Update on the pathological classification of gastritis

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CLASSIFICATION

GASTRITIS

1. Acute
2. Chronic
3. Uncommon Forms

GASTROPATHY

Chemical gastropathy (NSAID/Bile reflux)
CAUSES OF PEPTIC ULCER

100 Consecutive DU and 154 GU PATIENTS

VAMC, Houston

Percent of Group

Duodenal Ulcer

Gastric Ulcer

Hp POSITIVE

NSAID USER

NSAID ONLY

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Case 1: 45 year old with dyspepsia

Gastropathy = no acute inflammation (unless there is an erosion)

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Chemical gastropathy

1. Foveolar hyperplasia
2. Smooth muscle fiber hyperplasia
3. Paucity of chronic inflammatory cells
Q: Should we care?

1. OTC analgesics including NSAID are widely used, frequently taken inappropriately, and users are generally unaware of potential for adverse side effects.

2. Can cause serious side effects including dyspepsia, peptic ulcer, hemorrhage, and even result in death.
HOW TO IDENTIFY FOVEOLAR HYPERPLASIA?

2 things

1. LENGTH OF NECK REGION
2. MUCIN DEPLETION (50:50)

1. Foveolar region
   - Long & tortuous
   - normal
   - FH- 3x normal

2. Amount of mucin
   - normal - mucin 80% of cell
   - FH - mucin ≤ 50%

It's more blue
NORMAL SMOOTH MUSCLE FIBERS

Chemical gastropathy

Thinner than normal

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Q1: HOW OFTEN DO YOU SEE

Chemical gastropathy is common; you will not always see the triad; suggest it when suspected chronic NSAID users.

- Triad is most seen at incisura (less marked at other regions of the stomach).
- Remaining 70%:
  - edema
  - foveolar hyperplasia only
  - Fibrosis
  - FH only or SMF-H only

El-Zimaity et al Hum Pathol 1996; 27(12): 1348-54
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CLASSIFICATION

GASTRITIS

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GASTRITIS

• ACUTE
  – *H. pylori*
  – Other
    ▪ Other bacteria (Heilmanni, mycobacteria)
    ▪ Syphilitic
    ▪ Viral
    ▪ Parasitic
    ▪ Fungal

• Chronic
  – *H. pylori* (chronic atrophic gastritis)
  – Autoimmune (body predominant)
GASTRITIS

• ACUTE
  – *H. pylori*
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    ▪ Other bacteria (Heilmanni, mycobacteria)
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    ▪ Fungal

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  – *H. pylori* (chronic atrophic gastritis)
  – Autoimmune (body predominant)
Anatomy of The Stomach
WHAT IS NORMAL?

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Anatomy of The Stomach

- corpus
- antrum
- Acid
Anatomy of The CORPUS

- Antrum-corpus junction
- G cells
- D cells
- Parietal cells (ECL)

Mucous
ECL
Chief
Corpus

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NORMAL CORPUS
Anatomy of The ANTRUM

- Antrum-corpus junction
- G cells
- D cells
- Parietal cells
- ECL

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Acid Secretion Pathophysiology

Food

G cell

Gastrin

ECL

Parietal cell

ACID

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OUTCOMES OF *H. PYLORI* INFECTION

Environmental Factors

Acute Gastritis

Childhood

Acute & Chronic Gastritis

Mid-life---Old

Duodenal Ulcer

Gastric Ulcer

Gastric Cancer

Lymphoma

Short, cardiovascular disease, colon cancer, etc.
Should you care?

• If you speak “Arabic” you have *H. pylori*!
• Yes, you should care.
No bacteria likes too much acid including *H. pylori*

*H. pylori* starts its life in the antrum where it is less acidic.
No bacteria likes acid

Starts in the antrum

*H. pylori* surrounds itself with a bicarbonate cloud to counter gastric acidity

(it produces urease which converts urea (abundant in saliva & gastric juices) to ammonia and bicarbonate)

\[ C=0(NH2)2 + H+ +2H20 \rightarrow \text{urease} \rightarrow HCO3- + 2(NH4) \]
Acid Secretion Pathophysiology

- Food/H. pylori
- G cell
- ECL
- Parietal cell
- Gastrin

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Duodenal Ulcer

100 G cells

Gastrin

100 Parietal cells

Parietal cell

Acid

ACID

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Inflammation Depth - Duodenal Ulcer

- MNC
- PMN
- \(H.\ pylori\)

ACID

Zone 1

Zone 2

Zone 3

Body

Antrum

Inflammation in antrum only

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Inflammation Depth-Duodenal Ulcer

- MNC
- PMN
- H. pylori

Zone

1

2

3

Antrum

H. pylori → toxins → Cytokines → Massive inflammatory response → Destroy stomach

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Acid Secretion

GASTRIC ATROPHY

Destroyed corpus = no acid = bacteria moves proximal

Food/H. pylori

Parietal cell

ECL

G cell

Gastrin

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Inflammation Depth-Gastric Ulcer

MNC
PMN
H. pylori

Inflammation in both antrum and corpus

Acid

Zone

1
2
3

Body

Antrum

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Duodenal Ulcer Antral Predominant

Duodenal → Gastric Ulcer

Zone 1

Body

Zone 2

Body

Antrum

Zone 3

Gastric ulcer Pan Gastritis

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Why is this important?

• *If patient is H. pylori positive*
  – Receives acid suppressor therapy without treating the infection (e.g. GERD patient and *H. pylori* infection missed)
  – You will help him develop gastric atrophy
Acid Secretion

PPI treatment = high pH

Food/H. pylori

Parietal cell

G cell

ECL

HYPERGASTRINAEMIA

ECL HYPERPLASIA

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ANTRAL MUCOSA

Before

After PPI

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CORPORUS MUCOSA

VAMC, Houston

Before

After PPI

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Gastritis Stages

Antral Predom.  Corpus gastritis  Pan-atrophic

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Atrophic border (antral corpus junction) moves proximally and towards greater curve with disease progression.

El-Zimaity et al Am J Gastro 2001;96:666-672

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Endoscopic Recognition of the Atrophic Border
Kimura and Takemoto 1969

Eastern (Japanese) beliefs

Endoscopy 1969;1:87-97

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Normal Antral corpus junction
Lesser curvature

Advancing atrophic border

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3 questions to answer if you already decided it is *H. pylori*

1. Is it in the antrum only or antrum and corpus?
2. If in the corpus, is inflammation superficial or deep?
3. Is there corpus atrophy?
Gastric atrophy

• Absence of what is normally there:
  – Simple absence of glands (reduced thickness, increased fibrosis)
  – Replacement of what is normally there (with intestinal metaplasia or pseudopyloric metaplasia)
Atrophy in Gastric cancer (Intestinal type)
(a) advancing atrophic border
(b) total atrophy of antrum

12%  
n = 2

88%  
n = 14

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Isolated intestinal metaplasia = not important

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Continuous sheets of atrophy (IM and/PPM) is ominous irrespective of IM subtype
Continuous sheets of atrophy (IM and/PPM) is ominous
• We know how to recognize intestinal metaplasia
• How do we recognize pseudo-pyloric metaplasia?
Pepsinogen I (PG I) Normal Corpus

NORMAL CORPUS

PGI

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PSEUDOPYLORIC METAPLASIA

Normal corpus
In Anatomic corpus

Antral looking
In Anatomic corpus
Pepsinogen I (PG I) Anatomic Corpus (pseudopyloric metaplasia)

ANATOMIC CORPUS   PGI

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Pepsinogen I (PG I) Anatomic Corpus 
(pseudopyloric metaplasia)

ANATOMIC CORPUS

Gastrin

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**PSEUDO-PYLORIC METAPLASIA**

- PPM starts as early as 9 years old.
- Atrophy always starts at antral corpus junction and moves proximally and towards the greater curve.


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Two things to remember

1. Look for the Atrophic Front (starts at antral corpus junction)
2. Recognize all forms of atrophy (absence of normal or replacement with intestinal metaplasia and/or pseudopyloric metaplasia)
What about Pernicious Anaemia?

- Scandinavian decent
- Auto immune gastritis
- Parietal cell and Intrinsic Factor antibodies-
megaloblastic anemia
- Three to five fold increased risk of gastric cancer

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GASTRITIS PATTERN

A. Antral (Type B)
B. Fundic gland (Type A)
C. Pangastritis (Type AB)
pernicious anaemia

Big overlap in the literature since most PA studies were done before *H. pylori* era; some deny its existence!
In any *H. Pylori* Gastritis

- *H. pylori* positive patient
- Use patient’s serum as primary antibody
- Parietal cells stain dark blue

= autoantibodies in every day *H. pylori* gastritis

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PERNICIOUS ANEMIA

1. Parietal cells disappear early
2. G cells increase in number
3. ECL cells keep growing

Acid production drops much faster in PA; so, \textit{H. pylori} and associated inflammation moves proximally much faster.

Parietal cell antibodies
Many folds higher

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CORPUS
ECL HYPERPLASIA

Chromogranin

Grimelius

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PERNICIOUS ANAEMIA

Corpus atrophy with gastric cancer risk (intestinal type)

ECL hyperplasia and eventually carcinoids

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QUESTIONS TO ANSWER IN GASTRIC BIOPSIES?

1. Is it normal? Is it a gastritis or a gastropathy?
2. Why it looks like *H. pylori* but no bacteria found?
3. Is there atrophy?
Landmark for NORMAL lymphoid infiltrates muscularis mucosae
Lymphoid infiltrate:
Loose next to muscularis mucosae = Normal

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Lymphoid Follicles in *H. pylori* infection

**Pre-treatment**
Have marginal zone, mantle, and follicle center

**Post treatment**
Lymphoid tissue first disappear from marginal zone, followed by mantle zone.
More Mononuclear cells MNC in lamina propria means more likely gastritis

Few mononuclear cells = normal (scale 1-2)
To Diagnose Chronic inactive *H. pylori* infection (post treatment)

Lamina propria should have more than a few MNC (score of 3)

Lymphoid aggregates should have signs of organization

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If you found this in a 45 year old with dyspepsia (mucosa looks normal) is this *H. pylori*?
Safety Pin Appearance HP

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NOT ALL BACTERIA IN THE STOMACH ARE *H. pylori*

- With PPI use, the gastric pH increases which allows other bacteria to survive in the stomach.
- Make sure you are really looking at *H. pylori*. Look for squiggle bacteria with safety pin appearance.
Causes of (apparent) *H. pylori* negative gastritis

- Proton pump inhibitors (omeprazole etc.)
- Recent antibiotics or eradication therapy
- Missed organisms - few bugs
- Focal chronic active colitis - Crohn’s disease
- Other types of gastritis (e.g. lymphocytic gastritis)
GASTRITIS

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- Lymphocytic
- Eosinophilic
- Crohn's disease
- Sarcoidosis
- Isolated granulomatous
Lymphocytic Gastritis

• Protein loss.
• Ratio of 25 CD3+ IEL/100 epithelial cells (focal).
• Usually accompanied by lamina propria plasmacytosis

• Celiac Disease, Gastric Lymphoma, Menetrier’s Disease.
• *H. pylori* (low *H. pylori* count)
Lymphocytic Gastritis

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Crohn’s Gastritis

Same as any other part of the gastrointestinal tract

1. Focal enhanced inflammation
2. Granulomas
Gastritis (acute and chronic) is multifocal

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Granuloma’s in the Stomach

Crohn’s

1. Focally enhanced gastritis (acute and chronic)
2. Granuloma

- **H. pylori**
- Granuloma basics:
  - IBD
  - T.B.
  - Sarcoid
  - Foreign body
Reporting gastritis

1. Where am I? (Site - Antral, Oxyntic, Cardiac, Pangastritis, Focal)
2. Is it a gastritis or a gastropathy?
3. Are there epithelial/vascular changes (e.g. dysplasia or cancer)?