarged rugae

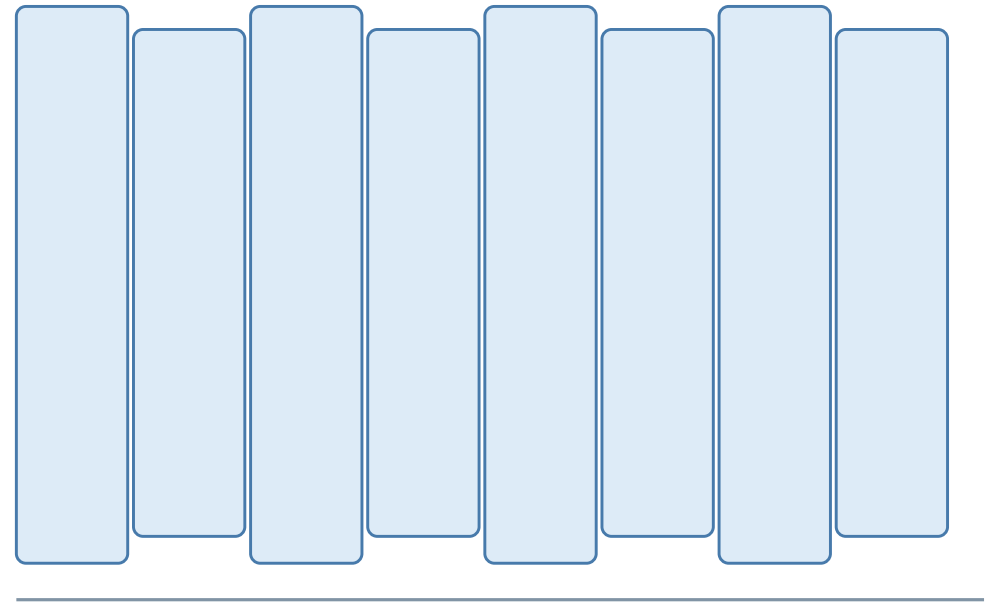
Antrum

Generally spared

Giant folds are a mucosal proliferation pattern

- Hypertrophic rugae may look cerebriform or convoluted.
- Their enlargement reflects epithelial hyperplasia rather than a specific neoplasm.
- Gross pattern recognition should prompt cellular characterization.

Giant cerebriform rugae (schematic)



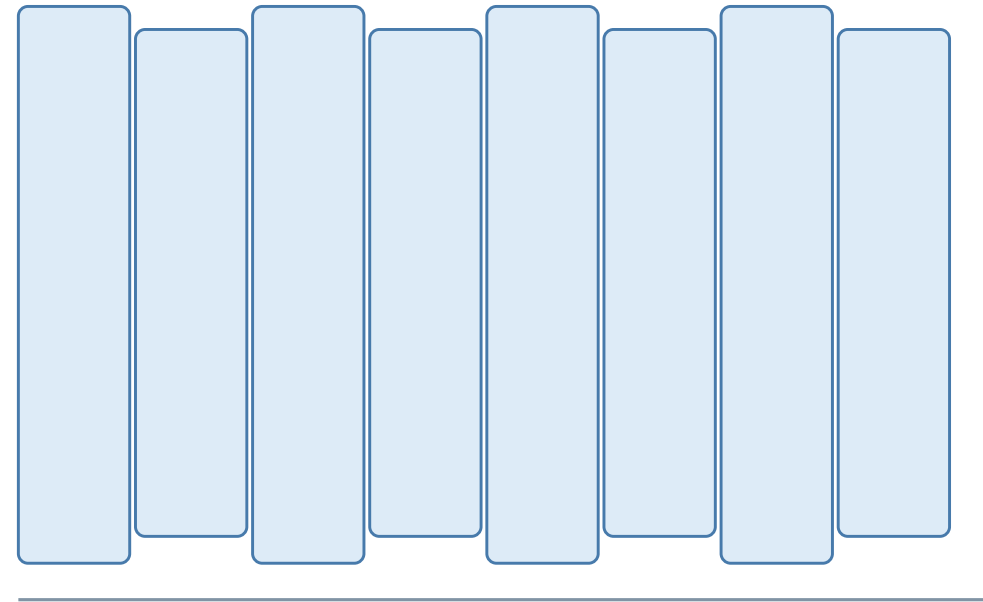
Fold enlargement $\neq$ proof of malignancy

Conceptual fold profile • not specimen imagery

The enlarged folds can appear polypoid

- Some mucosal regions project in a polypoid fashion.
- Polypoid appearance alone is not equivalent to a discrete neoplastic polyp.
- The diffuse rugal pattern remains a key clue.

Giant cerebriform rugae (schematic)

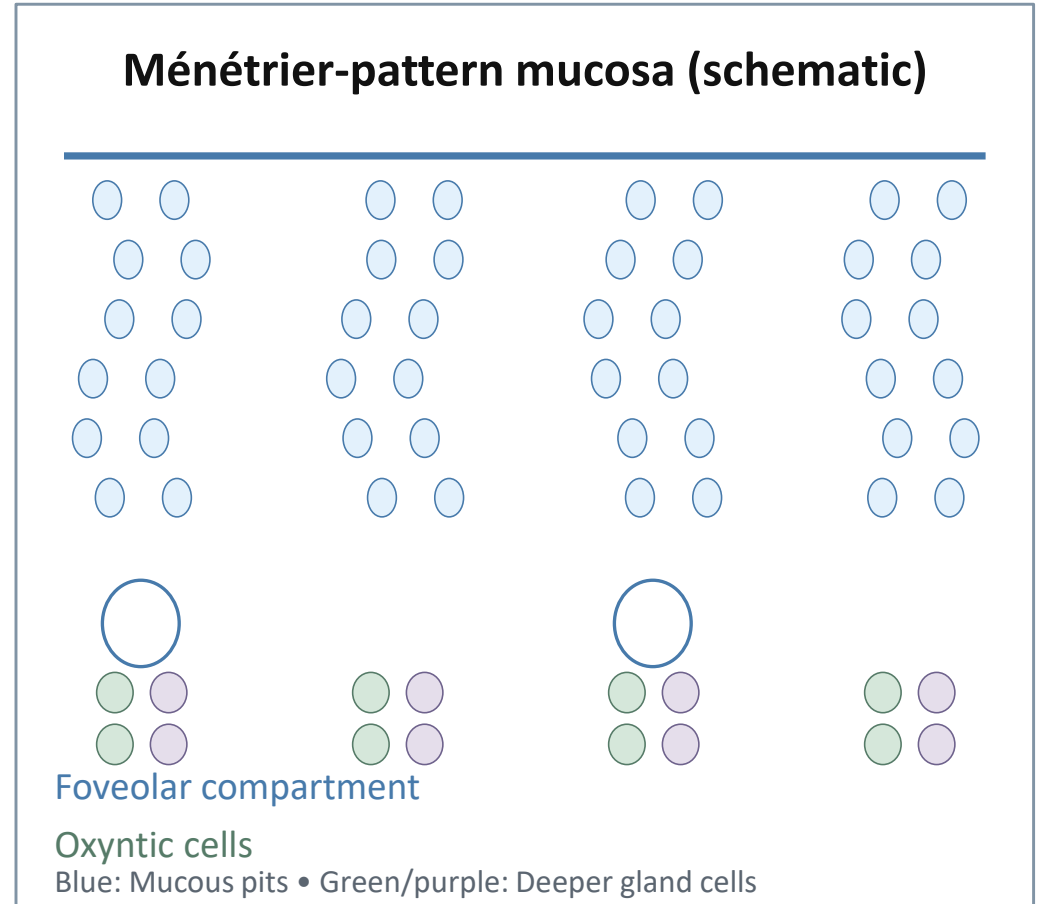


Fold enlargement $\neq$ proof of malignancy

Conceptual fold profile • not specimen imagery

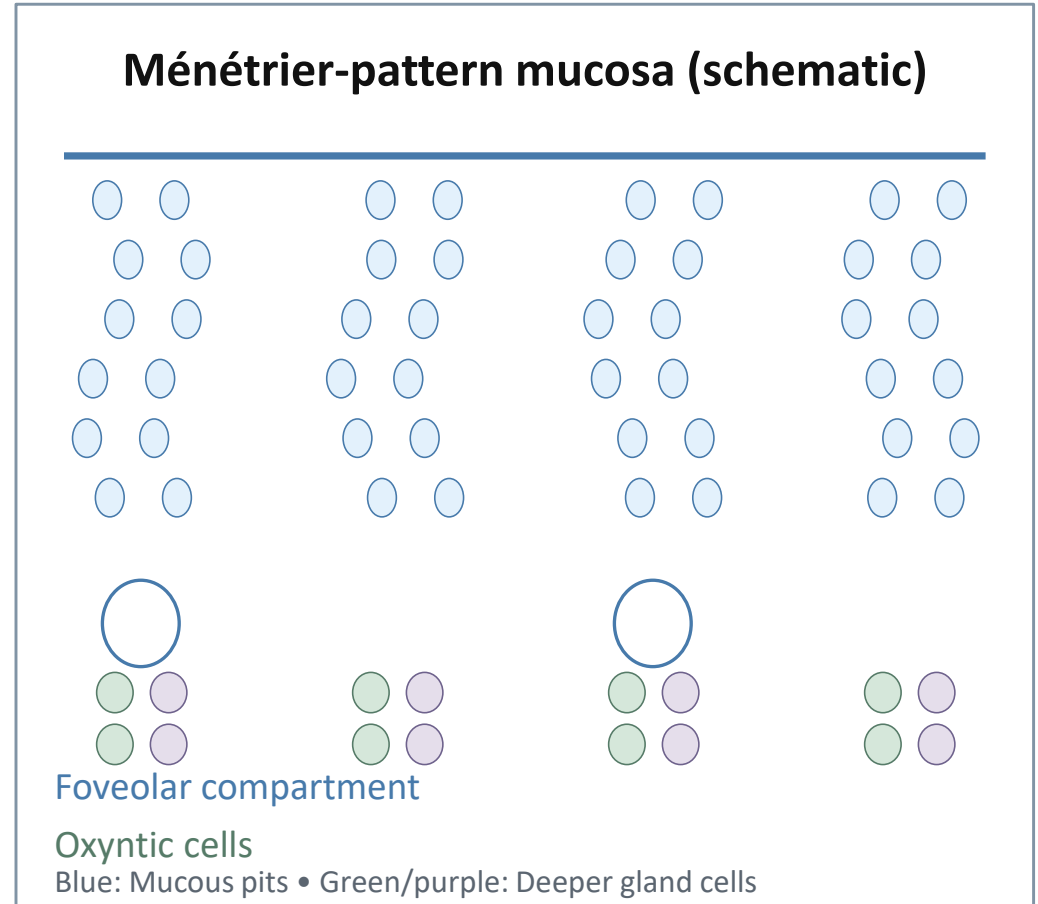
Histologic hallmark: Foveolar mucous hyperplasia

- The most characteristic microscopic change is expansion of foveolar mucous cells.
- The surface/pit epithelium becomes conspicuously elongated and convoluted.
- This defines the predominant epithelial cell type.



Corkscrew-like gland elongation

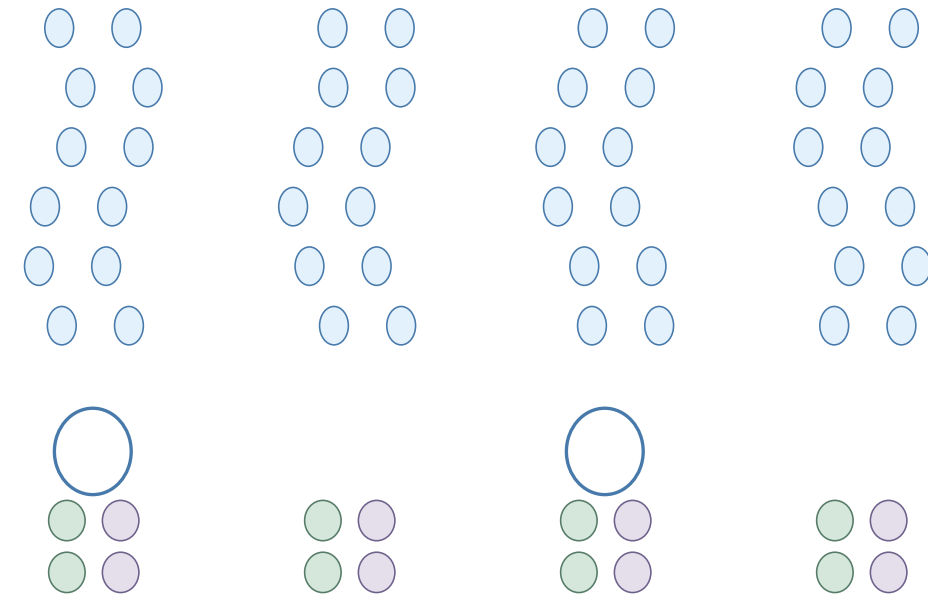
- Glands become long and tortuous, creating a corkscrew-like profile.
- Convolution is a morphologic expression of increased mucous epithelial mass.
- Look for the pattern in the context of fold enlargement.



Cystic dilation is common

- Dilated glandular lumina accompany the elongated mucous epithelium.
- Cystic dilatation should not be interpreted in isolation.
- The combination with foveolar hyperplasia is more discriminating.

Ménétrier-pattern mucosa (schematic)



Foveolar compartment

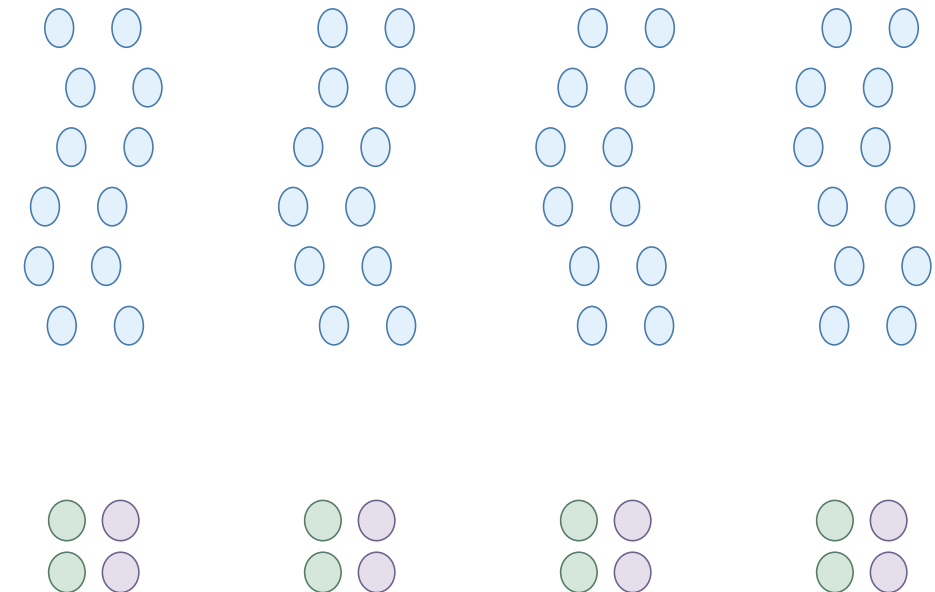
Oxyntic cells

Blue: Mucous pits • Green/purple: Deeper gland cells

Reduced parietal-cell compartment

- The source describes diffuse or patchy glandular atrophy.
- Parietal-cell hypoplasia may be intermixed with the hyperplastic epithelium.
- Mucosal enlargement does not imply intact acid-producing glands.

Ménétrier-pattern mucosa (schematic)



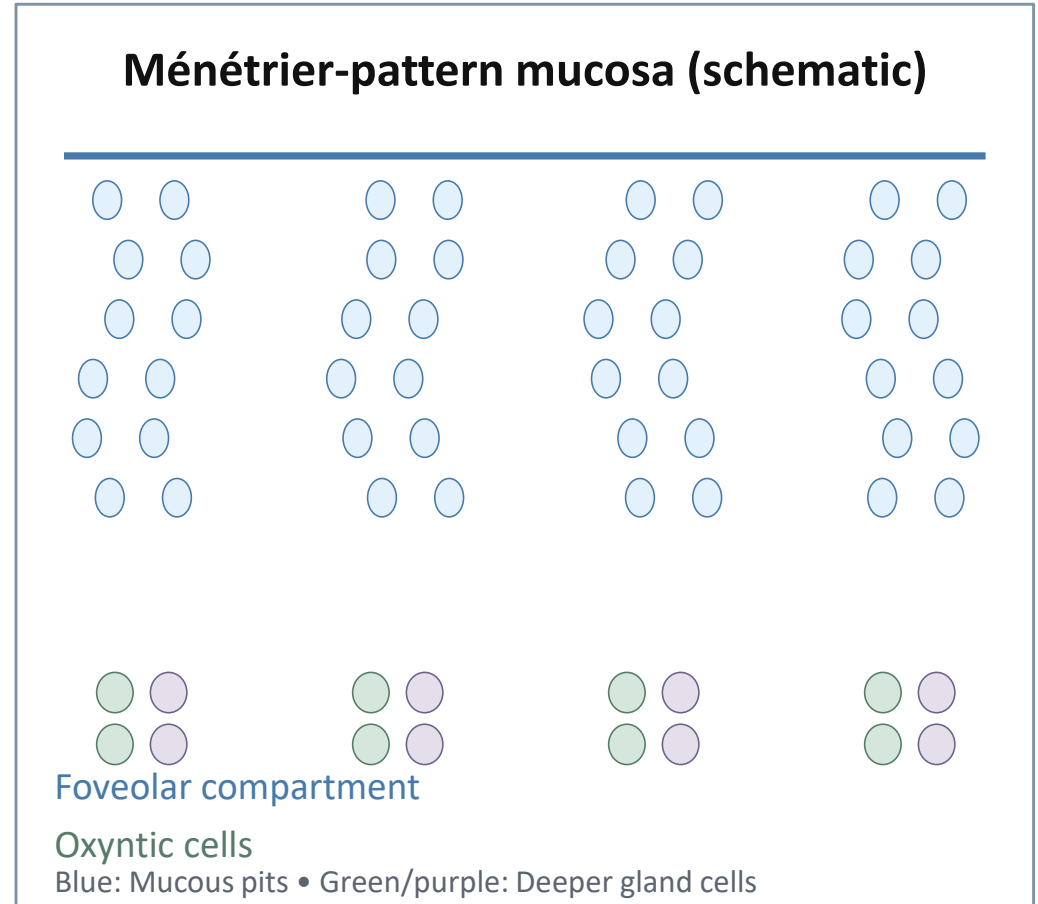
Foveolar compartment

Oxyntic cells

Blue: Mucous pits • Green/purple: Deeper gland cells

Reduced chief-cell compartment

- Chief cells may also be hypoplastic in affected mucosa.
- Their decline marks loss of the differentiated oxyntic gland component.
- Interpret this alongside foveolar expansion, not as a separate disease.



The signature microscopic combination

- Foveolar cell hyperplasia, corkscrew-like glands and cystic dilation favor the pattern.
- Patchy or diffuse parietal/chief-cell hypoplasia adds specificity.
- A cell-compartment assessment is more informative than mucosal thickness alone.

Expanded

Foveolar mucous cells

Elongated / dilated pits

Reduced

Parietal and chief cells

Oxyntic gland atrophy

Schematic • contrasting patterns

Inflammation is usually modest

- Ménétrier disease is classified with hypertrophic gastropathies.
- Inflammatory infiltrates are usually limited.
- Prominent inflammatory activity may raise the importance of alternative or associated lesions.

Intraepithelial lymphocytes may be conspicuous

- Some cases show marked intraepithelial lymphocytosis.
- This exception does not replace the characteristic foveolar hyperplasia.
- Assess inflammation as one feature within the overall architecture.

A histologic reading sequence

- First: Identify disproportionate foveolar epithelial expansion.
- Second: Assess pit/gland elongation and cystic dilation.
- Third: Evaluate the parietal/chief compartment and inflammatory infiltrate.

1. Foveolar expansion



2. Gland remodeling



3. Oxyntic cell depletion

Schematic • assessment sequence

Ménétrier versus Zollinger–Ellison

- Ménétrier disease primarily expands mucous/foveolar cells and produces hypoproteinemia.
- Zollinger–Ellison syndrome expands parietal cells in oxyntic mucosa and causes peptic ulceration.
- Both may produce enlarged folds, but cellular identity and symptoms distinguish them.

Ménétrier	Zollinger–Ellison
Foveolar cells	Parietal cells
Protein loss	Peptic ulceration

Schematic • contrasting patterns

Hypertrophic gastropathy: Mechanism comparison

Characteristic	Ménétrier disease	Zollinger–Ellison syndrome
Dominant signal	TGF- α $\rightarrow$ EGFR	Gastrin (gastrinoma)
Cellular pattern	Foveolar mucous hyperplasia	Parietal-cell hyperplasia
Clinical signature	Hypoproteinemia; Edema	Peptic ulcers; Diarrhea
Cancer association in table	Yes (adult Ménétrier)	No (ZES)

Ménétrier versus hyperplastic polyps

- Ménétrier disease favors enlarged body/fundus rugae with diffuse foveolar change.
- Inflammatory/hyperplastic polyps may occur in antrum or body and are linked to chronic gastritis.
- Neutrophils and lymphocytes are more prominent in the polyp category in the Robbins comparison.

Ménétrier

Diffuse folds

Limited inflammation

Hyperplastic polyps

Polyp formation

Chronic gastritis
setting

Schematic • contrasting patterns

Ménétrier versus fundic gland polyps

- Both can involve the body and fundus.
- Fundic gland polyps feature parietal/chief-cell-associated gland changes, rather than dominant foveolar hyperplasia.
- The source links fundic gland polyps with PPIs and familial adenomatous polyposis.

Ménétrier

Foveolar proliferation

Protein loss

Fundic gland polyps

Oxyntic elements

PPI / FAP context

Schematic • contrasting patterns

Ménétrier versus gastritis cystica

- Gastritis cystica features epithelial-lined cysts displaced into the gastric wall.
- The source places gastritis cystica in a trauma/prior-surgery context.
- Cystic change alone cannot establish Ménétrier disease.

Ménétrier

Foveolar expansion

Body/fundus folds

Gastritis cystica

Epithelial entrapment

Prior injury/surgery

Schematic • contrasting patterns

Ménétrier versus gastric adenoma

- Ménétrier disease is a hyperplastic mucous-cell process.
- Gastric adenomas are dysplastic epithelial lesions, frequently associated with atrophy or intestinal metaplasia.
- A mass-forming or cytologically abnormal area requires evaluation beyond the hypertrophic fold label.

Ménétrier

Foveolar hyperplasia

Diffuse rugal process

Gastric adenoma

Dysplastic epithelium

Focal neoplastic lesion

Schematic • contrasting patterns

Location and predominant cell type

Lesion	Usual location	Dominant cells
Ménétrier disease	Body and fundus	Mucous / foveolar
Zollinger–Ellison	Fundus	Parietal, mucous, endocrine
Hyperplastic polyps	Antrum and body	Mucous
Fundic gland polyps	Body and fundus	Parietal and chief
Gastric adenoma	Antrum and body	Dysplastic intestinal-type

Clinicopathologic evaluation of enlarged folds

- Establish whether fold enlargement is diffuse and where it is concentrated.
- Correlate foveolar versus parietal-cell prominence with clinical protein loss or ulceration.
- Consider other proliferative lesions when morphology or clinical context does not fit.

1. Topography



2. Cellular pattern



3. Clinical correlation

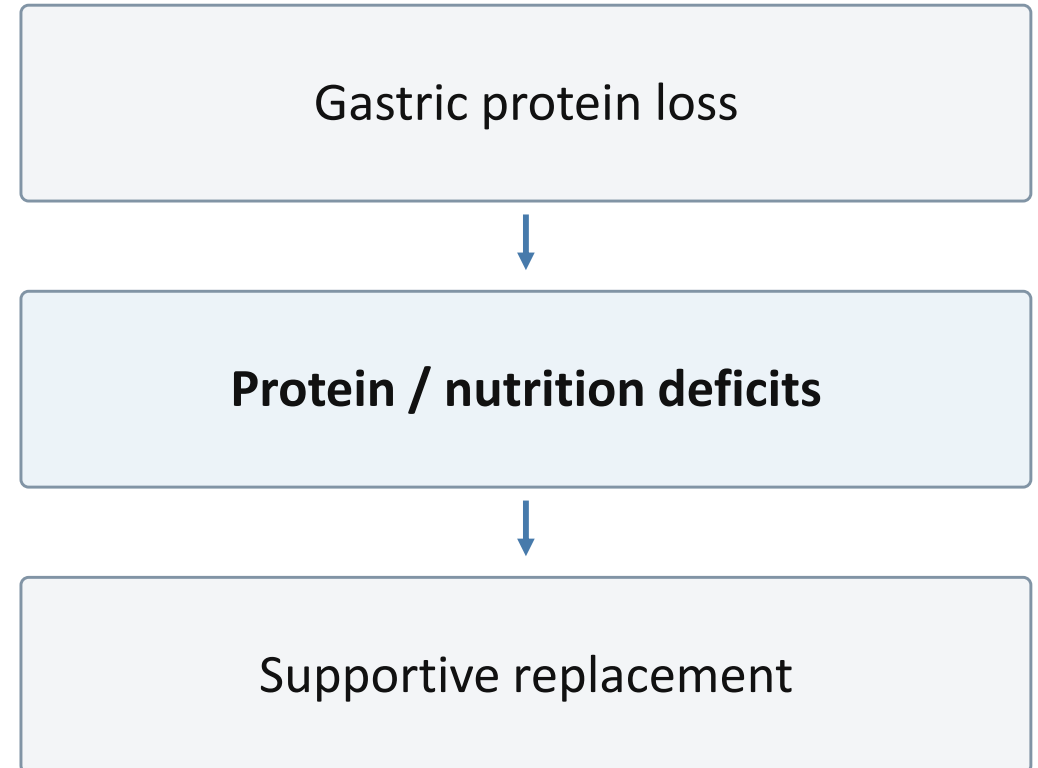
Schematic • assessment sequence

Sampling logic: Avoid a single-feature diagnosis

- The disease is defined by a combined anatomic, microscopic, and clinical pattern.
- Patchy atrophy means that one field may not reveal every feature.
- This is a reasoned teaching approach, not a Robbins-specified biopsy protocol.

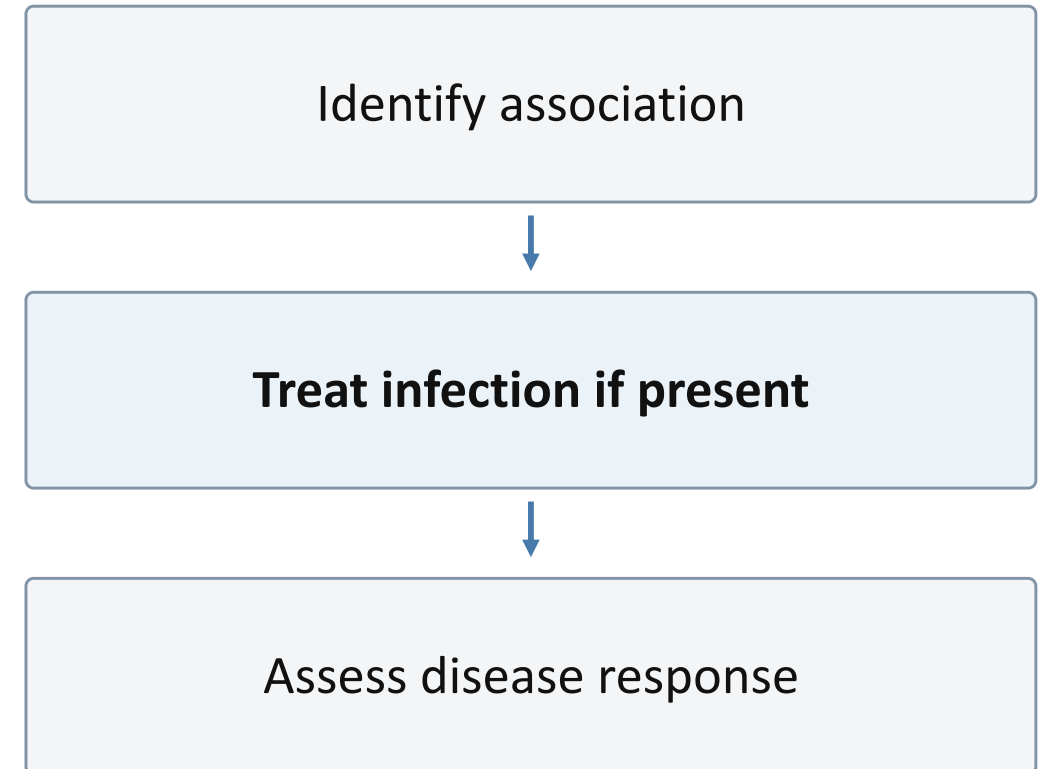
Supportive care targets the consequences

- The source includes intravenous albumin and parenteral nutritional support.
- These approaches address protein depletion and nutritional compromise.
- They do not, by themselves, identify or reverse the upstream growth-factor signal.



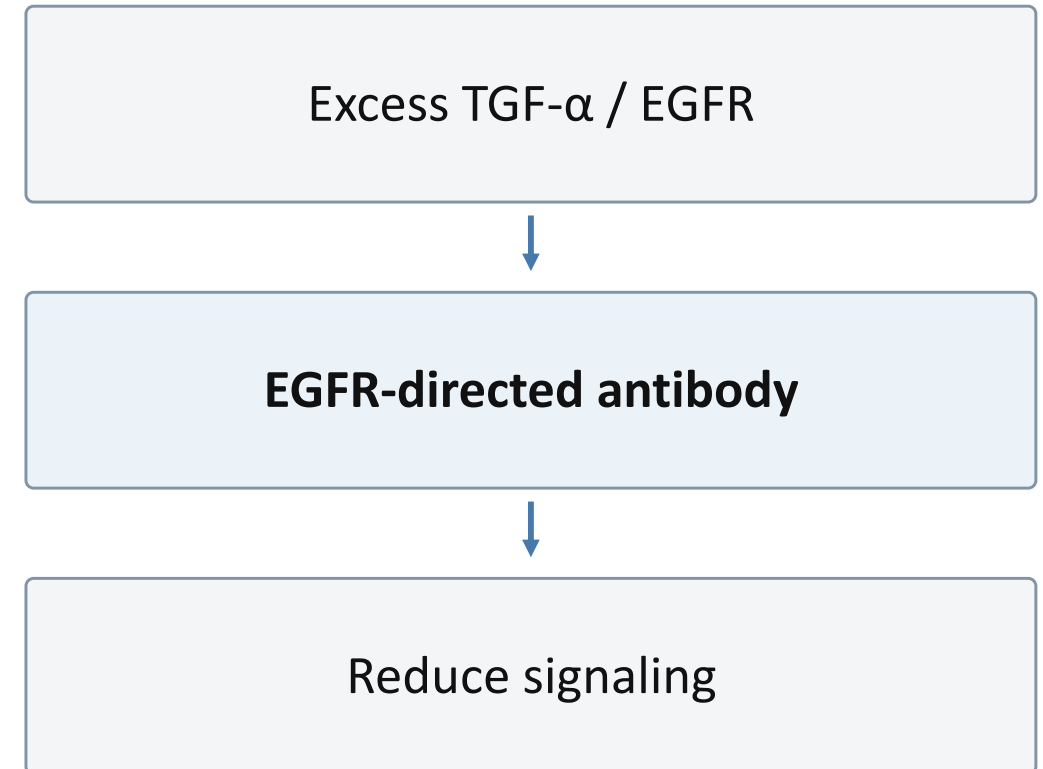
Treat associated infections when relevant

- For herpesvirus, CMV, or H. Pylori associations, treatment of the infection may help.
- This is not an assertion that infection is the cause of every case.
- Etiologic context matters especially in postinfectious pediatric disease.



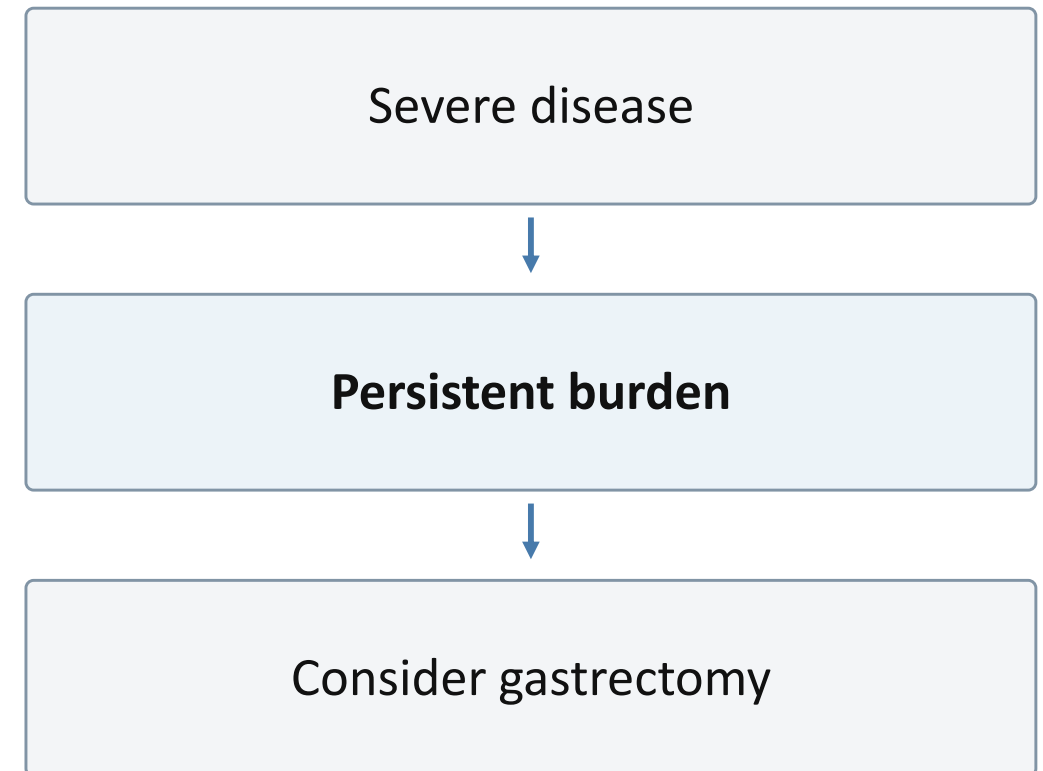
EGFR blockade addresses disease signaling

- The source reports that antibodies blocking EGFR activation can be effective.
- The therapeutic target aligns with the TGF- α → EGFR pathogenic mechanism.
- No dose, regimen, response rate, or guideline recommendation is specified by the supplied text.



Gastrectomy remains an option in severe disease

- Severe cases may require gastrectomy.
- The rationale is to remove a mucosal source of ongoing pathology when less invasive measures are insufficient.
- Surgical candidacy and detailed indications are beyond the supplied textbook excerpt.



Management approaches and intended targets

Approach	Immediate target	Source caveat
Albumin / nutritional support	Protein depletion / nutrition	Supportive, not receptor-directed
Infection treatment	Associated infection	Helpful in selected cases
EGFR-blocking antibody	Receptor activation	Can be effective
Gastrectomy	Severe gastric disease	Reserved option in severe cases

Clinical reasoning: Adult presentation

- Hypothetical: An adult has enlarged body/fundus rugae, peripheral edema, and low circulating protein.
- A tissue sample shows exuberant foveolar mucous epithelium with tortuous and dilated glands.
- Which pattern unifies the anatomy, histology, and systemic findings?

Reasoning target: Ménétrier disease: Foveolar hyperplasia plus gastric protein loss.

Clinical reasoning: A child after infection

- Hypothetical: A child develops gastric fold enlargement and protein loss after an infectious illness.
- The source describes a frequently self-limited pediatric pattern, often linked to CMV.
- What biological event can accompany return of normal architecture?

Reasoning target: Viral clearance with normalization of epithelial proliferation.

Diagnostic reasoning: Giant folds and ulcers

- Hypothetical: A patient has markedly thick gastric folds together with prominent peptic ulcers.
- Biopsy shows expansion of the parietal-cell compartment rather than foveolar predominance.
- Which hypertrophic gastropathy is the better match?

Reasoning target: Zollinger–Ellison syndrome (gastrinoma-associated).

Morphology challenge: A cystic gland is not enough

- Hypothetical: A gastric sample contains cystically dilated glands.
- The distribution, dominant cell type, and injury/surgery context are not yet known.
- Can cystic dilation alone distinguish Ménétrier disease from gastritis cystica?

Reasoning target: No. Use gland compartment, tissue depth, distribution, and context.

High-yield diagnostic synthesis

- Body/fundus-predominant giant folds plus dominant foveolar hyperplasia define the morphological core.
- Elongated tortuous/cystically dilated glands coexist with parietal/chief-cell hypoplasia.
- Gastric albumin loss explains hypoproteinemia and edema.

High-yield mechanism and clinical synthesis

- Excess TGF- α stimulates EGFR signaling on gastric epithelium.
- Children often have infection-associated, reversible disease; Adults have an increased gastric cancer association.
- Supportive replacement, selected infection treatment, EGFR blockade, and surgery are described options.

Selected source

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 17, “Hypertrophic Gastropathies” and “Ménétrier Disease,” pp. 702–703; Table 17.5 and Fig. 17.18 caption.

Lecture concepts are drawn from the supplied Robbins excerpt and its immediately adjacent stomach/hypertrophic-gastropathy context. Original textbook figure 17.18 was not reproduced.