Nutritional Alterations

Nancy Thompson, RN, MS, AOCNS
Swedish Cancer Institute

- Diarrhea
- Constipation
- Nausea & Vomiting
- Mucositis
- Taste Alterations
- Anorexia / Cachexia

GI Symptoms - Why does it matter?

- GI toxicity can result in dose reductions and treatment delays
- Quality of Life Issues
- Lead to a cascade of other symptoms

Diarrhea

Greater than 200 g/day of fecal output with a volume of 300 ml that is 70 – 90% water and more than three stools per day.
Types

- Acute - 24 – 48 hours of contact with an agent and resolves within 7 – 14 days or earlier with intervention
- Chronic diarrhea - late onset, lasts for 2 – 3 weeks, occurs as the result of an unidentified agent or as the result of tissue injury related to a treatment modality that interferes with normal bowel function.
- Radiation induced - typically occurs within 2 weeks of beginning radiation therapy

Types

- Osmotic – large volume that resolved with fasting or elimination of the provoking agent
- Secretory – large volume that persists despite fasting
- Exudative – inflammation, necrosis and sloughing of the colonic mucosa. Occurs more than 6 times per day of variable volume
- Chemotherapy induced - frequent, watery to semisolid stools with abdominal pain, cramping & fecal incontinence
- Radiation induced
- Dysmotility associated - uncoordinated control of intestinal propulsions with rapid transit of stool . Small frequent semisolid stools of variable amounts

Diarrhea Assessment

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Increase of &lt; 4 stools per day over baseline; mild increase in stool; not interfering with ADL</td>
<td>Increase of 4 – 6 stools per day over baseline; IV fluids indicated; 24 hrs moderate increase in stool; not interfering with ADL</td>
<td>Increase of &gt; 7 stools per day over baseline; IV fluids indicated; 24 hrs moderate increase in stool; not interfering with ADL; hospitalization with ADL</td>
<td>Life threatening consequences (e.g., hemorrhagic collapse)</td>
<td>Death</td>
</tr>
</tbody>
</table>


Diarrhea Risk Factors

- Radiation therapy
- 5-FU + high dose leucovorin or weekly 5FU
- Immunosuppression
- Bowel surgery
- Neutropenic sepsis - C. difficile, candida

- GVHD
- Dietary causes
- Inflammatory conditions
- Malabsorption
- Anxiety and stress
Diarrhea
High-Risk Agents

- Chemotherapy:
  - Irinotecan
  - 5-FU
  - Paclitaxel
  - Dactinomycin
  - Dacarbazine
  - Capecitabine
- Biotherapy:
  - IL-2
  - Interferons
- Targeted agents
  - MoAbs
  - Imatinib mesylate
  - Dasatinib
  - Erlotinib
  - Bortezomib
  - Lapatinib
  - Gefitinib
  - Sunitinib malate
  - Temsirolimus
  - Revlimid and thalidomide
  - Zolinza

Diarrhea
Clinical Manifestations

- Dehydration (especially children)
- Life-threatening electrolyte imbalances
- Cardiovascular compromise, orthostasis
- Impaired immune function
- Skin breakdown
- Reduced absorption of oral meds
- Pain
- Anxiety
- Exhaustion/decreased quality of life

Diarrhea
Management

- Monitor stool number, amount, consistency
- Consider other medications that could contribute
- Consider diet and herbal supplements
- medication that are contributing
- Replace fluid and electrolytes
- Administer antidiarrheal medication
  - Diphenoxylate
  - Loperamide
  - Octreotide
  - Anticholinergics
  - BRAT diet
- Increase clear fluid intake (with electrolytes)
- Skin care in the peri-rectal area, especially if neurogenic
- Early and aggressive patient education

Constipation

Affects 40% - 70% of cancer patients

Causes:
- Presenting symptom of cancer
- Side effect of treatment
- Result of tumor progression
- Unrelated to cancer or treatment
**Constipation Assessment**
- Patterns of elimination
- Dietary intake
- Activity level
- Abdominal pain or cramping
- Characteristics of last BM
- Current medications
- Laboratory values
- Abdominal/rectal exam
- Radiographic studies

**Agents that decrease motility of the large intestine**
- Vinca alkaloids
- Agents that increase nausea and vomiting (thereby decreasing oral intake)
- Opioids
- Anti-depressants
- Iron supplements
- Diuretics
- OTC analgesics (Tylenol, non-steroidal)

**Incidence**
- Vinblastine: 20-35%
- Vinorelbine: 35%
- Thalidomide: 55%
- Bortezomib: 41%

**Constipation Clinical Consequences**
- Abdominal or rectal discomfort
- Nausea/vomiting
- Anorexia
- Impaction
- Ileus
- Anal fissures
- Hemorrhoids
- Ruptured bowel and life-threatening sepsis

**Constipation Laxative Options**
- Bulk forming
- Lubricants and emollients
- Saline laxatives
- Osmotic laxatives
- Polyethylene glycol (with or without electrolytes)

- Detergent laxatives
- Stimulant laxatives
- Suppositories
- Prokinetic agents
- Methylnaltrexone
- Combination laxative-stool softener
  prophylactically for patients receiving vinca alkaloids.
**Constipation**

Non-pharmacologic interventions

- Increase physical activity or passive exercise
- Maintain usual bowel habits during hospitalization
- Increase fluid and fiber intake
- Do not perform rectal exams, use suppositories or enemas if myelosuppressed
- Consider rotating opioids

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**Nausea & Vomiting: Defined**

- **Nausea**: An unpleasant subjective experience that is described as a "wavelike" feeling occurring in the stomach and/or the back of the throat that may be accompanied by vomiting.

- **Vomiting**: The forceful expulsion of gastric, duodenal or jejunal contents through the mouth.

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**Therapy-Related Emesis Patterns**

- **Anticipatory**: Occurs before or during treatment from associated stimuli; a conditioned response
  - 25% incidence

- **Acute**: Occurs within 24 hours
  - Incidence determined by agents

- **Delayed**: Occurs at least 24 hours after therapy and may persist up to 6 days
  - Cisplatin associated with highest incidence

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**Risk Factors for CINV: Patient Characteristics**

- Female
- Age < 50 years
- History of low alcohol intake (<1.5 oz/day)
- History of motion sickness
- History of morning sickness during pregnancy
- History of prior CINV
- Extreme anxiety

- Other factors
  - pain, constipation, medications

**Risk Factors for CINV: Chemotherapy-Specific Factors**

- Use of moderately or highly emetogenic regimens, such as:
  - Cisplatin-based regimens
  - Cyclophosphamide-based regimens (e.g., CHOP)
  - AC (anthracycline + cyclophosphamide)
  - Carboplatin-based regimens
  - ABVD (doxorubicin + bleomycin + vinblastine + dacarbazine)
  - FOLFOX/FOLFIRI (oxaliplatin + leucovorin + 5FU/irinotecan + leucovorin + 5FU)
- Short IV infusion time
- Repeated cycles of chemotherapy

**Classification of Acute Emetogenic Potential of Single Chemotherapeutic Agents**

<table>
<thead>
<tr>
<th>Level</th>
<th>Emesis Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Emesis in &gt;90% of patients</td>
</tr>
<tr>
<td>4</td>
<td>Emesis in 60%–90% of patients</td>
</tr>
<tr>
<td>3</td>
<td>Emesis in 30%–60% of patients</td>
</tr>
<tr>
<td>2</td>
<td>Emesis in 10%–30% of patients</td>
</tr>
<tr>
<td>1</td>
<td>Emesis in &lt;10% of patients</td>
</tr>
</tbody>
</table>

**Single Chemotherapeutic Agents With Highest Potential for Acute Emetesis**

<table>
<thead>
<tr>
<th>Level</th>
<th>Frequency of Emetesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>4</td>
<td>60%–90%</td>
</tr>
</tbody>
</table>

**Agent Details**

- **Carmustine**: >250 mg/m²
- **Cisplatin**: 50 mg/m²
- **Cyclophosphamide**: >1,500 mg/m²
- **Dactinomycin**
- **Mechlorethamine**
- **Streptozotocin**
- **Cyclophosphamide**: >250 mg/m²
- **Cisplatin**: <50 mg/m²
- **Cyclophosphamide**: >750 mg/m² ≤1,500 mg/m²
- **Cyramzine**: >1 g/m²
- **Doxorubicin**: >60 mg/m²
- **Melphalan**: >1,000 mg/m²
- **Procarbazine**: (oral)

**Single Chemotherapeutic Agents With Moderate Potential for Acute Emetesis**

<table>
<thead>
<tr>
<th>Level</th>
<th>Frequency of Emetesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>30%–60%</td>
</tr>
<tr>
<td>2</td>
<td>10%–30%</td>
</tr>
</tbody>
</table>

**Agent Details**

- **Cyclophosphamide**: >750 mg/m²
- **Cyclophosphamide**: (oral)
- **Doxorubicin**: 30–60 mg/m²
- **Etoposide**: 150–250 mg/m²
- **Irinotecan**: 85 mg/m²
- **Hexamethylmelamine**: (oral)
- **Itenimide**: (oral)
- **Raspamycin**: (oral)
- **Epothilone**: (oral)
- **Mechlorethamine**: (oral)
- **Streptozotocin**: (oral)
- **Melphalan**: 200–1,000 mg/m²
- **Mitoxantrone**: ≤15 mg/m²

**Note:**

Both Peripheral and Central Pathways Play a Role in CINV


Illustration by Kirk Moldoff.

CINV: Differential Involvement of Neurotransmitters Over Time

<table>
<thead>
<tr>
<th>Acute (Day 1)</th>
<th>Delayed (Days 2–5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predominantly serotonin-dependent mechanisms (peripheral)</td>
<td>Predominantly substance P-dependent mechanisms (central)</td>
</tr>
</tbody>
</table>

Hours After Cisplatin Treatment

Nausea & Vomiting Pharmacologic Management

- Prevention of nausea and vomiting is the goal
- Select appropriate antiemetic based on treatment regimen
- Consider cumulative effects
- Administer through entire anticipated period of nausea & vomiting
- Oral and IV antiemetic have equivalent effectiveness
- Consider other potential causes of emesis

Serotonin Antagonists

- Indications:
  - High & moderate to high emetogenic chemotherapy
- Common side effects:
  - Headache, diarrhea, constipation, fever
- Examples:
  - Ondansetron, granisetron, dolasterson, palonosetron
**NK-1 Antagonist**

- **Indications:**
  - Acute and delayed nausea / vomiting
  - Highly emetogenic chemotherapy
- **Common side effects:**
  - Diarrhea, hiccups, fatigue
- **Examples:**
  - Aprepitant (oral)
  - Fosaprepitant (IV)

**Other agents**

- Corticosteroids - used in combination with other meds. Mechanism of action is unknown
- Cannabinoids - used for refractory CINV when other agents are ineffective. Many side effects
- Dopamine antagonists - used for low potential and for breakthrough
- Benzodiazepines - used for anticipatory CINV and breakthrough

**CINV Cheat Sheet**

<table>
<thead>
<tr>
<th>Phase of CINV</th>
<th>Acute Events</th>
<th>Delayed Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of Action</td>
<td>Peripheral Pathway</td>
<td>Central Pathway</td>
</tr>
<tr>
<td>Neurotransmitter</td>
<td>Serotonin</td>
<td>Substance P</td>
</tr>
<tr>
<td>Class of Drug</td>
<td>5HT₃ Receptor Antagonist</td>
<td>NK₁ Receptor Antagonist</td>
</tr>
<tr>
<td>Drug Examples</td>
<td>Dolasetron, Granisetron, Ondansetron, Palonosetron</td>
<td>Aprepitant Fosaprepitant</td>
</tr>
</tbody>
</table>

**Non-pharmacologic Management**

- Music therapy
- Moderate exercise
- Acupressure
- Acupuncture
- Behavioral interventions
- Dietary interventions (small frequent meals)
- Patient education
  - Notify if N/V > 24 hrs or unable to maintain fluid intake
  - Take antiemetics before arriving
  - Follow-up in 24-48 hours
Mucositis: Defined

- **Mucositis** - Inflammatory process involving the mucous membranes of the oral cavity and gastrointestinal tract
- **Stomatitis** – inflammatory disease of the mouth.
- Mucosal membranes proliferate with a high turnover rate every 7 – 14 days

Phases of Mucositis Development

Patient Related Assessment Areas for Mucositis

- Age (very young and very old)
  - Young recover more quickly
- Gender (females > males)
- Poor oral health and hygiene
- Low body mass index
- Renal Toxicity (increased creatinine, increased toxicity)
- Smoking History
- Previous cancer treatment
- Hyposalivation (or increased viscosity)
- Ill-fitting prostheses
- Hematologic malignancy (to some extent, related to treatment regimen)

Risk Factors for Mucositis

Regimen-related

- Cytotoxic agent used
- Prolonged or repetitive administration (vs. bolus)
- Radiation therapy to the head/neck region in combination with chemotherapy
- Cumulative radiation dose
- Number of cycles and intensity of treatment
- History of previous episodes of mucositis
- Blood/stem cell transplantation
Agents Most Commonly Associated with Mucositis

- actinomycin D
- amsacrine
- bleomycin
- cytarabine
- daunorubicin
- docetaxel
- doxorubicin
- etoposide
- floxuridine
- 5-fluorouracil
- methotrexate
- mitoxantrone
- plicamycin
- thioguanine
- vinblastine
- vindesine

Mucositis: Consequences

- Pain - *** The hallmark of oral mucositis
- Difficulty swallowing
- Difficulty in communication
- Infection
- Bleeding
- Dose reduction and dose delays
- Increased fatigue
- Increased need nutritional support

Mucositis: Assessment

- Perform a thorough oral assessment
  - Use a penlight
  - Use a gloved finger to gently manipulate tongue and cheek
  - Inspect under the tongue and along inner cheeks and gums, inspect hard and soft palate
- Ask the right questions

- Subjective:
  - pain, burning, increased sensitivity, altered taste
- Objective:
  - erythema, ulceration, saliva, bleeding, cracked lips, hoarse voice
- Functional:
  - Ability to chew, difficulty swallowing or speaking

*Systematic oral assessment at least daily or at each patient visit*
Mucositis: Management

- **Prevention**
  - Collaborate with a multidisciplinary team
  - Oral care products
  - Patient education (written, verbal, demonstration)
  - Treat dental problems before cytotoxic therapy
  - High protein diet
  - Fluid intake > 1500 ml/day
  - Cryotherapy for bolus 5-FU

- **Treatment**
  - Oral agents & hygiene
  - Systemic pain medications
  - Culture lesions

Mucositis: Oral Hygiene Program

- Keep oral cavity clean and moist
  - Daily oral self-exam, report signs of mucositis
  - Oral hygiene after each meal and at bedtime, increase to q 2 hours as needed
  - Floss daily with dental tape
  - Brush with soft toothbrush, 90 seconds bid
  - Swish after each meal, at bedtime, at other times with water or mouth rinse (Normal Saline, sodium bicarbonate)
  - Avoid oral irritants including tobacco and alcohol
  - Maintain adequate hydration
  - Use water based moisturizers to protect the lips

Cryotherapy for Bolus Mucotoxic Chemotherapy with Short Half Life

- Bolus 5-fluorouracil (5-FU) & Melphalan
- Instruct patients to hold ice chips in their mouth starting 5 minutes prior and for 30 minutes after.
- The effectiveness of this intervention is based on vasoconstriction of the circulation in the oral cavity and the short half life of these agents.
- Evidence is lacking to support the benefit with other chemotherapy agents.
- Do not use in patients receiving oxaliplatin

Mucositis – Oral Care Agents

- Palifermin – HSCT related mucositis
- **Effectiveness not established**
  - Amifostine – xerostomia protectant during RT
  - Gelclair – topical mucosal protectant
  - Anti-microbial agents
  - Anti-inflammatory rinses
  - Allopurinol
  - Caphosol
  - L-Glutamine
  - Aloe Vera
  - G-CSF
  - Chlorhexidine
  - Miracle Mouthwash - not a Miracle
### Taste Alterations: Defined

- An actual or perceived change in taste sensation or loss of taste
  - Hypogeusethesia: A decrease in the acuity of the taste sensation
  - Dysgeusia: An unusual taste perception, perceived as unpleasant
  - Ageusia: An absence of the taste sensation, “mouth blindness”

### Taste Alterations: Causes

- Disease related
  - Invasion of the tumor
  - Oral infections
  - Excretion of amino acid-like substances from the tumor cells

- Treatment related
  - Specific surgical sites
  - Radiation
  - Chemotherapy:
    - Lowered threshold for bitter taste
    - Increased threshold for sweet, sour and salty taste
    - Aversion to meats
    - Metallic taste

### Taste Alterations: Consequences

- Anorexia
- Decreased intake
- Altered or perverted sense of taste for certain foods
- * Can persist for up to 1 year *

### Taste Alterations: Management

- Experiment with spices and flavorings
- Use the aroma of foods to stimulate taste
- Encourage oral hygiene before and after meals
- Add increased sweeteners
- Substitute other sources of protein
- Marinate meats in sweet marinades
- Avoid the sight and smell of foods causing unpleasantness
- Avoid alcohol, commercial mouthwashes, smoking
- Consume hard candies and / or chew gum to change taste before meals and before chemotherapy treatment to reduce metallic taste
- Refer to dietitians for nutritional counseling
- Assess for weight loss
### Common Nutritional Challenges

- Anorexia
- Malnutrition
- Weight Loss
- Muscle Mass Loss
- Cachexia

- At diagnosis: 50% of patients present with nutritional issues
- Malnutrition is the most common secondary diagnosis to cancer

### Anorexia: Defined

- Involuntary loss of appetite accompanied by decreased food intake
- Often accompanied by weight loss
- Present in up to half of newly diagnosed patients
  - 70 – 80 of patients with advanced disease
- May be insidious and may only be obvious by weight loss
- Can lead to cachexia
- Often is not treated or diagnosed

### Malnutrition: Defined

- A state of nutrition in which a deficiency, excess or imbalance of energy, protein, and other nutrients causes measurable adverse effects on body function and clinical outcome

### Anorexia and Malnutrition: Causes

#### Physiologic: Concurrent symptoms
- Nausea/vomiting
- Early satiety
- Pain
- Dysphagia
- Mucositis
- Ascites
- Fatigue

#### Structural problems
- Abdominal tumors
- Surgical and dental changes

#### Medications
- Narcotics, iron, antibiotics

#### Psychological
- Anxiety, depression
- Loss of pleasure associated with food

#### Social factors
- Companionship
- Eating environment
- Issues associated with food preparation
Clinical Manifestations of Anorexia: Starvation & Wasting

- **Starvation** - Driven by inadequate dietary intake
  - Metabolism slows
  - Ketones used as fuel
  - Muscle and organs are spared
  - Predominant loss of fat
  - Reversed by improving dietary intake

- **Wasting** - Involuntary weight loss
  - Driven by inadequate dietary intake and anorexia
  - Greater than 10% loss from baseline weight
    - Greater than 5% loss in 6 months

Cachexia: Defined

- Condition of progressive deterioration with muscle wasting that occurs when protein and or calorie requirements are not met
- The nondeliberate loss of more than 5% of body weight in the prior 6 months (ONF, Sept 2010)
- A multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment (Fearon K., Lancet Oncol. 2011; 12(5) 489 – 495)

Patients with Weight Loss have worse outcomes

- Chemotherapy dose reductions
- Increase dose limiting toxicity
- Decreased Treatment response
- Decreased Quality of Life and performance status
- Shorter survival

Malnutrition’s Effect on Oncology Patients

Just a small loss of weight may be a sign of a nutritional decline that leads to:

- Treatment Delays
- Complications
- More frequent hospitalizations
- Reduced key outcomes such as quality of life

**Symptoms and Consequences**

**Symptoms:**
- Loss of lean body mass
- Loss of fat
- Muscle wasting
- Early satiety
- Loss of appetite
- Nausea and vomiting
- Dysphasia
- Weight loss

**Consequences:**
- Fatigue
- Impaired immune response
- Significant negative nitrogen balance
- Catabolic hormones and cytokines released
- Hypermetabolic state results
- Energy demand increases causing rapid depletion of muscle and fat

**Anorexia / Cachexia: Assessment**

- **Dietary factors**
  - Diet history
  - Ability to purchase & prepare food
  - Food preferences / aversions
  - Calorie count / food diary
  - Educational needs
- **Physical Exam**
  - Weight loss
- **Laboratory Data**
  - pre-albumin, albumin, transferrin

**Laboratory Results**

- **Serum albumin**
  - Measures visceral protein stores
  - Less than 3.5 g/dl shows recent protein depletion

- **Serum prealbumin**
  - Less than 15 mg/dl
  - Indicates protein depletion

- **Serum transferrin**
  - Less than 200 mg/dl
  - Reflects a decrease in the body's ability to make serum proteins

**Anorexia / Cachexia: Management**

- Treat the tumor - Cancer related anorexia
- Early and regular assessment
- Manage anorexia causes
- Consider appetite stimulants
  - Corticosteroids, progestins
- Dietary Counseling
- Non-pharmacological
  - small, frequent meals, oral hygiene, exercise, high calorie, high protein foods & supplements
Recommended Appetite Stimulants

- **Corticosteroids**: Prednisolone, Dexamethasone
  - Improve appetite, food intake, sense of well-being and performance status
  - Most effective type, dose or route not established
  - Benefit is significant yet short in duration
  - Long term use is associated with significant toxicities
- **Megestrol acetate** (Megace) - 160 - 1600 mg daily
  - Most widely studied
  - Dose related benefit on appetite, caloric intake and body weight and sensation of well-being.
  - Not to be used in patients at risk for thromboembolic disease, heart disease or serious fluid retention

Individualized Dietary Counseling

- Improved nutritional intake and body weight
- Reduction in the incidence of anorexia
- Improved quality of life

Tried but Failed....

- **Effectiveness NOT Established**
  - Fish oils contain: EPA (eicosapentaenoic acid) & DHA (docosahexaenoic acid)
  - Erythropoietin
  - Metoclopramide
  - Thalidomide
  - Oral branch chained amino acids

- **Effectiveness Unlikely**
  - Cannabinoids
  - Hydrazine Sulfate
  - Melatonin

Non-pharmacological

- Exercise/strength training - improved lean muscle mass
- Refer to cancer rehabilitation or PT
- One of the most effective things we can do!
In addition to decreasing inflammation, corticosteroids:

- Improve muscle tone
- Stimulate weight loss
- Stimulate the appetite
- Reduce anxiety

Nursing interventions for the management of nausea include encouraging patients to:

- Use sauces and gravies
- Eat foods that are cold or at room temperature
- Eat high protein / high potassium foods
- Avoid brushing their teeth when they are nauseated

Cachexia in the patient with cancer may result in increased:

- Bone density
- Infection rates
- Glucose turnover
- Lipoprotein lipase activity

Cancer associated nutritional problems, rather than treatment related nutritional problems are best reversed by:

- Extensive verbal counseling
- Self-care actions
- Medications
- Successful treatment of the tumor
Jim complains that food does not taste the same and that everything tastes like cardboard. He especially dislikes the taste of red meat. This is best explained by the fact that persons with cancer commonly experience which of the following?

a) Intolerance to bland foods
b) Difficulty digesting their food
c) An increased threshold for sweet, sour, and salt and a decreased threshold for bitter foods.
d) A decreased threshold for sweet, sour, and salt and an increased threshold for bitter foods