Medical Bacteriology 423

Helicobacter pylori

Advanced pathogenesis, diagnostic reasoning, and treatment update

Prepared for today’s bacteriology lecture
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Avoids repeating the previous basics; focuses on advanced concepts.

Today’s focus: beyond the previous H. pylori slides

This lecture adds depth without repeating the introductory material.

What we add today

- General morphology and growth requirements
- Urease as a survival factor
- Basic transmission and epidemiology
- Simple colonization-pathogenesis summary
- Basic symptoms and old treatment examples

- Virulence factor map: CagA, VacA, adhesins, OMVs
- Molecular pathogenesis: inflammation + epithelial disruption
- Disease-outcome logic: ulcer vs cancer phenotype
- Test selection + false-negative pitfalls
- 2024 guideline-based treatment principles

Reference foundation: Malfertheiner et al., Nat Rev Dis Primers 2023; Chey et al., ACG Guideline 2024.

Objectives

By the end of this lecture, students should be able to:

1. Explain how H. pylori virulence factors alter epithelial and immune signalling.
2. Link gastritis patterns to ulcer risk, atrophy, metaplasia, cancer, and MALT lymphoma.
3. Choose suitable diagnostic tests and recognize situations causing false-negative results.
4. Describe why antibiotic resistance changed modern treatment recommendations.
5. Apply test-of-cure and treatment selection principles in a simple clinical case.

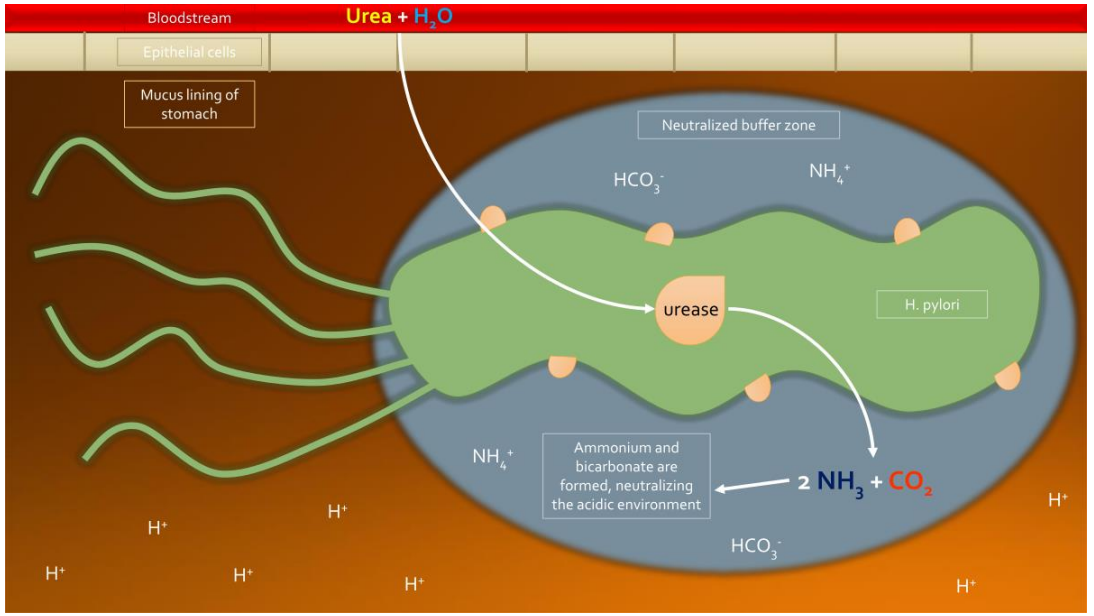
Sources: Nat Rev Dis Primers 2023; WGO H. pylori guideline; ACG Guideline 2024.

Helicobacter Pylori characteristics

- Slender, curved rods with polar flagella.
- Typical gram-negative cell wall structure.
- Requires a microaerophilic atmosphere for growth.
- Slow growth (3-5 days).
- Rapidly motile due to multiple polar flagella.

Helicobacter Pylori
Unique Bacteriologic Features:

- **Urease**:
  - Allows persistence in low pH environments by generating ammonia.
  - High production (6% of bacterial protein).
  - Demonstrable action within minutes in the presence of urea.



H. pylori infection is a disease spectrum

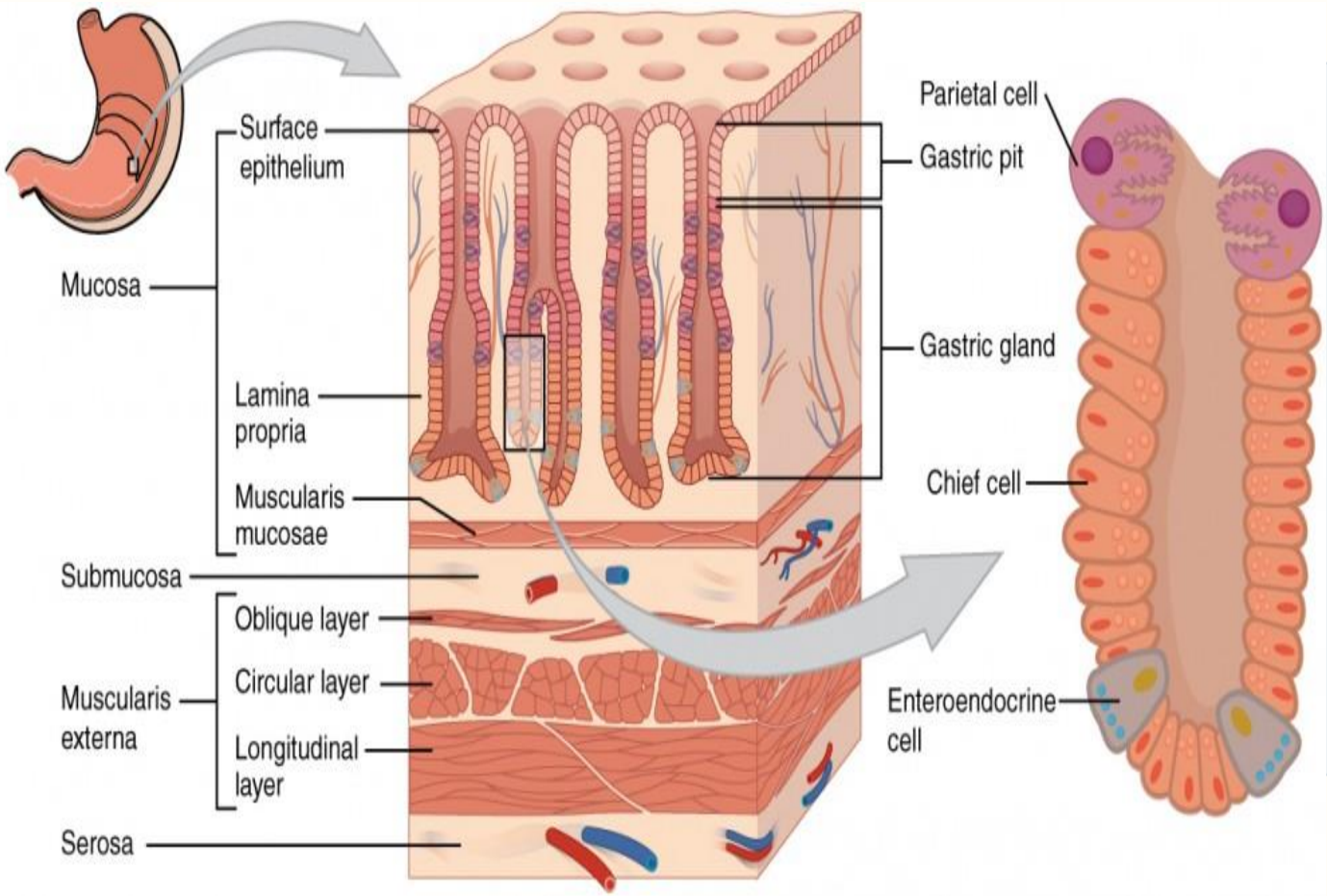
The same organism can lead to different outcomes depending on bacterial strain, host, and environment.

Clinical outcome = bacterial virulence + host immune response + acid physiology + environmental risk factors

Malfertheiner et al., Nature Reviews Disease Primers, 2023.

The gastric niche: why colonization is difficult

H. pylori does not live freely in acid; it localizes to the protected mucus-epithelial zone.



Bacteria swim away from extreme acidity and accumulate near the epithelium

Key teaching message

- The stomach is not one uniform acidic space.
- A mucus pH gradient creates a safer niche near epithelial cells.
- Motility, chemotaxis, adhesion, and immune evasion help long-term persistence.

Salama et al., Nat Rev Microbiol 2013; Malfertheiner et al., Nat Rev Dis Primers 2023.

Colonization: a stepwise process

This slide expands the basic survival story into a full pathogenesis chain.

1

Survive transit

Temporary buffering and stress responses allow survival during passage through gastric acidity.

2

Move to mucus

Flagella and chemotaxis direct movement toward the less acidic mucus layer.

3

Attach

Adhesins bind epithelial receptors and stabilize colonization.

4

Manipulate host cells

Virulence effectors alter junctions, signalling, and immune responses.

5

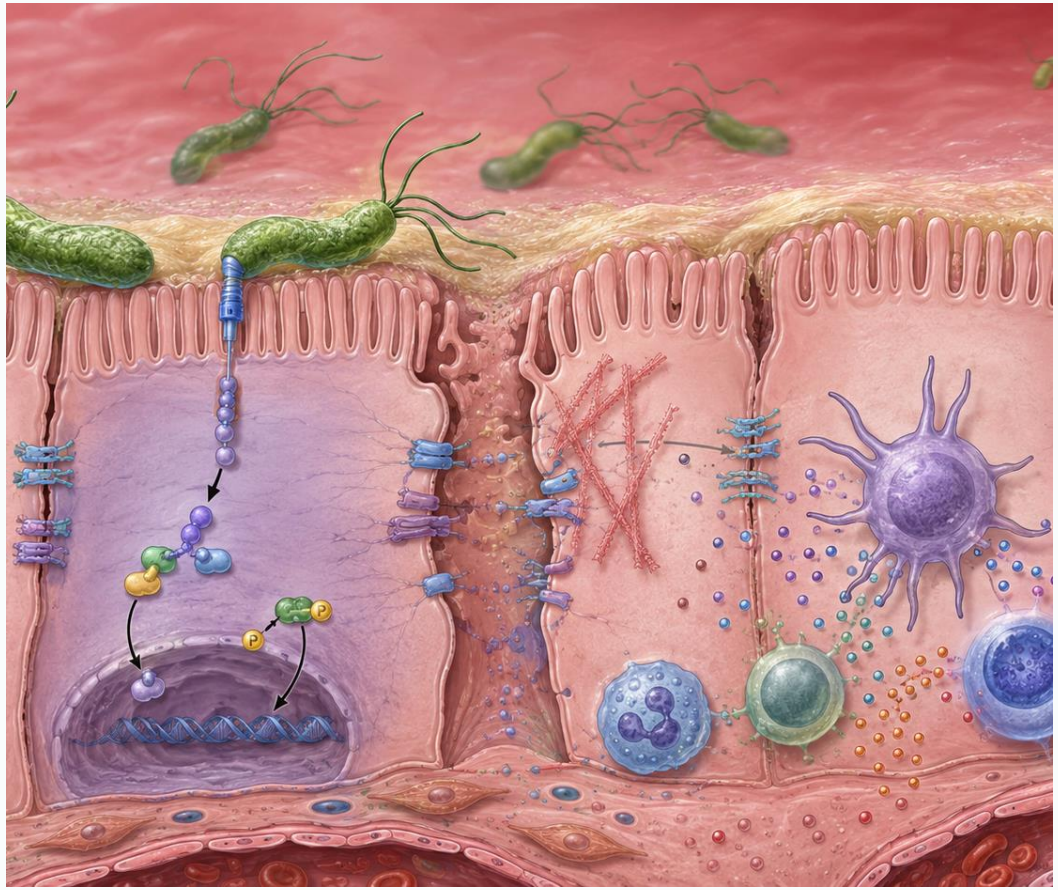
Persist

Chronic inflammation continues for years unless eradicated.

Malfertheiner et al., Nat Rev Dis Primers 2023; Sun et al., Front Cell Infect Microbiol 2023.

Virulence factor map

Focus on mechanisms that were not detailed in the introductory lecture.



CagA + type IV secretion

Injected into epithelial cells; alters signalling and junctions.

VacA toxin

Vacuolation, mitochondrial injury, apoptosis and immune modulation.

Adhesins: BabA, SabA, HopQ

Bind gastric receptors and define tissue tropism.

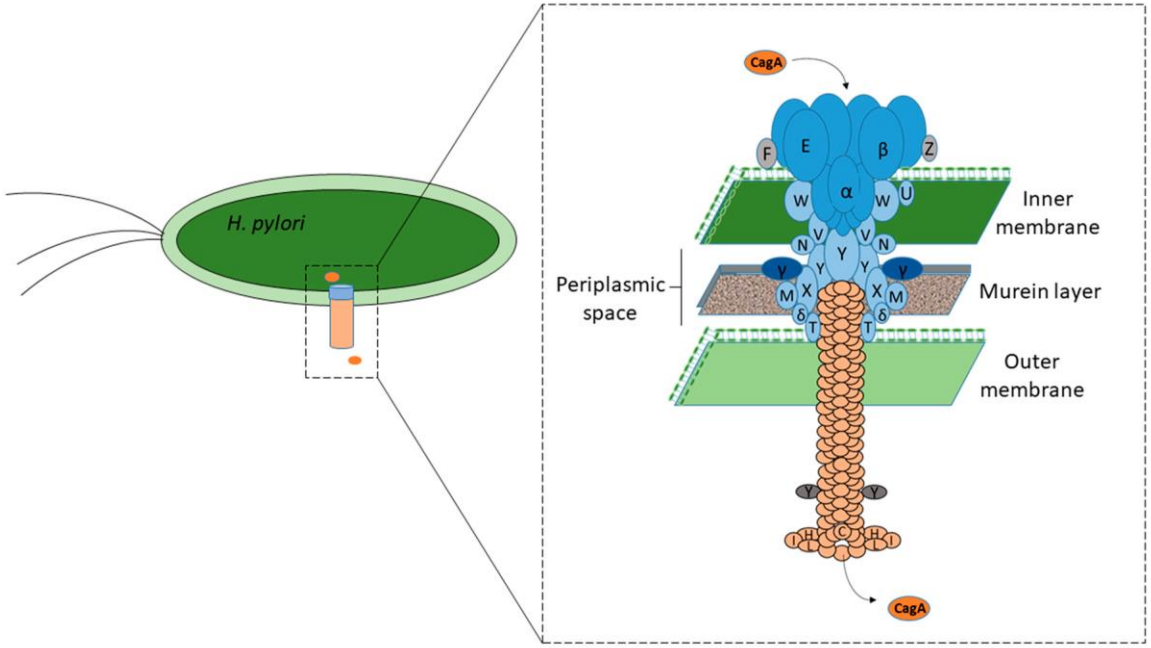
OMVs + HtrA + NAP

Deliver inflammatory signals, damage barriers and recruit neutrophils.

Virulence factors: Roesler et al., 2014; Malfertheiner et al., 2023; Sun et al., 2023.

CagA: the “injected effector” concept

CagA-positive strains use a type IV secretion system to alter epithelial cell behaviour.



SHP-2 / MAPK

cell shape + proliferation

β-catenin

oncogenic signalling

junction disruption

barrier leakage

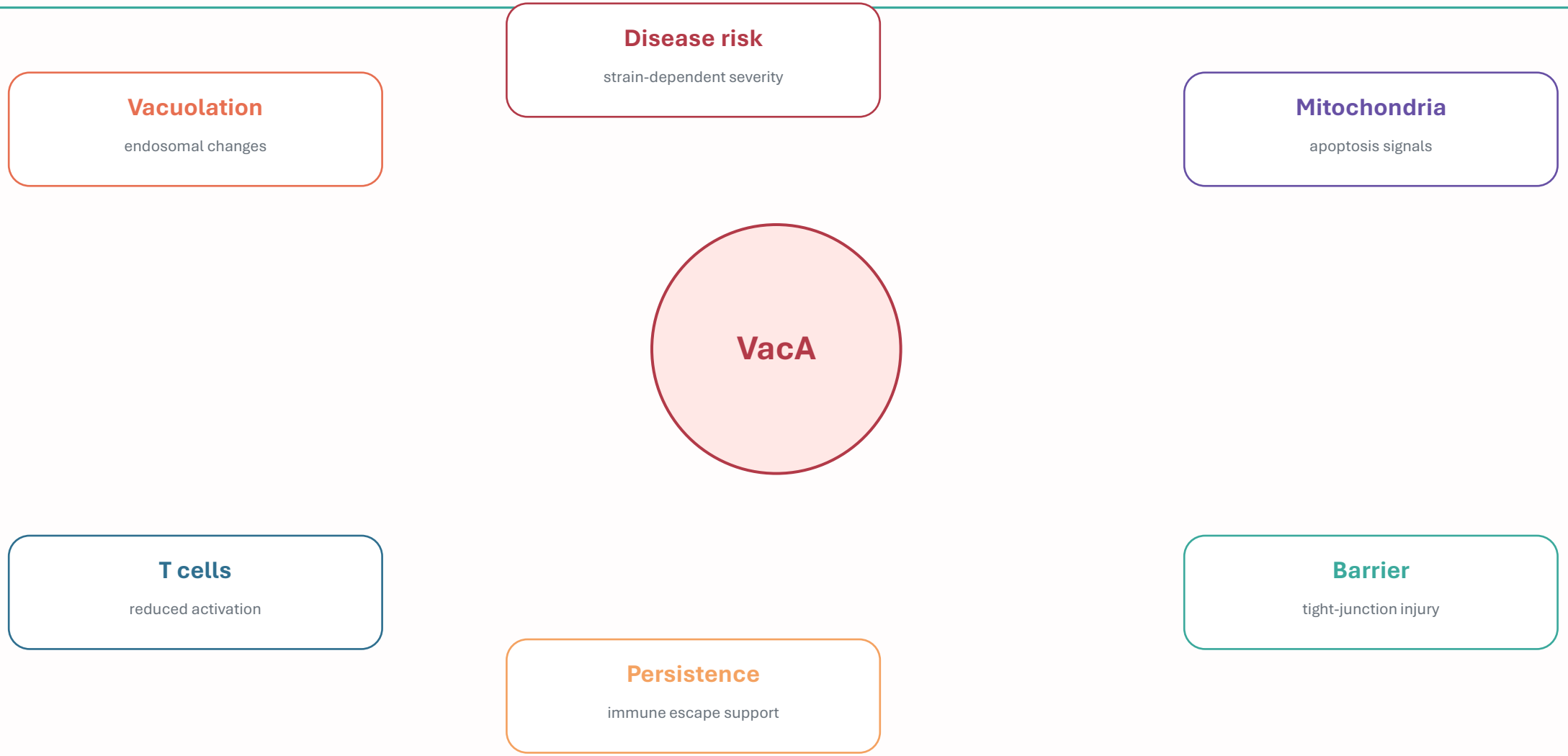
IL-8 induction

neutrophil recruitment

CagA signalling: Wang et al., Front Cell Infect Microbiol 2023; Roesler et al., 2014.

VacA toxin: more than “vacuoles”

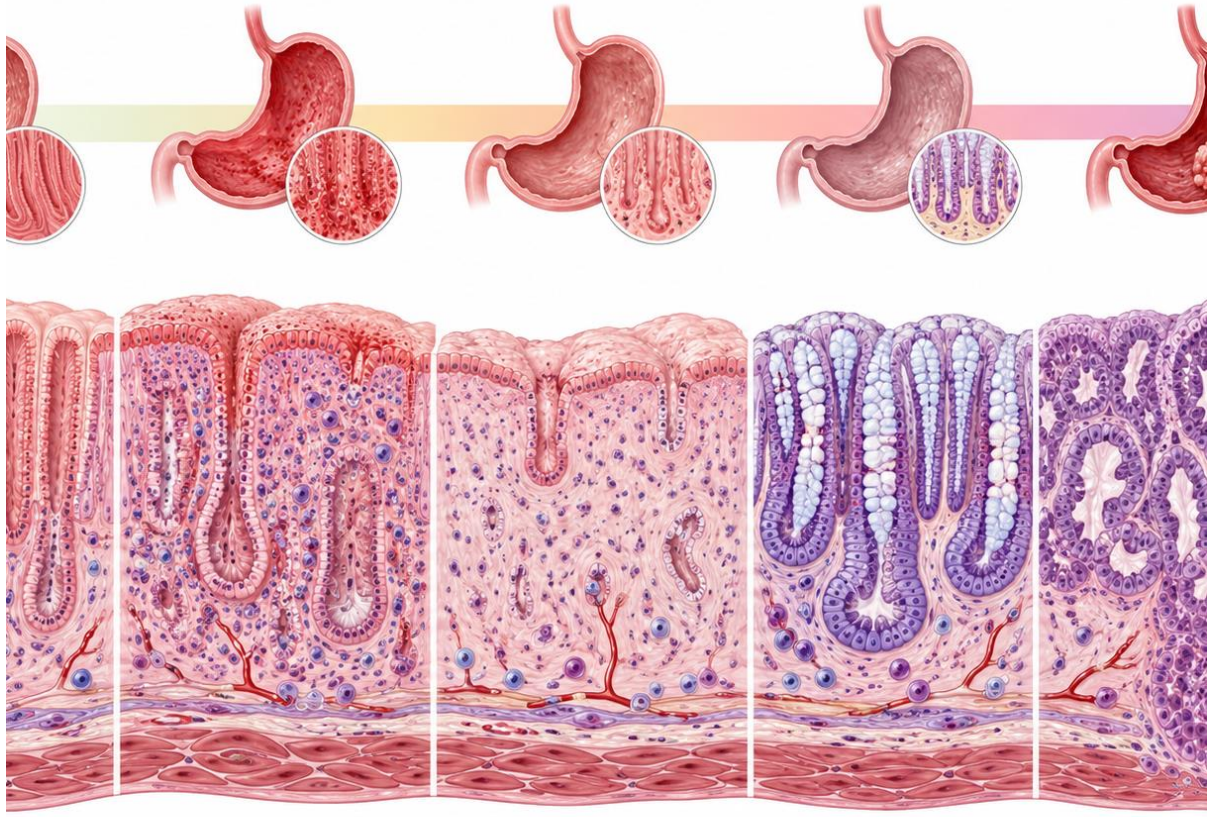
VacA helps explain epithelial injury and immune modulation.



VacA: Roesler et al., Clin Exp Gastroenterol 2014; Sun et al., Front Cell Infect Microbiol 2023.

Gastric carcinogenesis: the Correa cascade

H. pylori is a modifiable driver of chronic inflammation and premalignant change.



Progression model

1. Chronic active gastritis
2. Glandular atrophy
3. Intestinal metaplasia
4. Dysplasia
5. Adenocarcinoma

Eradication before advanced premalignancy gives the strongest preventive benefit.

Gastric cancer mechanisms: Salvatori et al., Int J Mol Sci 2023; Malfertheiner et al., 2023.

Diagnosis: choose the test according to the question

Do we need active infection, tissue damage, resistance, or treatment success?

Test	Best question answered	Teaching note
Urea breath test	Active infection	Non-invasive; very useful before/after treatment
Stool antigen test	Active infection	Non-invasive; useful for test-of-cure
Serology	Past exposure	Not suitable for cure confirmation
Endoscopy + biopsy	Histology / ulcers / premalignancy	Needed when alarm signs or histological staging
Culture / molecular resistance	Antibiotic susceptibility	Guides tailored therapy when available

Diagnostic approach: WGO H. pylori guideline; Malfertheiner et al., Nat Rev Dis Primers 2023.

Antibiotic resistance changed the treatment logic

Treatment is no longer “one standard triple therapy for everyone.”

1

Clarithromycin

macrolide resistance → triple therapy failure

2

Levofloxacin

fluoroquinolone resistance limits salvage use

3

Metronidazole

resistance common; high-dose/combination may still help

4

Amoxicillin

resistance remains relatively uncommon

Stewardship message: avoid empiric clarithromycin- or levofloxacin-containing regimens unless susceptibility is known.

Antibiotic resistance: Chey et al., ACG Guideline 2024; Tshibangu-Kabamba & Yamaoka, Nat Rev Gastroenterol Hepatol 2021.

Treatment update: 2024 guideline principles

A modern lecture should emphasize resistance-aware regimens and confirmation of cure.

Preferred empiric option

Optimized bismuth quadruple therapy for 14 days when susceptibility is unknown

Empiric alternatives

Rifabutin triple therapy or PCAB dual therapy may be suitable in selected patients without penicillin allergy

Avoid empirically

Clarithromycin or levofloxacin regimens unless antibiotic susceptibility is confirmed

After treatment

All treated patients need test-of-cure using appropriate timing and test choice

Chey et al., ACG Clinical Guideline: Treatment of H. pylori Infection, Am J Gastroenterol 2024.

Post-treatment test-of-cure algorithm

Eradication should be proven, not assumed.

1

Complete regimen

Confirm adherence and side effects

2

Wait ≥4 weeks

After antibiotics/eradication therapy

3

Hold PPI ~2 weeks

Use H2 blocker/antacid if needed

4

Test active infection

Urea breath test or stool antigen; biopsy if endoscopy needed

5

If positive

Assess previous antibiotics and select salvage regimen

Reason: traditional eradication rates have declined, so persistent infection must be detected early.

ACG 2024 guideline: universal post-treatment test-of-cure.

Prevention and public-health thinking

H. pylori is not only an individual ulcer problem; it is also a cancer-prevention topic.

Transmission reduction

Sanitation, clean water, reduced crowding, household-level prevention.

Screen-and-treat

May be considered in high gastric-cancer-risk populations.

Family clustering

Infected household members can share similar strains.

Antibiotic stewardship

Poor regimen choice increases resistance and future failures.

WGO H. pylori guideline; Malfertheiner et al., Nat Rev Dis Primers 2023.

Case discussion

Use this as an interactive class activity.

Case

A 38-year-old patient has recurrent epigastric pain. Stool antigen is positive for H. pylori. She previously received clarithromycin for respiratory infection several times. Local susceptibility testing is unavailable.

Questions

- Which first-line regimen is more logical?
- Why should clarithromycin triple therapy be avoided?
- When should test-of-cure be performed?
- Which test is appropriate for cure confirmation?

Case designed from ACG 2024 treatment principles.

Lecture summary

The advanced message in one slide.

CagA / VacA / adhesins

Chronic gastritis

Diagnosis strategy

H. pylori persistence

Resistance-aware therapy

Ulcer phenotype

Cancer / MALT risk

Synthesis of referenced literature and 2024 treatment guideline.

Quick review questions

Can be used as oral discussion or written exit-ticket.

1. What does the type IV secretion system deliver into gastric epithelial cells?
2. Name two effects of VacA on host cells or immunity.
3. Which gastritis pattern is more associated with gastric cancer risk?
4. Why is old clarithromycin triple therapy no longer a safe default choice?
5. Why should every treated patient undergo test-of-cure?

Questions designed to assess higher-level understanding beyond introductory facts.

References

Main sources used to prepare this lecture

1. Chey WD, Howden CW, Moss SF, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024;119(9):1730–1753. doi:10.14309/ajg.0000000000002968

2. Malfertheiner P, Camargo MC, El-Omar E, et al. Helicobacter pylori infection. Nat Rev Dis Primers. 2023;9:19. doi:10.1038/s41572-023-00431-8

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4. Tshibangu-Kabamba E, Yamaoka Y. H. pylori infection and antibiotic resistance—from biology to clinical implications. Nat Rev Gastroenterol Hepatol. 2021;18:613–629.

5. Wang H, Zhao M, Shi F, et al. Signal pathways induced by H. pylori CagA. Front Cell Infect Microbiol. 2023;13:1062803.

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7. Roesler BM, Rabelo-Gonçalves EMA, Zeitune JMR. Virulence Factors of Helicobacter pylori: A Review. Clin Exp Gastroenterol. 2014;7:9–17.

8. Sherris Medical Microbiology; Jawetz, Melnick & Adelberg's Medical Microbiology; Prescott's Microbiology.