Objectives

- Define entity
- Etiology
- Differentiation of UGI ulcers
- Pathophysiology
- Identify population at risk/risk factors
- Clinical presentation and diagnosis
- Prevention and treatment/prognosis
- Research and practice guidelines
Definition

- Multiple shallow erosions in the stomach and/or duodenum secondary to severe and unremitting physiologic stress that tend to cause hemorrhage but not perforation
- The GI component of multi-organ failure
Etiology

- Shock
- Sepsis
- CNS tumors/trauma
- Burns
- Multi-trauma
Differentiating stress ulcers

- Stress ulcers

- Variants
  - Cushing’s ulcers
  - Curling’s ulcers
Differentiating stress ulcers

- Stress ulcers
  - Shallow discrete lesions but can coalesce
  - Congestion and edema
  - Little inflammatory reaction at the margins
  - Predilection for parietal mucosa
  - Duodenal involvement 30%
  - Sometimes both
Differentiating stress ulcers

- Cushing’s ulcers
  - 2° to CNS trauma
  - ↑ vagal activity from ↑ ICP
  - High acid output and ↑ circulating gastrin
  - Solitary
  - Morphologically similar to ordinary gastroduodenal ulcer
  - Tendency to perforate
Differentiating stress ulcers

- Curling’s ulcer
  - ° to thermal injuries/burn victims
  - gastric secretions
  - Perforation more common than stress ulcers
  - May be anywhere along GI tract
Pathogenesis

- Acute in onset
- Multiple in number but can coalesce
- Commonly located in proximal stomach
- Not associated with hypersecretion of acids
- Failure of cytoprotective factors
Pathophysiology

1. ↓ gastric blood flow/mucosal ischemia
   - ↓ supply of blood buffers
   - ↓ neutralization of H⁺ ions

2. ↓ mucosal resistance
   - Circulating toxins
   - ↓ mucosal renewal
   - ↓ production of endogenous prostanoids
   - Thinning of surface mucus layer
   - ↑ corticosteroid secretion/administration
   - Bile reflux
   - Drug exposure (ASA, NSAIDS)
Pathophysiology

- **Gastric protection**
  - Mucus secretion
  - $\text{HCO}_3^-$ secretion
  - Epithelial restitution
  - ‘Alkaline tide’ that neutralizes acid
  - Energy mismatch when metabolic demand of acid secretion not met with sufficient blood flow
- None appears to contribute to stress ulceration
- ↓ blood flow is major factor
3. ↑ back diffusion of H\(^+\) and subsequent acid-induced injury
   - ? Relation to acid hypersecretion
   - Theory is disputed
   - Formation of ulceration is function of:
     - Rate of decline in intramucosal pH
     - Absolute intramucosal pH
     - Duration of intramucosal pH outside normal limits
Pathophysiology

- Animal model:
  - Neutralization of pH - ↓ stress ulceration
  - ↑ acid secretion with stress
    - No evidence that ↑ acid secretion in ulceration area
  - ↑ acid secretion in burn & CNS trauma victims
    - More common to manifest as serious bleeding
    - More benign in other etiologies of stress ulcers
    - Neutralization of pH does not prevent ulceration
Pathophysiology

- Back diffusion seen in less than $\frac{1}{2}$ of patients
- Mucosal damage in absence of acid
- $R_x$ neutralization of acids – modest results
  - ? Acids only have a modest role

- Acid does play a role – extent unknown
- ? Effect rather than a cause
Population at risk

- UGI bleed from stress ulceration
  - ICU – 5%
  - Severe trauma – 20%
  - Burns (>35% TBSA) – up to 50%
Risk factors

• Risk Factors
  – Etiologic factor present
  – Large transfusion requirements
  – ARDS
  – Ventilator > 48 hr
  – ICU > 1 week
  – Oliguric renal failure
  – Post-traumatic hepatic dysfunction
  – Coagulopathy (complications moreso than cause)
  – High dose steroids
Natural History

- Precipitating insult
- Superficial mucosal erosion
- Progression and coalescence (20% if untreated)
- Overt bleeding (3-5 d post insult)
- Clinically important bleeding (4-5 d post insult)
- Anemia and hypovolumia

- All bleeding stops eventually
Natural history

- Overt bleeding
  - Hematemesis, bloody gastric aspirate
  - Melena
  - Hematochezia
Natural history

• Clinically significant bleeding
  – Overt bleeding +
    • ↓ BP 20 mmHg in 24 hr
    • ↓ BP 10 mmHg + ↑ HR 20 on orthostatic change
    • ↓ Hgb 20 g/L + transfuse 2U blood in 24 hr
    • Requiring surgery
Clinical presentation

- Precipitating insult – asymptomatic (GI)
  - Within 24-48 hr: >60% have erosions
- UGI bleed ~ 20% of susceptible patients
  - Painless hematemesis (NG tube aspirate)
  - Melena/hematochezia – uncommon initial presentation
  - Clinical onset of hemorrhage 3-5 d post insult
  - Massive bleeding 4-5 d post insult
Clinical presentation

- Perforation
  - 10% of cases (not initial presentation)
- Manifestations of etiology
  - Shock, sepsis, burns, CNS, multi-trauma
  - Deteriorating vital signs – hypovolumia
  - Autopsy
Diagnosis

• H & P
  – Risk factors
  – Precipitating insult causing stress
  – Vital signs – hypovolumia
  – Stool for occult blood

• Index of suspicion
  – critically ill patient with painless UGI bleed
  – Presence of risk factors
Diagnosis

- **Barium swallow**
  - Inaccurate because superficial in nature
- **Arteriography**
  - Not 1st line
- **Endoscopy**
  - Correctly identify bleeding source in 90%
  - Erosions 24-48 hr post insult
  - Subclinical diagnosis
  - ? Coag or diathermy – diffuse process
Treatment

- Resuscitation
- Control of hemorrhage
- Prevention of recurrence
- Patient survival – underlying cause
Treatment

- ABCs
  - Resuscitation (Burn victim - 3cc/kg/%TBSA)
  - Restore circulating blood volume
  - Restore cardiac output
    - IVF, blood, clotting factors
  - Aggressive monitoring
    - Art line, Swan-Ganz, ins and outs
- Treat underlying cause
  - Ulceration is superficial – resolve with removal of etiology
- Correct acid-base imbalance
**Treatment**

- **Prevention**
  - **Prophylaxis**
    - Reduce amount of intraluminal acid
      - Intragastric antacid (titrate pH > 3.5-4)
      - H₂ blockers
      - PPI
      - sucralfate
  - Early institution of feeding reduces incidence
  - TPN patients seem to be protected – No benefit from H₂ blockers in this group
  - Avoid surgery if possible
Treatment

- Studies of cimetidine vs. intragastric antacid
  - pH > 3.5
    - Antacid better irrespective of cimetidine dosage
  - Bleeding
    - 2-18% with cimetidine
    - 0-5% with antacid
  - Endoscopic
    - No difference in mucosa
Treatment

- Why cimetidine fail?
  - Inadequate drug delivery
  - ↓ secretion but ↓ buffer
  - ? Importance of ↓ acid secretion in stress ulcers
Treatment

- Gastric lavage with chilled solutions
  - Combat sepsis
- H$_2$ blockers
  - not effective for treating active bleeding
  - ↓ rate of rebleed
  - ↓ acidity – theoretically ↑ risk nosocomial pneumonia
    - Not supported by experience
- Some success with vasoconstrictors
  - percutaneous vasopressin into Left gastric artery
  - Before surgery
Treatment

- Surgery
  - Vagotomy and drainage
  - Vagotomy and pyloroplasty – ? treatment of choice
    - With oversewing of bleeding areas
  - Vagotomy and extensive subtotal gastrectomy
    - With oversewing of bleeding areas
  - Total gastric devascularization
  - Total gastrectomy – if needed for extent of ulcers
    - Inadvisable if other option due to ↑ operative mortality
Treatment

- Vagotomy
  - Reduce gastric secretion
  - Favors opening of AV shunts
    - Divert blood from engorged mucosa
Prognosis

- Dependent on etiology and PMH of patient

- Mortality
  - 30-40% in any circumstance
Research

- Many studies in literature
- Different patient populations
- Different clinical problems
- Different outcomes
  - Some clinically insignificant
Cook et al.
- 269 studies of stress ulcer prophylaxis
- 63 comparable and included in meta-analysis

- **H₂ Blockers**
  - ↓ overt bleeding
  - ↓ clinically important bleeding

- **Sucralfate**
  - ↓ overt bleeding
  - Insufficient data on clinically significant bleeding
  - Less pneumonia and better overall survival than other regimens
Cook et al. – also prospective multicentre study on risk factors for clinically significant GI bleeding in ICU patients

- Incidence low – 33/2252 (1.5%)

- Risk factors
  - Coagulopathy
  - Ventilation > 48 hr
Practice guidelines

? How we judge bleeding as significant
- Endoscopic evidence with no occult blood
- No overt bleeding
  - Therapy doesn’t change outcome
  - Potential unnecessary side effects
  - $$$
- Clinically significant bleeding
  - Incidence low
  - Treat those with risk factors
American Society of Hospital Pharmacists

- Prophylaxis provided for:
  - Ventilated > 48 hr
  - ICU with coagulopathy
  - H$_x$ of GI ulceration or bleeding 1 year prior to admission
  - 2 or more of the following risk factors
    - Sepsis, ICU > 1 week, occult bleeding > 6 days, high dose steroids (>250 mg hydrocortisone or =)
Practice guidelines

- Prophylaxis recommended for:
  - ICU with GCS $\leq 10$ or inability to obey simple commands
  - Thermal injury $> 35\%$ TBSA
Practice guidelines

- Prophylaxis beneficial for:
  - Partial hepatectomy or liver failure
  - Multi-trauma
  - Spinal cord injuries
  - Transplant patients

- Patients not in ICU do not benefit from prophylaxis
Practice guidelines

• Studies supporting these recommendations show
  – ↓ clinically significant bleeds with H$_2$ blockers and sucralfate
  – Insufficient data for efficacy of PPI or misoprostol
  – Measuring gastric pH does not help manage the problem
  – Major complication is pneumonia
    • Not supported by experience
Conclusion

- Very high morbidity and mortality
- High index of suspicion in patients at risk
- Aggressive resuscitation
- Prophylaxis
  - $H_2$ receptor blockade
- Treat underlying cause
  - Ulcerations are superficial and reversible
References

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  – Sabiston (1987)

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