Care Guide: *Chemotherapy-Induced Diarrhea (CID)*

**At First Report of Diarrhea: Evaluate Patient**
- Obtain history of onset and duration of diarrhea
- Have patient describe number of stools and stool composition (e.g., watery, bloody, mucus, nocturnal)
- Assess for fever, dizziness, abdominal pain/cramping, weakness (rules out risk for sepsis, bowel obstruction dehydration)
- Obtain medication profile to identify any diarrheogenic agents
- Obtain dietary profile to identify any diarrhea-enhancing foods

**Uncomplicated**
CTCAE grade 1 or 2 diarrhea with no complicating signs or symptoms

**Management**
- Stop all lactose-containing products, alcohol, and high-osmolar supplements
- Drink 8-10 large glasses of clear liquids per day (e.g., Gatorade, broth)
- Eat frequent small meals (bananas, rice, applesauce, toast, plain pasta – BRAT diet)
- Instruct patient to record number of stools and report symptoms of life-threatening sequelae (e.g., fever, dizziness upon standing)
- For grade 2 diarrhea, hold cytotoxic chemotherapy until symptoms resolve and consider dose reduction

**Treatment**
Administer loperamide; initial dose 4 mg, followed by 2 mg q 4 h or after very unformed stool

**Complicated**
CTCAE grade 3 or 4 diarrhea or grade 1 or 2 with one or more of the following:
- Cramping
- Nausea/vomiting (> grade 2)
- Decreased performance status
- Fever
- Sepsis
- Neutropenia
- Frank bleeding
- Dehydration

**Progression to severe diarrhea**
(CTCAE grades 3 – 4 ± fever, dehydration, neutropenia, and/or blood in stool)

**Re-assess 12 – 24 h** → **Diarrhea unresolved**
Diarrhea Resolving
- Continue instructions for dietary modification
- Gradually add solid foods to diet
- Discontinue loperamide after 12 h diarrhea-free interval

Consider:
- If recently on antibiotics, check for *C. difficile*
- If on prolonged steroids, check for amoeba, ova and parasites, and strongyloides

Persistent Diarrhea (CTCAE grades 1 – 2)
- Administer loperamide 2 mg q2h
- Start oral antibiotics
- Observe patient for response

Diarrhea resolved

Diarrhea unresolved

Evaluate in Office or Outpatient Center
- Check stool workup*
- Check CBC and electrolytes/consider abdominal/pelvic CT scan
- Perform abdominal exam
- Replace fluids and electrolytes as appropriate
- Discontinue loperamide; begin second-line agent
  - Octreotide (100 to 150 mcg SQ tid with dose escalation up to 500 mcg tid)
  - Other second-line agent (e.g., tincture of opium)

Persistent diarrhea (CTCAE grades 1 – 2)
(no fever, dehydration, neutropenia, and/or blood in stool)

Re-assess 12 – 24 h

Progression to severe diarrhea
(CTCAE grades 3 – 4 ± fever, dehydration, neutropenia, and/or blood in stool)

Admit to Hospital †
- Administer octreotide (100 – 150 mcg SQ tid or I. V. [25 – 50 mcg/h] if dehydration is severe, with dose escalation up to 500 mcg tid)
- Start I.V. fluids and antibiotics as needed (e.g., fluoroquinolone)
- Stool workup, CBC, and electrolyte profile
- Discontinue cytotoxic chemotherapy until all symptoms resolve; restart chemotherapy at reduced dose

* Check for blood, fecal leukocytes, *Clostridium difficile*, *Salmonella*, *Escherichia coli*, *Campylobacter*, infectious colitis.
† For RT-induced cases and select patients with chemotherapy-induced diarrhea, consider intensive outpatient management, unless the patient has sepsis, fever, or neutropenia.

CTCAE, common terminology criteria for adverse events; CBC, complete blood count; SQ, subcutaneous; RT, radiotherapy
Risk Factors for Chemotherapy-Induced Diarrhea (CID)

1. Medicare age
2. Female gender
3. Poor performance status (Eastern Cooperative Oncology Group (ECOG) level 2 or higher)
4. Associated bowel pathology (e.g., inflammatory bowel disease, tumor in bowel, etc.)
5. Change in emotional state (e.g., anxiety, stress)
6. Prior history of CID
7. Concomitant abdominal-pelvic radiation and chemotherapy
8. Chemotherapy agents with significant incidence of causing diarrhea: capecitabine (Xeloda), cisplatin (Platinol), cyclophosphamide (Cytoxan), docetaxel (Taxotere), paclitaxel (Taxol), 5-fluorouracil (5-FU, Adrucil), irinotecan (Camptosar), leucovorin, oxaliplatin (eloxatin), erlotinib (Tarceva)
9. Travel
10. Irritable Bowel Syndrome
11. Surgery related:
   - Gallbladder, gastrectomy, esophagogastrectomy, pancreaticoduodenectomy (Whipple procedure) intestinal resection

ECOG Performance Status

<table>
<thead>
<tr>
<th>Version</th>
<th>Level 0</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
<th>Level 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG</td>
<td>Fully active, able to carry out all pre-disease performance without restriction.</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature e.g., light housework, office work.</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.</td>
<td>Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.</td>
<td>Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair.</td>
<td>Dead</td>
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</table>

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Increase of &lt;4 stools per day over baseline; mild increase in ostomy output compared to baseline</td>
<td>Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline Not interfering with ADLs</td>
<td>Increase of &gt;=7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADLs</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
<td>Death</td>
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Definition: A disorder characterized by frequent and watery bowel movements.

Non-Chemotherapy Drugs that Can Cause Diarrhea

1. Antacids with Magnesium
2. Antibiotics, e.g., ampicillin, erythromycin, amoxicillin
3. Bile salts, lactulose
4. Colchicine
5. Potassium chloride
6. Prokinetic agents, e.g., Reglan
7. Non Steroidal Anti Inflammatory Drugs (NSAIDs)
8. Theophylline
9. H-2 blockers, proton pump inhibitors
Confounding Factors in Cancer Patients with Diarrhea

Diet
- High-fiber diet
- High-osmolar dietary supplements
- Laxative abuse
- Milk or milk products
- Lactose products

Endocrine Factors
- Hyperthyroidism
- Neuroendocrine tumors

Infection

Inflammatory bowel conditions

Malabsorption

Goals of treatment of CID*

1. Avoid associated mortality and morbidity
2. Reduce patient discomfort and inconvenience
3. Enhance recovery of the intestinal mucosa from the effects of chemotherapy
4. Reduce hospitalization and use of other health care resources
5. Enhance treatment outcomes

Agents Utilized in the Treatment of Chemotherapy-Induced Diarrhea

**Absorbents**
- Charcoal
- Kaolin + pectin (generic or Kaopectate)

**Anticholinergics**
- Atropine
- Belladona
- Scopolamine

**Antisecretory Agents**
- Bismuth subsalicylate (Pepto-Bismol)
- Octreotide (Sandostatin LAR Depot)
- Sulfasalazine (Azulfidine)

**Opioids**
- Diphenoxylate (Lomotil)
- Loperamide (Imodium)
- Tincture of Opium (Paregoric)

**Probiotic Agents**
- Lactobacillus
- Bifidobacteria

Preventive measures against Chemotherapy-Induced Diarrhea

<table>
<thead>
<tr>
<th>WHAT TO AVOID</th>
<th>WHAT TO DO</th>
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<tbody>
<tr>
<td>Caffeine products</td>
<td>Drink 8-10 glasses of clear liquids daily (water, Gatorade, broth, clear juices)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Eat small frequent meals</td>
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<tr>
<td>Raw fruits/vegetables, raw eggs</td>
<td>Diet should be low residue</td>
</tr>
<tr>
<td>Spicy, fatty or greasy foods</td>
<td>Diet should be high in protein and calories</td>
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<tr>
<td>Milk and dairy products</td>
<td>BRAT diet</td>
</tr>
<tr>
<td>Un-refrigerated foods</td>
<td>- Bananas</td>
</tr>
<tr>
<td>Lactose-containing foods</td>
<td>- Rice</td>
</tr>
<tr>
<td>High-fiber foods</td>
<td>- Applesauce</td>
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<tr>
<td>Sugar-free gum and other sorbitol containing products</td>
<td>- Toast</td>
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<tr>
<td>Foods containing olestra</td>
<td>- Plain pasta</td>
</tr>
<tr>
<td></td>
<td>Decaffeinated tea and soft drinks</td>
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Key Points: Management of Chemotherapy-Induced Diarrhea (CID)

1. CID is a common, often dose limiting toxicity associated with cancer chemotherapy treatment. Patients who experience CID undergo changes in their planned chemotherapy including dose reductions, delays in treatments, reduction in dose density and discontinuation of therapy. CID impacts Quality Of Life and can inhibit activities such as, work, travel and recreation.

2. CID occurs in 10% of all patients with advanced cancer. However, as many as 80% of those treated with 5-FU or irinotecan (Camptosar), alone or in combination, experience diarrhea, and of those 30% or more have grade 3-5 diarrhea. There is a small but significant mortality associated with CID, especially when it occurs concomitantly with mucositis and neutropenia.

3. Patients with uncomplicated CTCAE Grade 1-2 CID (see chart) should be placed on the BRAT diet (bananas, rice, applesauce, toast, plain pasta) and drink 8-10 large glasses of clear liquids such as Gatorade, broth, and water. They should eat small frequent meals.

4. A severe complication of CID that is difficult to treat is pseudomembranous colitis caused by *Clostridium difficile* ²

References:

1. National Oncology Alliance: Diarrhea Management V. 2. 4/11/06.

2. NCI Gastrointestinal complications (PDQ). Health professional version. Diarrhea. 2010


