Introduction

- Patients are at increased risk for developing diarrhea in the hospital, with as many as 40% to 70% of some ICU patient populations affected.
- Diarrhea is the most common non-hemorrhagic gastrointestinal complication in this population.
- Diarrhea adversely impacts critically ill patients by contributing to:
  - Fluid losses, dehydration, electrolyte imbalances
  - Hemodynamic instability
  - Increased risk pressure sores
  - Malnutrition
  - Delayed wound healing
  - Acid/base problems
  - Contamination of wounds and catheters
• **Definition**

  • Stools with increased fluidity
  • Increased frequency
  • Increased quantity (≥200g or ≥300ml/day)
Classification

- **Diarrhea secondary to increase in faecal water**

  1. **Secretory diarrhea** – excessive secretion by mucosal cells
     - Osmolar gap < 70 mOsm
     - Infective causes
  2. **Osmotic diarrhea** – excessive amount of high osmol molecules in lumen causing water shift into lumen.
     - Osmolar gap > 70 mOsm
     - Drugs (Duphalac)
  3. **Exudative disease** – increased abdominal mucosa permeability
  4. **Accelerated transport**
  5. **Decreased transit time**: Motility disturbances

- **Diarrhea not secondary to increased faecal water**
  - Partial bowel obstruction
  - Overflow diarrhea
Etiologies

Most cases of diarrhea are non infectious

- Enteral feeding
- Fecal impaction
- Bacterial overgrowth
- Medications: Histamine Antagonists, Peristalsis promoting drugs (metoclopramide, erythromycin), Cholinergics, Sorbitol containing drugs (KCl, Theophylline, Digitalis)
- Psychological stress
- Diagnostic test reagents
- Endocrine disorders
- Immunosuppressants used in transplantation
- Malabsorption
- Hypoalbuminemia
- Intestinal ischemia
- Exacerbations of inflammatory bowel disease
Infectious causes

- Essential to consider an infectious etiology in an ICU patient with diarrhea, especially if the patient has
  - 3 bowel movements per day,
  - blood or mucus in the stool,
  - vomiting, severe abdominal pain, and/or fever
- Infectious diarrhea is typically more severe than noninfectious diarrhea
- Infections: *Clostridium Difficile*
  - Enteric pathogens (*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *Cryptosporidium*)
  - Rotavirus, Norovirus
C. difficile

- Organism first reported in the stools of healthy infants in 1935
- C. difficile was relatively unnoticed for the next four decades, until Tedesco et al. recognized the association of clindamycin with colitis in 1974
- Anaerobic, spore-forming bacillus producing two exotoxins, toxin A and toxin B
- Toxins cause intestinal pathology, disruption of the actin cytoskeleton and induction of neutrophil migration and mucosal inflammatory cascades
- In adults, C. difficile is the leading cause of infectious hospital-associated diarrhea in the United States, Canada, and Europe
- Interacting variables might explain the increased prevalence and severity of CDI
- These include:
  - clonal expansion of the hypervirulent BI/NAP1/027 epidemic strain of C. difficile
  - lack of timely recognition of severe CDI
  - changes in medication-prescribing practices
  - increased and more complex patient comorbidities in an increasingly aging or immunocompromised population
Antibiotics

- Some studies show a definite correlation between antibiotic usage and incidence of diarrhea.
- Historically clindamycin, ampicillin, and cephalosporins were the antimicrobials associated with the greatest risk for CDI.
- More recently, fluoroquinolones have emerged as another strongly associated with CDI.
- Alterations in intestinal flora, breakdown of dietary carbohydrate products are postulated mechanisms.
Enteral nutrition

- Diarrhea is a known and problematic complication of enteral nutrition
- Number of factors contribute to the pathogenesis of diarrhea in enteral nutrition, including:
  - Altered physiological response
  - Elevated risk of Enteropathogenic infection
  - Antibiotics
  - Too high flow rates/volume
  - Hyperosmolar feeds
  - Too little residue formula
Enteral nutrition may result in deleterious effects on the gastrointestinal microbiota, including reductions in bifidobacteria and key butyrate producers.

Studies on healthy individuals found that intragastric enteral nutrition results in abnormal water secretion into the ascending colon.

Above exacerbated by suppression of distal colonic motor activity that accelerates colonic transit and reduces the opportunity for water absorption.

If these occur in patients receiving enteral nutrition, then in the absence of compensatory absorptive mechanisms, diarrhea may result.

Many patients receiving enteral nutrition also receive concomitant antibiotics, and a number of studies have shown that diarrhea is associated with the prescription, number, or duration of antibiotics.
Elevated risk of enteropathogenic infection?

- A case-control study found that *Clostridium difficile* colonization was three-fold higher, and *C. difficile* associated diarrhea (CDAD) was nine-fold higher, in patients receiving enteral nutrition, and this is despite similar antibiotic use.

- More recently, in an analysis of 233 patients undergoing percutaneous endoscopic gastrostomy (PEG), 15 (6.4%) patients developed CDAD within 1 month, six (2.6%) of whom entered a cycle of recurrent CDAD, resulting in a major interruption to the delivery of enteral nutrition.

- Prophylactic antibiotics are frequently given during PEG insertion, and following multivariate analysis, the duration of antibiotic prescription (but not actual antibiotic prescription) was an independent predictor of subsequent development of CDAD.
Mx Enteral nutrition-associated diarrhea

- The addition of sodium chloride and trace elements to the formula may counteract the effects of active gastrointestinal water secretion.
- Some authors recommend predigested enteral formulas containing peptides and medium-chain triglycerides rather than whole proteins and long-chain triglycerides.
- ASPEN combined different approaches and stated that if there is evidence of diarrhea, soluble fiber-enriched formulas or predigested formulas may be utilized.
Enteral nutrition should not be interrupted or stopped.
Continued bowel rest exacerbates bacterial overgrowth and gastrointestinal dysmotility, which perpetuates the diarrhea, and protein and energy goals will not be reached.
Reducing the delivery rate, while still achieving target volumes.
Another option is to reduce enteral nutrition provision and to replace protein and energy with supplementary parenteral nutrition, tapering down once diarrhea abates and the volume of enteral nutrition is increased.
Fibre enriched formulas

- May prevent diarrhea through:
  - reducing the rate of gastric emptying
  - improving gut barrier function
  - increasing epithelial cell turnover or regeneration
  - increasing colonic fluid and electrolyte absorption
- Some fibers undergo fermentation and produce SCFAs that reverse the abnormal colonic water secretion in enteral nutrition
- A systematic review and meta-analysis of prospective RCTs reported a preventive effect of fiber-enriched enteral nutrition on diarrhea, with a significant reduction in the percentage of patients with diarrhea
Algorithm for clinical management of enteral nutrition-associated diarrhea

- Diarrhea for more than two days
  - Kwashiorkor? (Yes/No)
    - Yes: Add trace elements
    - No pump: Use pump
  - No cause found: Try partially hydrolysed guar gum formulae or a FODMAP-free formula, loperamide
- Check EN output
  - No pump: Use pump
  - Pump: Reduce output
- Rectal examination
  - Fecal impaction: Extraction
  - No fecal impaction: Stop if possible
- Antibiotics? (Yes/No)
  - Yes: Stop if possible
  - Metronidazole
- Laxatives? (Yes/No)
  - Yes: Stop
Probiotics

- Probiotics are ‘live microorganisms’ which when administered in adequate amounts can confer a health benefit on the host.
- Commonly used strains: lactobacilli, bifidobacteria, and saccharomyces.
- Rationale for using probiotics is based on the assumption that:
  - They modify the composition of colonic microflora.
  - Modulate immune function.
  - Counteract enteric pathogens.
- Several RCTs and meta-analyses suggest that probiotics are effective in primary and secondary prevention of gastroenteritis.
- Promising in preventing antibiotic-associated diarrhea.
Prebiotics

- Prebiotics are defined as the selective stimulation of growth and/or activity of one or a limited number of microbial species in the gut microbiota.
- The most commonly used prebiotics are Inulin-type fructans (inulin, oligofructose, fructo-oligosaccharides).
- When added to enteral formulas, prebiotics have been shown to increase fecal bifidobacteria in healthy individuals.
- But no studies have investigated the ability of prebiotic formulas to stimulate growth of bifidobacteria in in-patients with acute illness.
Evaluation

1. **History**
   - Review Medications received + feeding regimen
   - Medical & surgical history
   - Onset / duration / frequency stools
   - Stool details (amount / fluidity / color / smell / + blood)

2. **Examination**
   - Full systemic, Abdominal and rectal exam

3. **Stool Exam**
   - MC&S
   - Ova, Parasites, Toxins
   - Biochemistry

4. **Other as indicated**
   - Gen. Lab studies (FBC, UK&E, LFT, CMP, CRP)
   - Abdominal radiographs are sometimes helpful: may show signs of ischemia, partial obstruction, perforation, or a toxic megacolon associated with colitis
   - Flexible or rigid proctosigmoidoscopy useful in diagnosing antibiotic-associated colitis, distal ischemic colitis, GVHD, and vasculitis, to name a few
   - Mucosal biopsy can be useful in some cases with negative endoscopic findings
   - Contras studies
Management

- Identify and treat the cause > As per evaluation above
- Monitor and correct fluid and electrolyte abnormalities
- Antimotility agents such as loperamide and codeine can be used; however, exclude fecal impaction and C. difficile infection
- There is no evidence to support the use of probiotics or prebiotics in treating patients who already have diarrhea
- TPN - if enteral route not advisable
- Medications should be reviewed
- Rectal catheter
  - Increase nursing ease
  - Quantify losses
Establishing the diagnosis is important not only to initiate specific treatment for the patient with diarrhea but also to implement measures to prevent the spread of the causative organism to other patients and staff in the ICU.
References

- Irwin and Rippe's Intensive Care Medicine
- Critical Care Medicine 2010, Vol. 38, No. 8
- Current Opinion in Gastroenterology 2011, 27, 152–159