Disease of the Stomach

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I have no relationship with any commercial firm having products related to topics I will discuss at this conference.
Disease of the Stomach

1. Neuromuscular disorders
   Gastroparesis
   Dumping syndrome and Rapid Gastric Emptying

2. Gastritis and Gastropathies
   Autoimmune Metaplastic Atrophic Gastritis
   Environmental Metaplastic Atrophic Gastritis
Disease of the Stomach (cont’d)

3. Peptic Ulcer Disease
   Epidemiology
   Risk Factors
   Other Causes of Ulcer Disease
   - Gastrinoma with or without MEN Type 1
   - Systemic Mastocytosis
   - Miscellaneous Disorders

4. Upper GI Bleeding

5. Granulomatous Gastritides
   - Sarcoidosis
   - Xanthogranulomatous Gastritis
6. Distinctive Gastritides
   Colagenous Gastritis
   Lymphocytic Gastritis
   Eosinophilic Gastritis

7. Miscellaneous Forms of Gastritis
   IBD (Crohn’s disease
   Gastritis Cystica Profunda
   GVHD

8. Carcinoid Tumor in AMAG
Gastric & Intestinal Motility Disorders *(Classifications)*

- **Neuropathy**
  - Diabetic Gastroenteropathy
  - Post-Vagotomy
  - Neuropathic variety of intestinal pseudo-obstruction

- **Myopathy**
  - Scleroderma
  - Myopathic variety of intestinal pseudo-obstruction

- **Drugs/Humoral**
- **Undefined**
  - ?N.U.D.
  - ?I.B.S.
SOME OF THE SYMPTOMS OF DELAYED AND ACCELERATED GASTRIC EMPTYING OVERLAP

Delayed Gastric Emptying
- Belching
- Vomiting

Early Satiety
- Feeling of Fullness
- Epigastric Pain
- Nausea
- Heartburn
- Anorexia
- Weight Loss

Accelerated Gastric Emptying
- Abdominal Cramping
- Diarrhea
- Vasomotor Changes
- Pallor
- Rapid Pulse
- Perspiration
- Syncope

Acute Gastric Emptying
- Weight Loss
- Dehydration
- Hyperglycemia
- Hypokalemia
- Hypomagnesemia
Diabetic Gastroenteropathy
A Wide Spectrum of Dysfunction and Symptomatology

- **Esophageal Dysfunction**
  - Dysphagia

- **Gastroparesis**
  - Nausea/Vomiting
  - Post-prandial fullness
  - Abdominal Pain

- **Accelerated Emptying**
  - “Dumping” syndrome

- **Delayed Intestinal Transit**
  - Constipation
  - Abdominal Pain

- **Rapid Intestinal Transit**
  - Diarrhea

- **Gallbladder Dysfunction**
  - Gallstones

- **Anal Sphincter Neuropathy**
  - Incontinence
Diabetic Gastropathy

Clinical Features

• Common (50% of long-standing Type 1)
• Most prevalent in Type 1 but also occurs in Type 2
• Usually (50-70%) associated with autonomic neuropathy
• High blood sugar levels can exacerbate gastropathy
• Consequences may include:
  – Delayed emptying of solids and indigestible particles
  – Rapid emptying of liquids
  – Bezoar formation
  – Poor blood sugar control (tendency to hypoglycemia)
  – Malnutrition/weight loss
Dumping Syndrome

- Occurs in patients after vagotomy and pyloroplasty
- Abnormal post-op anatomy causes rapid emptying of food into the duodenum
- Symptoms 1st hour
  - Pain, bloating, nausea, vomiting
- Symptoms 2 to 4 hours later
  - Sweating, lightheadedness, cramps, diarrhea
- (Later symptoms due to rapid absorption of carbs
Rapid Gastric Emptying

• Definition: When more than 30% of the meal leaves the stomach within 30 minutes or more than 70% at 60 minutes

• Causes:
  - Idiopathic
  - Early Diabetes Mellitus Type 2
  - Zollinger-Ellison Syndrome
  - Surgeries
Gastropathy and Gastritis - Definitions

- **GASTROPATHY** - Literally, any gastric lesion
  Used as substitute for “gastritis” when inflammation absent or minimal

- **GASTRITIS** - Leukocyte infiltration in stomach
  - **ACTIVE (=ACUTE) GASTRITIS** - Neutrophil infiltration present

- **CHRONIC GASTRITIS** - Mononuclear leukocytes increased

- **CHRONIC ACTIVE GASTRITIS** - Mixed chronic and active inflammation
<table>
<thead>
<tr>
<th>Features</th>
<th>Autoimmune (Type A)</th>
<th>Environmental (Type B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes</td>
<td>Antoimmunity Genetic?</td>
<td>Dietary Duodenal reflux?</td>
</tr>
<tr>
<td>Parietal Cell Ab’s</td>
<td>All</td>
<td>None</td>
</tr>
<tr>
<td>Pernicious Anemia</td>
<td>Common</td>
<td>None</td>
</tr>
<tr>
<td>Serum Gastrin</td>
<td>High (often)</td>
<td>Low or Normal</td>
</tr>
<tr>
<td>HCl Secretion</td>
<td>Absent</td>
<td>Low</td>
</tr>
<tr>
<td>Gastric Ulcer</td>
<td>Rare</td>
<td>Increased</td>
</tr>
<tr>
<td>Gastric Cancer</td>
<td>? Increased</td>
<td>Increased</td>
</tr>
</tbody>
</table>
Metaplastic Atrophic Gastritis - Distributions of Autoimmune vs Environmental Types

Autoimmune

Environmental

Early

Late
Granulomas In Gastritis – Typical Causes

- **SYSTEMIC DISEASE-ASSOCIATED** (non-infectious)
  - Crohn’s disease
  - Sarcoidosis
  - Wegener’s granulomatosis (rare)

- **CONFINED TO STOMACH** (non-infectious)
  - Isolated (idiopathic) granulomatous gastritis
  - Foreign material
  - Tumor-associated (eg, MALT Lymphoma)

- **INFECTIONOUS**
  - *H pylori*
  - Tuberculous
  - Tertiary syphilis (gummatous)
  - Whipple’s disease
  - Histoplasmosis
Lymphocytic Gastritis – Associated Conditions

- Varioliform gastritis
- Celiac disease
- *H. pylori* gastritis
- Hypertrophic lymphocytic gastritis
- Ticlopidine administration
- Lymphocytic colitis
- Collagenous colitis
Large Gastric Folds: Classification

- **Gastrin-Stimulated Rugal Hypertrophy**
  - Z-E associated Some DU patients

- **Hypertrophic Hypersecretory Gastropathy**
  - Not gastrin-stimulated
  - Protein-losing gastropathy

- **Menetrier’s Disease**

- **Miscellaneous Causes**
  - Hyperplastic polyps
  - Neoplasia (carcinoma, lymphoma)
  - Inflammatory (various)
  - Infiltrative (amyloid)
Gastric Amyloidosis with Large Rugal Folds – Endoscopy and Histology (Congo Red)
Hyperplastic Gastropathies - Gross

Zollinger-Ellison

Ménétrier's
Non-Ulcer Dyspepsia

- *H. pylori* frequency about the same as in asymptomatic population
- Prospective clinical trials of anti-\(H. pylori\) therapy generally have had disappointing results
- As yet unable to identify subpopulation that achieves long term symptomatic benefit from *H. pylori* therapy
The Gastric Mucosa is Protected by a Multi-layered Defense

- Mucus
  - Mucus
  - Bicarbonate
- Epithelial Defenses
  - Hydrophobic surface
  - Tight intercellular junctions
  - Rapid restitutions
- Subepithelial Defenses
  - CGRP
  - NO
  - NK/SP
  - Other Protective Mechanisms
  - PG
- Arteriole/Venule
  - Vasodilatation
  - Increased Blood Flow
  - Splanchnic Afferent Nociceptive Neuron
Causes of Peptic Ulcer

• *Helicobacter pylori* infection
• NSAID use
• Rare causes
  – Pathologic hypersecretory states
  – Herpes simplex infection
  – Crohn’s disease, etc.
  – Systemic Mastocytosis
Ulcers May Be Caused by Non-acid/peptic Disorders

**Esophagus**
- herpes simplex
- tablet induced tetracycline
- KCl
- others
- cytomegalovirus

**Stomach**
- carcinoma
- Kaposi’s
- lymphoma
- pancreatic rest
- syphilis
- candida

**Duodenum**
- Crohn’s disease
- pancreatic carcinoma
Gastric Cancers May Ulcerate and Resemble Gastric Ulcers

X-Ray

Endoscopy

Histology

Gastric Cancer

Gastric Ulcer
EM of spiral flagellated *H. pylori*
Helicobacter Pylori

- Gram-negative
- Spiral rod
- Fastidious
- Microaerophilic
- Urease-positive
- Unipolar flagella
Pathophysiology
Postulated Steps in Infection

• Ingestion of *H. pylori*
• ‘Swim’ through mucus
• Attach to mucosa
• Multiply
• Damage tissue
• Internalization into epithelium?
Clinical Outcomes & Sequelae of *Helicobacter pylori* Infection

Acute infection (usually unrecognized)

Acute gastritis (transient hypochlorhydria)

Chronic Active *H. pylori* gastritis (life-long infection)

Asymptomatic

Peptic Ulcer (GU or DU)

EMAG

AMAG

Gastric Carcinoma

Gastric MALT Lymphoma
Pathophysiology
Duodenal Abnormalities

• Alterations in duodenal structure and function
  – Damage to surface cells
  – Increase in proportion of surface covered by gastric metaplasia; some with ability to make acid
  – Scarred, deformed smaller bulb (altered motility?)
  – Abnormal bicarbonate secretion
Diagnostic Tests

• **Non-invasive**
  – Antibody tests
  – Urea Breath Tests
  – Stool antigen

• **Invasive**
  – Rapid Urease Tests
  – Histology
  – Culture
Antibody Tests

- Used for initial diagnosis
- FDA approved tests are for serum IgG, antibody tests and are sensitive, specific, and cost effective
- IgA or IgM tests: unapproved and poor
- Titers decline slowly, limiting use for follow-up
- Saliva and urine tests are experimental
Urea Breath Tests
Diagnose Active Infection

- [13C] - urea
  - stable isotope
  - non-radioactive

- [14C]- urea
  - radioactive isotope
  - special handling and disposal
Conclusions:

- There is sufficient evidence in humans for the carcinogenicity of infection with *H. pylori*.
- *H. pylori* is a Group 1 or definite carcinogen
GASTRIC MALT LYMPHOMA

MALT: Mucosa-Associated Lymphoid Tissue - a benign reactive process consisting of lymphoid follicles

MALT LYMPHOMA: monoclonal proliferation of neoplastic B-lymphocytes infiltrating gastric glands (lymphoepithelial lesions)
Gastric Malt Lymphoma
Presentation

• Clinical
  – Asymptomatic!
  – Dyspepsia
  – Weight Loss
  – Ulcer

• Endoscopic
  – Mucosa appears normal
  – Thick folds
  – Ulcerations
Gastric Malt Lymphoma

Effect of Treatment of *Hp*

- Cure of *H. pylori* infection results in remission of approx. 75% of gastric MALT lymphomas
- Regression usually occurs within 6 months, but may take longer
- No features predict unresponsiveness
- Recurrence of MALT lymphomas associated with reinfection
Antimicrobial Drugs
Used for *H. pylori*

- Amoxicillin
- Bismuth
- Clarithromycin (macrolides)
- Metronidazole
- Tetracycline
- Proton pump inhibitors
**H. PYLORI** Treatment

PPI Therapies X 14 days

- **TRIPLE THERAPY (OAC)**
  - Omeprazole 20 mg b.i.d.
  - Amoxicillin 1000 mg b.i.d.
  - Clarithromycin 500 mg b.i.d.
- Lansoprazole can substitute for Omeprazole
Parietal Cell Secretion is Regulated by Site-Specific Agonists and Antagonists
NSAID ULCER Clues

- **History**
  - NSAID use, arthritis

- **Location**
  - Greater curve GU
  - Giant DU

- **Presentation**
  - UGI Bleeding

- **H. pylori tests**
  - neg. for *H. pylori*

- **Clinical Course**
  - Difficult to heal
Peptic Ulcer - Therapeutic Endoscopy

- Initial Control: 80%
- Permanent Control
- Rebleed: 20%
- Permanent Control: 50%
- Rebleed: 50%
- Surgery
- Angiography
UGI BLEEDING
Adverse Clinical Prognostic Factors

- Shock, red blood
- Cause of bleeding (varices or cancer)
- Comorbid disease
- Older age
- Onset in hospital
- Recurrent bleeding
UGI Bleeding
Outcome

% Patients

- varices
- Gastric Cancer
- Peptic Ulcer
- Gastric erosions
- Mallory Weiss
- No diagnosis

Rebleed
Death
UGI Bleeding – Stress Ulcer
Indications for Prophylaxis

• Critical illness
  – ventilator dependent > 48 hours
  – coagulopathy

• Burns
  – > 30% surface area

• Head injury
  – Neurosurgical patients
UGI Bleeding
Vascular Anomalies

GUT
- Vascular ectasia
  - angiodysplasia
  - watermelon stomach
  - congestive gastropathy
- Vascular tumor
- Dieulafoy’s lesion
- AVM

GUT + skin
- Olser-Weber-Reineu
- CRST
- Blue rubber bleb
- Ehlers-Danlos
UGI Bleeding

- Duodenal ulcer
- Gastric erosions
- Rare causes
- Tumors
- Mallory-Weiss
- Duodenitis
- Esophagitis
- Gastric Ulcer
- Unknown
UGI Bleeding

- AVMs
- Stomal ulcer
- Dieulafoy’s lesion
- Watermelon stomach
- Hemobilia
- Connective tissue disorder
- Kaposi’s sarcoma
- Aorto-enteric fistula
- Benign tumors
- Others
Zollinger-Ellison Syndrome
Is a Clinical Triad Consisting of:

- Gastric acid hypersecretion
- Severe peptic ulcer disease
- Non-beta islet cell tumors of the pancreas

• The tumors produce gastrin (G17 & G34); referred to as “gastrinomas”
• Tumors localized usually to head of pancreas, duodenal wall or regional lymph nodes
• About 1/2 of gastrinomas are multiple and 2/3 are malignant
• About 1/4 have multiple endocrine neoplasia syndrome (MEN I) - tumors of parathyroid, pituitary, and pancreatic islets
Clinical Features that Distinguish ZE Syndrome from DU

- Diarrhea
- Weight loss/steatorrhea
- Large gastric folds
- Large amounts of gastric secretions
- Family history of endocrine tumor
- Intractable or post-surgical recurrence of ulcer disease

- Increased gastric acid secretion, decreased duodenal/jejunal pH
  Inactivation of lipase
- Mucosal Inflammation
  - Trophic effect of gastrin
  - Secretory effect of gastrin
  - MEM I - parathyroid tumor/hyperplasia
  - Acid hypersecretion due to gastrin-secreting tumor
Carcinoid Tumor in Autoimmune Metaplastic Atrophic Gastritis With Infiltrating Tumor

Polyps & Atrophic Mucosa

Carcinoid Tumor

Infiltrating Tumor
### Gastric Carcinoid Tumors: Main Features

<table>
<thead>
<tr>
<th>Precursor State</th>
<th>Serum Gastrin</th>
<th>Primary Cell Type</th>
<th>Percent of Gastric Carcinoids</th>
<th>Percent of Gastric Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune Metaplastic</td>
<td>↑</td>
<td>ECL</td>
<td>60-80</td>
<td>Low</td>
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<tr>
<td>Atrophic Gastritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEN 1 (Z-E)</td>
<td>↑</td>
<td>ECL</td>
<td>15-20</td>
<td>Intermediate</td>
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<tr>
<td>Sporadic</td>
<td>NL</td>
<td>Mixed</td>
<td>~5</td>
<td>High</td>
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</table>

*↑: Increased; NL: Normal*