PALLIATIVE CARE NETWORK OF WISCONSIN

Fast Facts Core Curriculum

GI

PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #10
TUBE FEED OR NOT TUBE FEED?

James Hallenbeck MD

Background Tube feeding is frequently used in chronically ill and dying patients. The evidence for much of this use is weak at best. The Fast Fact reviews data on the use of tube feeding in advanced illness.

For prevention of aspiration pneumonia

- Numerous observational studies have demonstrated a high incidence of aspiration pneumonia in those who have been tube fed. Reduction in the chance of pneumonia has been suggested for non-bed-ridden post-stroke patients in one prospective, non-randomized study. For bedridden post-stroke patients, no reduction was observed.

- Three retrospective cohort studies comparing patients with and without tube feeding demonstrated no advantage to tube feeding for this purpose.
- Swallowing studies, such as videofluoroscopy, lack both sensitivity and specificity in predicting who will develop aspiration pneumonia. Croghan's (1994) study of 22 patients undergoing videofluoroscopy demonstrated a sensitivity of 65% and specificity of 67% in predicting who would develop aspiration pneumonia within one year. In this study no reduction in the incidence of pneumonia was demonstrated in those tube fed.
- Swallowing studies may be helpful in providing guidance regarding swallowing techniques and optimal food consistencies for populations amenable to instruction. See *Fast Fact* #128 for discussion of the role of swallowing studies.

For life prolongation via caloric support

- Data is strongest for patients with reversible illness in a catabolic state (such as acute sepsis).
- Data is weakest in advanced cancer. No improvement in survival has been found (see exceptions noted below).
- Individual patients may have weight stabilization or gain with tube feeding. However, when cohorts of patients have been studied in non-randomized retrospective or prospective studies, no survival advantage between tube fed and hand fed cohorts has been demonstrated.
- Tube feeding may be life-prolonging in select circumstances:
  - → Patients with good functional status and proximal GI obstruction due to cancer
  - → Patients receiving chemotherapy/XRT involving the proximal GI tract.
  - → Selected HIV patients
  - → Patients with Amyotrophic Lateral Sclerosis

For enhancing quality of life

- Where true hunger and thirst exist, quality of life may be enhanced (such as in very proximal GI obstruction).
- Most actively dying patients (see *Fast Fact* #3) do not experience hunger or thirst. Although dry mouth is a common problem, there is no relation to hydration status and the symptom of dry mouth – see *Fast Fact* #133.
- A recent literature review using *palliative care* and *enteral nutrition* as search terms found no studies demonstrating improved quality of life through tube feeding (results were limited to a few observational studies).
- Tube feeding may adversely affect quality of life if patients are denied the pleasure of eating.

Summary

Although commonly used, current data does not provide much support for the use of artificial enteral nutrition in advanced dementia, or in patients on a dying trajectory from a chronic illness. A recommendation to use, or not use, tube feeding should be made only after first establishing the overall *Goals of Care* (see *Fast Fact* #16). Recommendations for how to discuss the issue tube feeding with patients/families can be found in *Fast Fact* #84.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #15
CONSTIPATION

James Hallenbeck MD

Constipation – it's not fun to have or to treat. As with other symptoms, rational therapy should be based on a sound understanding of underlying physiology. Our goal in treating constipation is generally not to "cure" something, but to help the patient return to the best possible balance that will allow a normal bowel movement to be passed. Four major components affect the production of a normal BM: solid waste, water, motility and lubrication.

Solid Waste – Too much or too little is a problem. The intestine is most efficient pushing intermediate volumes. Patients on fiber-poor diets may improve if fiber is added. **Note**: In patients on opioids or patients with minimal fluid intake or poor gut motility (e.g. the dying patient) additional fiber can worsen the situation, causing a 'soft impaction'.

Water Content – Stool water content depends on how much water we drink, our general hydration status, how much water is absorbed from and secreted into the intestine and how fast stool moves through the bowel. Any of these variables can be manipulated. It is easiest to limit absorption (and increase secretion into the gut) by adding osmotically active particles that retain water (e.g. Magnesium salts, non-absorbable sugars such as sorbitol and lactulose, or polyethylene glycol [PEG]). Note: Magnesium and phosphorus salts are contraindicated in renal failure. Hyperosmolar solutions may worsen dehydration by drawing body water into the gut lumen. Sickly-sweet sorbitol and lactulose may be difficult to for patients to tolerate. PEG is flavorless and may be better tolerated.

Motility – Patients with low-activity levels (bed-ridden, dying patients and patients with advanced neurodegenerative disorders) and use of certain drugs (see below) lead to motility problems. Senna preparations, which stimulate the myenteric plexus are generally favored. Use senna tablets (or granules, liquid, or tea), starting with 1 tab QHS, may be gradually increased to 4 tabs BID if needed. Before increasing motility, evacuate existing constipated stool with an enema or cramping can result.

Lubrication simply eases passage and minimizes pain that can interfere with excretion. Most commonly used is dioctyl sodium sulfosuccinate (DSS, or docusate), which decreases stool surface tension much like soap. Usual dosage is 240 mg PO daily or BID. DSS also tastes like soap, so liquid DSS should never be given PO, but may be given to tube-fed patients. Note: DSS is commonly used in combination with senna in opioid-induced constipation, but is generally inadequate as a sole agent. Mineral oil can be used as an enema but should not be given PO, as pneumonitis can result if aspirated. Glycerin suppositories can provide lubrication and draw-in water due to osmotically active particles.

Medications that can cause/exacerbate constipation: Opioids, anticholinergics (tricyclic antidepressants, scopolamine, oxybutinin, promethazine, diphenhydramine), lithium, verapamil, bismuth, iron, aluminum, aalcium salts. See *Fast Facts* #294 and #295 for more information on opioid induced constipation.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #25
OPIOIDS AND NAUSEA

David E Weissman MD

Background Why do patients get nauseated and vomit after receiving an opioid? Commonly described as an "allergy", opioid-induced nausea/vomiting is not an allergic reaction. In fact, rather than indicating a pathologic reaction, nausea indicates normal functioning of the brain. Opioid-induced nausea occurs through the following mechanisms:

- At the base of the 4th ventricle lies the chemoreceptor trigger zone (CTZ), a "sampling port", to detect substances that do not belong in the blood. Adjacent to the CTZ lies the medullary vomiting center which controls the complex muscular sequence of vomiting. When the CTZ detects a noxious chemical in the blood, a signal is sent to the VC and the vomiting reflex is initiated. Of note, this is the same mechanism when patients vomit after receiving chemotherapy.
- Opioids can directly stimulate the vestibular apparatus—patients note a spinning sensation with their nausea.
- Opioids cause constipation which can lead to nausea via stimulation of afferent cholinergic pathways.

Do all opioids produce the same degree of nausea? There is little research data on this topic. In clinical practice, morphine and codeine are often mentioned as the worst offenders. Some clinical studies along with preclinical data in rats suggest that the transdermal fentanyl patch may have less nausea and constipation than morphine.

Why are some patients more sensitive to the emetic effects of opioids than others? Unknown

What is the natural history of opioid-induced nausea? Most patients develop tolerance to the emetic effects, so that within 3-7 days, at a constant opioid dose, the emetic effect will abate.

What are management approaches?

- Dose adjustment—if good pain relief is achieved but associated with nausea, it may be possible to lower the opioid dose, still retain good analgesia, but eliminate the nausea.
- Switching opioids—there is variability in emetic reaction to different opioids. Note: since tolerance to nausea develops, one never knows if a reduction in nausea is from the change of drug or tolerance.
- Anti-emetics— Whenever possible, choose a drug directed at the most likely cause of nausea (see *Fast Fact* # 5). There are little published data to guide physicians in specific choice of anti-emetic for opioid-induced nausea.
  - Start with low-cost dopamine antagonists (e.g. prochlorperazine, haloperidol, or metoclopromide) or anti-cholinergics (e.g. scopolamine);
  - Anti-histamines may be helpful for patients who note a spinning sensation.
  - $5HT_3$ antagonists (e.g. ondansetron) can be used for more refractory cases. Two multi-center randomized trials have examined control of emesis associated with opioids not used for anesthesia. In one, 16 mg of ondansetron was more effective than 8 mg or placebo. In the other trial, stopped early due to lack of patient accrual, 24 mg ondansetron was no better than placebo or metoclopramide.
- Non-pharmacological approaches: there is little evidence to support non-pharmacological treatments for nausea outside of chemotherapy associated nausea; suggested approaches include acupressure and behavioral treatments.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #45
MEDICAL MANAGEMENT OF BOWEL OBSTRUCTIONS
Charles F von Gunten MD, PhD, J Cameron Muir MD, Sean Marks MD

Background Malignant bowel obstruction is a common oncologic complication; most common in ovarian and colon cancer. Symptoms include nausea, vomiting, and abdominal pain which can be colicky or continuous. Treatment options include surgical correction, placement of a venting gastrostomy tube, stent placement across the obstructed site, or medical management (see *Fast Fact* #119 for a discussion of interventional options). Total parenteral nutrition may be beneficial in select patients with longer prognoses who may die of starvation rather than the cancer itself (see *Fast Fact* #190). Still, the need to rely on medical management is common, especially when the patient's functional status is poor and expected survival is short. There has been significant advances in the medical management of this problem, so that many patients can avoid dying with the traditional approach of intravenous fluids and nasogastric tubes ("drip and suck").

Major Drugs

- Opioids and anti-emetics: usually dopamine antagonists (e.g. haloperidol) can be administered (intravenously or subcutaneously) to relieve pain and nausea.
- Antimuscarinic/anticholinergic drugs (e.g. atropine, scopolamine): are used to manage colicky pain due to smooth muscle spasm and bowel wall distension. In the US, scopolamine can be administered by parenteral (10 mcg/hr IV/SQ continuous infusion) or transdermal (10 mcg/hr) routes, but is only available as the hydrobromide salt. This penetrates the CNS and can lead to delirium. Glycopyrrolate, a quaternary ammonium antimuscarinic with similar clinical effects to scopolamine, but without the CNS side-effects (dosed at 0.2-0.4 mg IV/SQ q2-4h), may be a viable alternative.
- Somatostatin analogs: inhibit the secretion of GH, TSH, ACTH and prolactin, and decrease the release of gastrin, CCK, insulin, glucagon, gastric acid and pancreatic enzymes. They also inhibit neurotransmission in peripheral nerves of the gastrointestional tract leading to decreased peristalsis and a decrease in splanchnic blood flow. Octreotide (Sandostatin) is administered as a SQ injection (starting at 50-100 mcg q 8 hours) or as continuous IV or SQ infusion, beginning at 10-20 mcg/hr. Small randomized controlled trials suggest it may be more successful in improving nausea, vomiting, and colic than antimuscarinics for patients with a NG tube. One case report suggested it may help in partial bowel obstruction as well. The drug is titrated every 24 hours until nausea, vomiting, and abdominal pain are controlled. A once monthly injection of a long-acting formulation can be used for patients on a stable dose. A more recent randomized controlled trial suggested that dexamethasone with ranitidine may be a more cost-effective alternative to octreotide 600 mcg/day for MBO however.
- Corticosteroids: have been recommended to decrease the inflammatory response and resultant edema, as well as relieve nausea, through both central and peripheral antiemetic effects. A meta-analysis found that 6-16 mg of IV dexamethasone/day decreased symptoms and improved bowel function in 60% of patients. In fact, a phase III trial suggested little benefit from octreotide in patients already on intravenous ranitidine 200 mg/day and intravenous dexamethasone 8 mg/day.

Minor Drugs

Prokinetic drugs (e.g. metoclopramide) may be beneficial if there is a partial obstruction. However, if there is total obstruction some advocate the discontinuation of prokinetic agents as they may exacerbate crampy abdominal pain. On the other hand metoclopramide may inhibit the reverse peristalsis from obstruction and decrease nausea. Olanzapine, an atypical anti-psychotic, blocks multiple neurotransmitters associated with nausea. It is available in a sublingual route with some published accounts of utility in refractory cases of nausea in cancer.

Care Plan Often medications must be used in combination to achieve clinical goals in malignant bowel obstruction. The goal of medical management is to decrease pain, nausea and

secretions into the bowel in order eliminate the need for a nasogastric tube and IV hydration. During the medication titration phase, IV fluids should be restricted to 50 ml/hr. When NG output is less than 100 cc/day, the NG tube can be clamped for 12 hours and then removed. Once out, patients are instructed that they may drink and even eat, although vomiting may occur. If a venting gastrostomy tube is already in place, oral intake can be normal without fear of vomiting. Supplemental parenteral hydration is only indicated if a) patients remain dehydrated despite oral intake, and b) use of hydration to extend life is consistent with the patients' goals (see *Fast Facts* #133, 134).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #81
MANAGEMENT OF HICCUPS

Chad Farmer MD

Background Hiccups (singultus) are distressing to patients and families; when chronic, they diminish quality of life. A hiccup is an involuntary reflex involving the respiratory muscles of the chest and diaphragm, mediated by the phrenic and vagus nerves and a central (brainstem) reflex center. A single episode can last for a few seconds to as long as several days. If they last longer than 48 hours hiccups are termed *persistent*; longer than one month, *intractable*. Etiologies range from stress/excitement to cancer, myocardial infarction, esophageal or gastric distension, liver disease, uremia, IV steroids, CNS lesions, chemotherapy, and idiopathic. Irritation of the vagus nerve or diaphragm is a common pathophysiologic mechanism.

Management Once hiccups have lasted beyond a time-limited annoyance, deciding on therapeutic intervention should be based on a thorough clinical assessment and, if possible, treatment directed at the underlying cause. A thorough history, review of medications, focused review of systems, and physical exam may help guide initial choice of treatment. Many drug and non-drug treatments have been used, but there is little evidence of any one superior approach to management; virtually all current data are anecdotal. The patient's prognosis, current level of function, and potential adverse effects from any proposed treatment should be considered.

Pharmacologic Therapy

- **Anti-Psychotics:** Chlorpromazine – the only FDA approved drug for hiccups. Dose: 25-50 mg PO TID or QID. Can also be given by slow IV infusion (25-50 mg in 500-1000 ml of NS over several hours). Haloperidol – a useful alternative to chlorpromazine; give a 2-5 mg (SubQ/PO) loading dose followed by 1-4 mg PO TID.
- **Anti-Convulsants:** Gabapentin – at doses of 300-400 TID has been described as effective in multiple case reports. Its dual role as an analgesic may make it an especially attractive therapeutic agent. Phenytoin – reportedly effective in patients with a CNS etiology of their hiccups. Dose: 200 mg slow IV push followed by 300 mg PO daily. Others: Valproic Acid and Carbamazepine have been reported to work for selected patients.
- **Miscellaneous:** Baclofen – the only drug studied in a double blind randomized controlled study for treatment of hiccups. 5 mg PO q8 hours did not eliminate hiccups but did provide symptomatic relief in some patients. Metoclopramide – 10 mg PO QID is an option, especially if stomach distension is the etiology. Nifedipine – 10 mg BID with gradual increase up to 20 mg TID has been suggested as a relatively safe alternative if other interventions have failed. Other drugs that have been tried with very limited success include: amitriptyline, sertraline, inhaled lidocaine, ketamine, edrophonium, methylphenidate, and amantidine.

Non-Pharmacologic Therapy There are many well known, time-honored home remedies: gargling with water, biting a lemon, swallowing sugar, or producing a fright response. Other approaches are directed at a) vagal stimulation such as carotid massage or valsalva maneuver; b) interruption of phrenic nerve transmission via rubbing over the 5th cervical vertebrae; or c) interrupting the respiratory cycle through sneezing, coughing, breath holding, hyperventilation, or breathing into a paper bag. Other interventions such as acupuncture, diaphragmatic pacing electrodes, or surgical ablation of the reflex arc can be considered when other treatments fail.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #84
SWALLOW STUDIES, TUBE FEEDING, AND THE DEATH SPIRAL

David E Weissman MD

Introduction The reflex by families and doctors to provide nutrition for the patient who cannot swallow is overwhelming. It is now common practice for such patients to undergo a swallowing evaluation and if there is significant impairment to move forward with feeding tube placement (either nasogastric or gastrostomy) – see *Fast Fact* #128. Data suggest that in-hospital mortality for hospitalizations in which a feeding tube is places is 15-25%, and one year mortality after feeding tube placement is 60%. Predictors of early mortality include: advanced age, CNS pathology (stroke, dementia), cancer (except early stage head/neck cancer), disorientation, and low serum albumin.

The Tube Feeding Death Spiral The clinical scenario, the *tube feeding death spiral,* typically goes like this:

1. Hospital admission for complication of "brain failure" or other predictable end organ failure due to primary illnesses (e.g. urosepsis in setting of advanced dementia).
2. Inability to swallow and/or direct evidence of aspiration and/or weight loss with little oral intake.
3. Swallowing evaluation followed by a recommendation for non-oral feeding either due to aspiration or inadequate intake.
4. Feeding tube placed leading to increasing "agitation" leading to patient-removal or dislodgement of feeding tube.
5. Re-insertion of feeding tube; hand and/or chest restraints placed.
6. Aspiration pneumonia.
7. Intravenous antibiotics and pulse oximetry.
8. Repeat 4 – 6 one or more times.
9. Family conference.
10. Death.

Note: at my institution, the finding of a dying patient with a feeding tube, restraints, and pulse oximetry is known as *Weissman's triad*.

Suggestions

- Recognize that the inability to maintain nutrition through the oral route, in the setting of a chronic life-limiting illness and declining function, is usually *a marker of the dying process.* Discuss this with families as a means to a larger discussion of overall end of life goals.
- Ensure that your colleagues are aware of the key data and recommendations on tube feedings (see *Fast Fact* #10).
- Ensure there is true informed consent prior to feeding tube insertion—families *must* be given alternatives (e.g. hand feeding, comfort measures) along with discussion of goals and prognosis.
- Assist families by providing information and a clear recommendation for or against the use of a feeding tube. Families who decide against feeding tube placement can be expected to second guess their decision and will need continued team support.
- If a feeding tube is placed establish clear goals (e.g. improved function) and establish a timeline for re-evaluation to determine if goals are being met (typically 2-4 weeks).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #91
INTERVENTIONAL OPTIONS FOR MALIGNANT UPPER GI OBSTRUCTION

James Ouellette DO, Lisa Patterson MD, and Paula Termuhlen MD

Background Patients with unresectable cancers of the upper gastrointestinal tract often suffer severe symptoms due to pain, nausea and vomiting, weight loss, cachexia, and poor food tolerance. This can be related to gastric and duodenal cancers causing intrinsic obstruction of the intestinal lumen or pancreatic and biliary cancers causing extrinsic biliary compression. Management options vary depending on the site of obstruction, the patient's functional status, the patient-defined goals of care, and estimated prognosis. *Fast Fact* #45 discussed medical management options. This *Fact Fact* reviews interventional approaches for upper GI obstructions, especially when further radiation, chemotherapy, medical management, or curative surgical options are longer helpful. Listed below are treatment options for managing different sites of obstruction (listed from least invasive to most invasive). Management decisions for these problems are complex, requiring a multi-disciplinary approach (involving surgery, gastroenterology, medical and radiation oncology, radiology, and palliative care) to achieve the best possible outcome with minimum morbidity.

Esophageal obstruction

1) External beam radiation therapy (successful in 40% of patients).
2) Endoscopic laser therapy (can be repeated every 4-6 weeks).
3) Endoscopic/fluoroscopic stenting (different stent materials are available for different situations).

Gastric or Duodenal obstruction

1) Nasogastric tube decompression (poor long-term solution due to patient discomfort).
2) Venting gastrostomy tube, which allows for drainage of intestinal contents (can be placed endoscopically, laparoscopically, or with open surgery).
3) Janeway gastrostomy (surgically created gastrocutaneous fistula).
4) Endoscopically/fluoroscopically placed stent across the site of obstruction (e.g. pylorus).
5) Laparoscopic gastrojejunostomy.
6) Open gastrojejunostomy.

If unable to restore continuity of the gastrointestinal tract with a surgical procedure to bypass the obstruction, a combination of a gastrostomy tube with a separate jejunostomy tube can be used. This can provide enteral nutrition to the small intestine while venting the stomach. Patients can enjoy the pleasure of eating, even if the food is drained through the G-tube.

Pancreaticobiliary obstructions

1) Stent placement (plastic or metal) across obstruction through an endoscopic procedure (ERCP).
2) Stent/drain placement across obstruction by a radiologic procedure (transhepatic).
3) Laparoscopic cholecystojejunostomy (after gallstone absence is confirmed).
4) Open choledochojejunostomy, cholecystojejunostomy or hepaticojejunostomy.

Adjuvant medications may augment the efficacy of these interventions.

- Proton pump inhibitor to reduce gastric secretions.
- Sucralfate (Carafate) slurry, 1 gram q6 hours, for patients with ulcerated esophageal or gastric lesions.
- Metoclopramide (Reglan) 10 mg tid to qid, as a prokinetic drug.
- Octreotide (Sandostatin) 50-100 micrograms q6-8 h for high volume output conditions.
- Dexamethasone 4-8 mg per day.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #96
DIARRHEA IN PALLIATIVE CARE

Jeffrey Alderman MD

Diarrhea is a debilitating and embarrassing problem, defined as an abnormal looseness of the stools (increased liquidity or decreased consistency). Patients with uncontrolled diarrhea are at increased risk for dehydration, electrolyte imbalance, skin breakdown, and fatigue.

Common Causes Diarrhea can usually be divided into different types and treatment will vary depending on cause: secretory, osmotic, mechanical, or disordered motility. In palliative care, the overuse of laxatives, typically seen when the management of constipation is suddenly 'stepped-up,' is a common cause. Other causes include partial intestinal obstruction, pancreatic insufficiency, *Clostridium difficile* infection, and radiation enteritis. Chemotherapeutics are another common cause, especially in advanced cancer where the incidence can be up to 60% (diarrhea may be even more common with chemotherapy regimens with 5 flourouracil boluses or combination of irinotecan and fluoropyrimidines). Infectious diarrhea is especially common in HIV infection (*Cryptosporidia*, *Giardia lambila*, *E. histolytica*, and Cytomegalovirus). Severe constipation and fecal impaction can also cause diarrhea as backed-up, liquefied stool may be all that the patient can pass ('overflow diarrhea').

Evaluation Review diet, medications, laxatives, procedures, timing of movements in relation to ingestion of food or liquids, and a description of quantity and quality of stool. When performing a physical exam, make sure to palpate the abdomen and do a rectal exam. Radiographs are often not necessary, but may help clarify a partial bowel obstruction or overflow diarrhea. Keep in mind that patients at the end-of-life are also at risk for developing the same diarrheal illnesses that occur in the general population (viral/bacterial gastroenteritis, adverse effects of medications).

Treatment

- **General** Ensure adequate hydration; encourage sips of clear liquids; parenteral hydration should be considered for severe dehydration. Simple carbohydrates, toast or crackers, will add back small amounts of electrolytes and glucose; milk and other lactose-containing products should be avoided.
- **Medications** include bulk forming agents, antimicrobials, adsorbents, and opioids.
  - **Kaolin and Pectin** (Kaopectate®) is a suspension of adsorbent and bulk-forming agents, which can provide modest relief from diarrhea. However, kaolin-pectin may take up to 48 hours to produce an effect and can interfere with the absorption of certain medications.
  - **Antibiotics:** infectious diarrhea should be identified and treated with appropriate antibiotics, particularly *C. difficile* enteritis.
  - **Bismuth** has an additional antimicrobial effect, and can be added for increased symptomatic control against organisms such as enterotoxigenic *E. Coli.*
  - **Loperamide** (Imodium®), an opioid, reduces peristalsis in the gut, increases water reabsorption, and promotes fecal continence, making it a potent anti-diarrheal agent. Because it only weakly crosses the blood-brain barrier, loperamide's side effect profile is more favorable than other opioids (e.g. codeine or diphenoxylate [Lomotil®]). The initial dose of loperamide is 4 mg, with titration to 2 mg after each loose stool, with the typical dose being 4 – 8 mg per day. Although the package insert recommends a maximum of 16 mg in a 24-hour period, up to 54 mg per day of loperamide has been used in palliative care settings with few adverse effects. Note: loperamide should be used with caution if an infectious diarrhea is suspected.
  - **Aspirin** and **Cholestyramine** can reduce the diarrhea in radiation-induced enteritis, as can addition of a stool bulking agent such as psyllium (Metamucil™).
  - **Mesalamine** and other antiinflammatories are used for inflammatory bowel disease.
  - **Pancreatic Enzymes** such as pancrelipase are used for pancreatic insufficiency.
  - **Octreotide**, although costly, is effective with profuse secretory diarrhea seen in HIV disease, chemotherapy induced diarrhea, and those with high effluent volume from a stoma. It may be given via continuous subcutaneous infusion at a rate of 10 – 80 mcg every hour until symptoms improve.

- **Budesonide, probiotics** and **activated charcoal** have been described in the literature for use in chemotherapy induced diarrhea, but there role in the clinical setting is not yet established.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #119
INVASIVE TREATMENT OPTIONS FOR MALIGNANT BOWEL OBSTRUCTION

Robert S Krouse MD

Background
Malignant bowel obstruction (MBO) is a common problem in patients with ovarian and colorectal cancers. MBO also occurs with other abdominal (e.g. gastric and pancreatic) and non-abdominal malignancies. MBO may be related to cancer (intraluminal or extraluminal tumor growth), its treatment (e.g. radiation enteritis), or benign etiologies (e.g. adhesions or internal hernias). Invasive treatment options should be considered for all patients except those who are actively dying (see *Fast Fact* #3). In cases where surgical management is not feasible, medical management can be very effective at relieving symptoms (see *Fast Fact* #45).

Goals of Treatment
The goals of treatment include relieving nausea and vomiting, allowing oral intake, alleviating pain, and permitting the patient to return to their chosen care setting. Although it is recognized that improvement in quality of life after surgery is variable (42-85%), there is no consistent parameter used to determine this clinical outcome. Operations may offer an advantage of an increased survival.

Surgical Approaches
The optimal procedure is that which offers the quickest, safest, and most efficacious ability to alleviate the obstruction and improve symptoms. Options include bowel resection (which may lead to the best overall outcome), bypass, or a gastrostomy. An intestinal stoma may be necessary after resection or to adequately bypass the blockage. Laparoscopic procedures may be attempted, although this approach may be difficult due to adhesions, carcinomatosis, or bowel dilatation. Cytoreductive procedures (resection of intraperitoneal tumor) frequently carry a high morbidity and usually are only considered with very low grade tumors, such as psuedomyxoma peritonii. Many patients are deemed inoperable (6.2-50%), with the most frequent reasons being extensive tumor spread, multiple partial obstructions, and inability to correct obstructions surgically.

Surgical risks must be carefully considered prior to an operation, as morbidity (42%) and mortality (5-32%) are common, and the re-obstruction rate is high (10-50%). Poor prognostic indicators for surgical intervention include ascites, carcinomatosis, palpable intra-abdominal masses, multiple bowel obstructions, prior obstructions and very advanced disease with poor performance status.

Endoscopic Approaches
Endoscopic procedures are suited for patients who are poor operative candidates or who decline an open operative intervention. The major approaches include stenting and percutaneous endoscopic gastrostomy (PEG) tube placement. Stenting may include procedures to initially canalize the lumen (e.g. laser or balloon dilatation). Endoluminal wall stents have a high success rate for relief of symptoms (64-100%) in complete and incomplete colorectal obstructions, and in over 70% of upper intestinal malignant obstructions including gastric outlet, duodenal and jejunal obstructions. While risks include perforation (0-15%), stent migration (0-40%), or re-occlusion (0-33%), stents can frequently lead to adequate palliation for long periods of time. Stent occlusion by tumor in-growth is usually amenable to another endoscopic intervention.

PEG tubes are generally well tolerated “venting” procedures that can alleviate symptoms of intractable vomiting and nausea for upper GI obstructions. In combination with other medical techniques, both open and percutaneous gastrostomy offer the possibility of intermittent oral intake. Complications are rare, even when puncturing other organs. The presence of significant ascites is a relative contraindication.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #128
THE SPEECH PATHOLOGIST AND SWALLOWING STUDIES

Carol Monteleoni MS, CCC-SLP

Background Speech pathologists can facilitate communication among members of the medical team, and between the team and the patient/family, to make treatment decisions that honor patient wishes. Speech pathology services for symptom control to enable the individual to maintain activities of daily living and basic functional skills are reimbursable under the Medicare Hospice Benefit (see *Fast Facts* #82, 87, 90). Swallowing studies are used to evaluate a patient's ability to safely ingest oral food and oral secretions, yet the role of swallowing studies to facilitate optimal care near the end of life is not clear. This *Fast Fact* will review the indications and contraindications for a swallowing study and the role of the speech pathologist.

Potential Indications for a swallowing evaluation (Bedside or Instrumental)

- Acute stroke or other neurological condition affecting oral motor function (see *Fast Facts* #201, 300).
- Tracheostomy or recent endotracheal extubation.
- Changes to oropharyngeal anatomy secondary to tumor, surgery, trauma, etc.
- Observed difficulty swallowing food or liquid.
- Recurrent upper respiratory infections or pneumonias.
- Reduced oral food intake; unexplained weight loss or fever.

Contra-indications for swallowing evaluation (Instrumental only)

- Imminent death—death expected within 2 weeks (See *Fast Fact* #3).
- Death expected within weeks from any progressive terminal illness.
- Reduced level of arousal (e.g. coma/obtundation).

Types of swallowing studies

- **Bedside dysphagia evaluation** involves an in-depth feeding/swallowing history, oral peripheral examination, and trial swallows of various food consistencies. Bedside evaluation cannot rule out silent aspiration.
- **Instrumental swallowing evaluation** is performed via modified barium swallow (videofluoroscopy), fiber-endoscopic evaluation of swallowing (FEES), or fiber-endoscopic evaluation of swallowing with sensory testing (FEEST). All of these instrumental assessments require the patient to be alert, cooperative, and able to follow simple commands.

Speech Pathologist Role The decision to perform a swallowing evaluation should be made based on the overall *goals of care* and expected prognosis. Consultation with your speech pathologist **prior** to ordering an evaluation can help clarify how you will use any new information to improve patient comfort and satisfaction. If performed, the speech pathologist will evaluate the patient's swallowing and recommend feeding strategies which may include:

- Appropriate food consistencies.
- Positioning of the head and neck.
- Timing of meals
- Promoting family involvement.

Using the Speech Pathologist's Assessment Decisions regarding feeding management *should not* be made based solely upon the speech pathologist's assessment of swallowing dysfunction, which may be a sign of the final stage of life in many terminal conditions. In addition, feeding tube placement decisions in this population *should not* be based on the likelihood of aspiration. In patients with advanced dementia and other terminal conditions, feeding tubes have not been found to reduce the incidence of aspiration and can significantly impair the dying patient's quality of life (see *Fast Facts* #10, 84).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #137
CARCINOID SYNDROME: SYMPTOM MANAGEMENT

Stacey Shaffer and Robert Arnold MD

Background The *carcinoid syndrome* (CS) is a symptom complex resulting from hormone secretion in patients with carcinoid tumors. Carcinoid tumors typically grow slowly, and patients may live for many years following diagnosis. CS becomes manifest only when sufficient concentration of hormones reach the systemic circulation, most commonly in the presence of liver metastases. This *Fast Fact* will focus on managing the symptoms of CS.

Symptoms and Causes The CS includes the complex of: flushing, diarrhea, abdominal cramping, cyanosis, bronchoconstriction, and symptoms of right heart failure. Compared with the general population and other cancer patients, CS sufferers may also be at increased risk for cognitive impairment. Other specific symptoms depend on the hormones the tumor secretes. Serotonin-secreting tumors cause diarrhea and cramping; bradykinin and histamine secretion lead to flushing and cyanosis. Carcinoid tumors may also produce somatostatin, norepinephrine, dopamine, gastrin, vasoactive intestinal peptide, and other hormones. Drugs that block the hormonal secretion can help to control the symptoms of carcinoid syndrome.

Somatostatin Analogs These drugs are the treatment of choice for CS. Three formulations are available: short-acting octreotide (continuous infusion or 50-500 mcg TID, IV or subcutaneously); depot octreotide (standard dose is 30 mg intramuscularly every 4 weeks; however, doses up to 40 to 60 mg every 4 weeks may offer added benefit); and lanreotide (standard dosing is 30 mg every other week intramuscularly). 50-70% of patients experience a significant reduction of diarrhea and flushing episodes within seven days. Efficacy and side effect profiles for the three preparations are similar. Side effects include pain at the injection site, abdominal bloating, fatigue, transient fever, elevated serum glucose, and asymptomatic biliary lithiasis.

Interferon Interferon alpha is effective in controlling both diarrhea and flushing, although it is inferior to the somatostatin analogs. The dose is 3-9 mU subcuteneously three to seven times per week. Interferon alpha therapy is often limited by its side effects: fever, anemia, thrombocytopenia, neutropenia, fatigue, depression, and flu-like symptoms.

Other Drugs & Symptom-Specific Treatments

- Diarrhea: Cyproheptadine is an alternative treatment for carcinoid-associated diarrhea. 60% of patients report improvement within one week. The dosage is 4 mg TID given orally as a tablet; it can be titrated up to 0.5 mg/kg per day. Side effects include sedation, dry mouth, dizziness, mild blurring of vision, nausea, and vomiting. Loperamide and opioids are non-specific anti-diarrheal agents that can be used for mild symptoms.
- Wheezing: bronchodilators.
- Heart failure: diuretics; tricuspid valve replacement.

Non-Drug Treatments Patients should be counseled to identify and eliminate stressors that reproducibly cause symptoms—this may include specific stressful situations, foods, or alcohol.

Other Other treatments for refractory symptoms include systemic chemotherapy, hepatic artery embolization, hepatic chemoembolization, or debulking surgery of hepatic metastases.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #176
EVALUATION OF MALIGNANT ASCITES

Karen LeBlanc and Robert Arnold MD

Background Malignant ascites is the accumulation of abdominal fluid due to the direct effects of cancer. This *Fast Fact* reviews the causes and diagnosis of malignant ascites. *Fast Fact* #177 will review its treatment.

Pathophysiology The pathophysiology of malignant ascites is incompletely understood. Contributing mechanisms include tumor-related obstruction of lymphatic drainage, increased vascular permeability, over-activation of the renin-angiotensin-aldosterone system, neoplastic fluid production, and production of metalloproteinases that degrade the extracellular matrix. Portal venous compression can also occur from metastatic invasion of the liver, leading to peritoneal fluid accumulation.

Natural History The most common cancers associated with ascites are adenocarcinomas of the ovary, breast, colon, stomach and pancreas. Median survival after diagnosis of malignant ascites is in the range of 1-4 months; survival is apt to be longer for ovarian and breast cancers if systemic anti-cancer treatments are available.

Presentation and Diagnostics Symptoms include abdominal distension, nausea, vomiting, early satiety, dyspnea, lower extremity edema, weight gain, and reduced mobility. Physical exam findings may include abdominal distention, bulging flanks, shifting dullness, and a fluid wave. Plain abdominal x-rays are not specific, but may show a hazy or a “ground glass” appearance. Ultrasound or CT scanning can confirm the presence of ascites and also demonstrate if the fluid is loculated in discrete areas of the peritoneal cavity.

There are many potential causes of ascites in the cancer patient: peritoneal carcinomatosis, malignant obstruction of draining lymphatics, portal vein thrombosis, elevated portal venous pressure from cirrhosis, congestive heart failure, constrictive pericarditis, nephrotic syndrome, and peritoneal infections.

Depending on the clinical presentation and expected survival, a diagnostic evaluation is usually indicated as it will impact both prognosis and treatment approach. Key tests include the serum albumin and protein level and a simultaneous diagnostic paracentesis, checking ascitic fluid white blood cell count, albumin, protein, and cytology.

Classification The old classification of exudative versus transudative ascites has been updated through the use of the serum-ascites albumin gradient (SAAG).

SAAG = (the serum albumin concentration) – (ascitic fluid albumin concentration).

A SAAG $\geq$ 1.1 g/dl indicates ascites due to, at least in part, increased portal pressures, with an accuracy of 97%. This is most commonly seen in patients with cirrhosis, hepatic congestion, CHF, or portal vein thrombosis.

A SAAG < 1.1 g/dl indicates no portal hypertension, with an accuracy of 97%; most commonly seen in peritoneal carcinomatosis, an infectious process of the peritoneum, nephrotic syndrome, or malnutrition/hypoalbuminemia.

Cytological evaluation is approximately 97% sensitive in cases of peritoneal carcinomatosis, but is not helpful in the detection of other types of malignant ascites due to massive hepatic metastasis or malignant obstruction of lymph vessels.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #177
PALLIATIVE TREATMENT OF MALIGNANT ASCITES

Karen LeBlanc and Robert Arnold MD

Background The natural history, presenting signs/symptoms, and diagnostic approach to the patient with malignant ascites are discussed in *Fast Fact* #176; readers are encouraged to read this *Fast Fact* to review the important role of determining the Serum Ascites-Albumin Gradient as a diagnostic and treatment aid. This *Fast Fact* will review treatment approaches.

1. **Diuretics:** Malignant ascites (SAAG < 1.1) generally does not respond to diuretic treatment although no randomized trials have been completed. Patients with evidence of portal hypertension (SAAG > 1.1) are more likely to respond to diuretics.

2. **Paracentesis:** Paracentesis can provide immediate relief of symptoms in up to 90% of patients. Drainage of uncomplicated large-volume ascites (4-6 L/session) can be done safely and quickly in the outpatient setting—including the home—or at the hospital bedside; ultrasound guidance is necessary only when there is loculated fluid.

3. **Drainage catheters:** For patients who require frequent paracentesis, external drainage catheters placed through the abdominal wall allow frequent or continuous drainage of ascites fluid without repetitive needle insertions. Patients or caretakers may perform the drainage, reducing visits to medical clinics. Several types of catheters are available:
   a. Pigtail Catheter: A simple, temporary all-purpose catheter; they are prone to complications when used over an extended duration (peritonitis, accidental removal, leakage, occlusion), hence are rarely used now.
   b. Tunneled Catheter: A catheter that prevents infection by promoting scarring around an antibiotic-impregnated Dacron cuff in subcutaneous tissue. Used conventionally for peritoneal dialysis, it is placed with ultrasound or fluoroscopic guidance and has lower risks of infection and leakage than the pigtail catheter. Complications are reduced by daily drainage for the first two weeks of cuff healing. The *PleurX catheter* is FDA approved for malignant ascites and features a one-way rubber valve to prevent leaks between draining sessions. Tunneled catheters are used in patients with life expectancy of at least one month.

4. **Vascular Shunts:**
   a. Peritovenous shunt (PVS) systems are designed to channel peritoneal fluid and proteins in benign ascites back into the circulation via the superior vena cava. PVS has not been shown to have clinically significant risk of disseminating tumor cells in malignant ascites. A PVS is placed by interventional radiology under conscious sedation, and patients typically require 24 hours of monitoring with a central venous line after the procedure. The best response to PVS (only about 50%) is in ovarian and breast cancers. PVS is recommended only in patients with a life expectancy of one to four months, considering that eventual occlusion rate is up to 24%.
   b. Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a shunt between the portal vein and hepatic vein, designed to reduce portal hypertension and improve sodium balance. Most patients with malignant ascites do not have portal hypertension although TIPS might be helpful in the occasional cancer with evidence of increased portal pressures (SAAG > 1.1).

5. **Hyperthermic Intraperitoneal Chemotherapy (HIPEC):** This procedure is performed by surgical oncology specialists and entails warmed chemotherapy being infused into the peritoneal cavity for a short period of time. Most commonly this procedure is done along with tumor debulking or cyto-reductive surgery (CRS). However, considering that recovery from HIPEC with CRS can take 3 to 6 months, CRS-HIPEC is typically reserved for low-

grade appendiceal primary cancers seeing that these cancers are associated with a longer survival. For patients with anticipated shorter survivals, HIPEC without CRS can be done laparoscopically (and is therefore associated with less morbidity) with high rates of ascites control.

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HEPATIC ENCEPHALOPATHY IN ESLD
Julie Wilson Childers MD and Robert Arnold MD

Background Hepatic encephalopathy (HE) is a neuropsychiatric syndrome with a fluctuating course associated with end stage liver disease (ESLD). HE symptoms, which are graded from 0 to IV, range from subtle personality or sleep disturbances to confusion and coma. Severe HE (grade III or IV) is manifested by gross disorientation, bizarre behavior, stupor, or coma (1). Without transplantation, severe HE signifies a poor prognosis (58% 1 year and 77% 3 year mortality in one case series) (2). In addition, 15% of patients awaiting liver transplantation die before receiving an organ (3).

Etiology The cause of HE is uncertain, but may be related to the accumulation of neurotoxic substances normally metabolized by the liver; these include ammonia and endogenous benzodiazepine-like substances that activate GABA-receptors to cause neurotoxicity.

Evaluation HE is a diagnosis of exclusion, and in one study 80% of cases were associated with an identifiable secondary cause such as gastrointestinal bleeding, infection (including spontaneous bacterial peritonitis), renal failure, alcohol withdrawal, excessive dietary protein, volume depletion, or drugs (particularly benzodiazepines) (4). Because of its association with coagulopathy, brain imaging often via a CT scan without contrast, may be needed to rule out intracranial hemorrhage. Serum ammonia levels are usually elevated in HE, although the utility of following ammonia levels has not been established.

Therapy begins with correction of the underlying causes if this is consistent with the goals of care. Specific therapy of HE is aimed at limiting production of and increasing excretion of intestinally derived toxins, particularly ammonia.

- **Nonabsorbable disaccharides** such as *lactulose* and *lactitol* are the mainstay of treatment though there is a lack of controlled evidence supporting their use (5). These agents not only cause increased transit time through the gut and less absorption of toxins, but also promote bacterial fermentation, leading to a hostile environment for ammonia-producing bacteria. The daily dose of lactulose should be titrated to result in two to four soft stools daily. For most patients the daily dose is between 30 and 60 grams. Side effects include gastrointestinal cramping, diarrhea, and flatulence.
- **Nonabsorbable antibiotics** such as *neomycin* and *vancomycin* were the first treatments for HE. They lower ammonia by combating urea-producing bacteria in the gut. Neomycin likely produces more rapid improvement than lactulose but its use is limited by its nephro- and oto-toxic effects (5). *Rifaximin* is a nonabsorbable derivative of rifampin which received orphan drug status from the FDA in 2005 for treatment of HE. Rifaximin, given at 400 mg orally three times a day, is as effective as neomycin or lactitol and better tolerated than other nonabsorbable antibiotics (6). Rifaximin costs $4.00 a pill (average wholesale price). Because of this and its lack of clear superiority to disaccharides rifaximin is considered a second-line agent for patients who cannot tolerate or who are not responding to disaccharide therapy.
- **Other therapies** have limited efficacy in treating HE and play no clear role in its management. These include branched chain amino acids (7), the benzodiazepine antagonist flumazenil (8, 9), zinc, L-ornithine–L-aspartate and limitation of dietary protein (10).

Advance care planning The patient's values, goals of care, and treatment options should be discussed in the context of HE's poor prognosis. A health care proxy should be established in patients with cirrhosis before cognitive impairment prevents this.

Supportive care The patient and family must be educated to recognize HE's symptoms, understand its fluctuating course, and avoid precipitating factors when possible. They should also be counseled about the risk of motor vehicle accidents. Patients who are confused should be reoriented and measures should be taken to prevent falls, skin breakdown, and aspiration. Intravenous fluids, nasogastric feeding, and airway protection are sometimes appropriate. Dose-adjusted acetaminophen (<2 gm/day) is the first line analgesic. Opioids can worsen HE but are

sometimes necessary to adequately treat pain; their use should be closely monitored and balanced with the patient's degree of suffering and goals of care (11). Dying patients should receive attentive comfort care. Besides pain – dyspnea, restlessness, edema, and secretion management are common challenges in dying ESLD patients.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #189
PROGNOSIS IN DECOMPENSATED CHRONIC LIVER FAILURE

Brigid Dolan MD and Robert Arnold MD

Background In 2009, chronic liver disease and cirrhosis resulted in approximately 30,000 deaths, making it the twelfth leading cause of death in the United States. Patients with compensated chronic liver failure (without ascites, variceal bleeding, encephalopathy, or jaundice) have a median survival of 12 years. After decompensation, median survival drops to ~ 2 years. This *Fast Fact* reviews prognosis in chronic liver failure, focusing on two validated prognostic indices. Of note, these indices predict prognosis for patients without liver transplantation.

The ***Child's-Turcotte-Pugh (CTP)*** score includes 5 variables, each scored 1-3:

	Numerical Value		
Variable	1	2	3
Ascites	None	Slight	Moderate/Severe
Encephalopathy	None	Grade 1-2	Grade 3-4
Bilirubin (mg/dL)	< 2.0	2.0-3.0	>3.0
Albumin (mg/L)	> 3.5	2.8-3.5	<2.8
Increase in seconds from normal Prothrombin time	1-3	4-6	>6.0

Patients are grouped into three classes based on the total CTP score, which is simply the sum of the scores for each of the 5 variables. Patients scoring 5-6 points are considered to have *'Class A*' failure*;* their 1 and 2 year median survivals are 95% and 90%, respectively. A score of 7-9 is considered *Class B* with median survivals of 80% at 1 year and 70% at two years. *Class C* patients (10-15) have far greater mortality: 1-year median survival is 45% and 2-year is 38%. Variations in the timing and subjectivity inherent in the scoring of the CTP (e.g. in grading ascites or encephalopathy) are its major limitations. In addition, the scale does not include renal function, an important prognostic factor in liver failure.

The ***Model for End-stage Liver Disease (MELD)*** score was developed in 2000 to overcome the above-mentioned limitations and determine survival benefit from transjugular intrahepatic portosystemic shunting. It is currently used to help determine organ allocation for liver transplantation, and there is increasing evidence that it can also be used generally to predict survival in patients with chronic liver failure. The MELD score relies on laboratory values alone (serum creatinine, total bilirubin, and INR). An additional benefit over CTP is that it can predict prognosis on the order of months with more precision – making it helpful for determining hospice eligibility in the US. The formula to calculate MELD score is complex, and a calculator can be found at: http://reference.medscape.com/calculator/meld-score-end-stage-liver-disease.

MELD Score	**Predicted 6 month survival**	**Predicted 12 month survival**	**Predicted 24 month survival**
0-9	98%	93%	90%
10-19	92%	86%	80%
20-29	78%	71%	66%
30-39	40%	37%	33%

Other important prognostic variables The hepatorenal syndrome (HRS) – renal failure from renal arterial under-filling due to decompensated liver failure – portends a particularly poor prognosis. Most patients with type-1 HRS (rapid and severe renal failure) die within 8-10 weeks even with therapy. Median survival with type-2 HRS (chronic, less severe renal failure with serum creatinine usually 1.5-2 mg/dL) is around 6 months. Both older age and hepatocellular carcinoma also adversely affect survival. While the CTP and MELD systems provide objective guidance to prognostication in liver failure, clinical judgment, patient comorbidities, the rate of decompensation, and the likelihood of transplantation all should additionally affect the assessment and communication of a patient's prognosis in liver disease.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #260
OPIOID USE IN LIVER FAILURE

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Background Most opioids are at least partially metabolized by the liver, complicating their use in liver failure. This *Fast Fact* discusses the use of opioids in patients with liver failure (see also *Fast Facts* #161 about opioid use in renal failure, #176 and #177 about managing ascites and #189 about prognostication in end-stage liver disease). **Note:** while there are plenty of pharmacokinetic data about opioids & liver failure, all the clinical recommendations below are empiric and not based on clinical outcomes research.

Hepatic Opioid Metabolism There are two different types of chemical reactions involved in hepatic drug metabolism. The first, *oxidation/reduction reactions*, occurs through the cytochrome (CYP) P450 enzyme system. The CYP450 enzymes most relevant in palliative medicine include CYP1A2, 2D6, 2C9, 2C19, 3A3 and 3A4; most opioids are metabolized by these enzymes. In hepatic failure, opioid clearance is reduced and drug bioavailability is increased. These changes can be secondary to reduced hepatic blood flow (limiting first-pass metabolism) or decreased CYP450 enzyme levels in these patients. *Conjugation and glucuronidation* comprise the second group of chemical reactions in the liver. These reactions are less affected in hepatic disease due to glucuronidation enzyme preservation and also because of extrahepatic glucuronidation processes. Glucuronidated opioid metabolites are generally renally excreted. Changes such as decreased serum albumin and ascites can also alter opioid volume of distribution which can lead to either increased or decreased drug concentrations, although there is no practical way to 'test' for or predict this apart from close clinical observation.

Morphine Morphine is metabolized by glucuronidation to two major metabolites, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G). M6G is an active analgesic that is more potent than morphine, while M3G has no analgesic effect but contributes to neurotoxic side effects such as confusion. Morphine accumulation has been reported in liver disease which can result from decreased plasma clearance and/or increased elimination half-life of the parent drug. In patients with early liver disease, initial lower doses should be used, but at normal dosing intervals. However, as the disease progresses to advanced hepatic failure, longer dosing intervals may be necessary.

Oxycodone Oxycodone is metabolized to two different metabolites by CYP2D6 and 3A4. However, neither metabolite contributes significantly to analgesia. In advanced liver failure, oxycodone's maximum concentration increases 40%, and immediate-release oxycodone's half-life increases to 4.6-24.4 hours (average 14 hours; its usual half-life is ~3.5 hours). Initial oxycodone dosing in patients with severe hepatic failure should be reduced to 30%-50% of the recommended starting dose.

Codeine & Meperidine Both these drugs should be avoided entirely in patients with liver failure. Codeine is a prodrug that is hepatically converted to morphine by CYP2D6. In patients with liver dysfunction, pain control can be compromised if codeine is not metabolized. Meperidine is metabolized by CYP3A4 to normeperidine and also by hydrolysis. In hepatic disease, meperidine clearance is reduced and its half-life is prolonged. Seizures, a major side effect of meperidine and normeperidine, can occur at reduced doses in patients with hepatic failure (see *Fast Fact* #71).

Hydromorphone & Hydrocodone **Hydromorphone** is glucuronidated to metabolites which have no analgesic properties but can be neurotoxic (see *Fast Facts* #57, 58, 142). **Hydrocodone** is a prodrug metabolized by CYP2D6 to hydromorphone and other metabolites, and is only available in combination with non-opioids such as acetaminophen. Hydrocodone dose titrations are limited by the non-opioid component, and overconsumption of acetaminophen-containing products is hepatotoxic. In patients with severe liver disease, initial starting doses of

each drug should be reduced to 50% of normal and as the disease progresses, prolonged dosing intervals may also be necessary.

Fentanyl Fentanyl is primarily metabolized by CYP3A4 and quickly redistributes to muscle and fat upon administration. In single-bolus studies, intravenous fentanyl's pharmacokinetics were unchanged by liver failure, however its half-life is prolonged in liver failure with repeated dosing or high dose therapy. Transdermal fentanyl has not been adequately studied in liver failure. Hepatic failure can alter skin permeability and drug absorption; the clinical relevance of this, if any, has not been determined. Some experts suggest fentanyl is a preferred opioid in liver failure (1, 4), although this judgment appears to be entirely empiric.

Methadone Methadone is metabolized by CYP3A4, 2D6 and 1A2. Methadone's clearance is reduced in severe liver disease. Notably, however, hepatitis C infection stimulates CYP3A4 activity and may actually increase methadone clearance, particularly early on (before overt liver failure occurs).

Clinical Management Pearls As in any clinical setting, the 'right dose' of an opioid analgesic medication is that which provides adequate pain relief in conjunction with an acceptable side effect profile. This statement is especially true in end stage liver disease (ESLD). Opioid doses should not be decreased solely out of concern for hepatic disease (e.g., if a patient with ESLD appears to tolerate and require q3 hour dosing of oxycodone, that dosage should continue). In general, lower doses of most opioids should be initiated in patients with ESLD, and clinicians should be cautious prescribing opioids at 'regular' dosing intervals until patients have demonstrated an ability to tolerate them. Patients with deteriorating liver function should be closely monitored for signs of drug accumulation and need for dose reductions, assuming the level of analgesia remains acceptable. Finally, potential drug interactions involving the CYP450 enzyme system must always be considered as there is potential for non-opioid medications to either induce or inhibit the metabolism of any opioid that is a CYP450 enzyme substrate.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #294
OPIOID INDUCED CONSTIPATION PART 1: ESTABLISHED MANAGEMENT STRATEGIES

Andrew Badke MD and Drew A Rosielle MD

Background Opioid induced constipation (OIC) affects 45-90% of patients (1, 2) and can cause significant morbidity. It is the most common reason patients avoid and/or discontinue opioids (3, 4) and can often result in an increase in hospital length of stay (5) and overall healthcare costs (6). This *Fast Fact* will describe the physiology of OIC and describe established treatment strategies. *Fast Fact # 295* will discuss newer management strategies.

Physiology OIC is mediated through several different mechanisms including ineffective GI motility, inhibition of mucosal transport of electrolytes and fluids, and interference with the defecation reflex (7). The greatest risk factor for developing OIC is duration of opioid therapy. Route of delivery or increased opioid dosing does not appear to affect the risk of developing OIC (2). While patients usually develop tolerance to most other side effects from opioids, they do not develop tolerance to OIC (1).

Non-pharmacologic Therapies Physical activity, scheduled toileting, fiber, and adequate fluid intake have been traditional non-pharmacologic mainstays for preserving GI regularity in constipation (8). However, there is no specific evidence in favor for any of these interventions to treat OIC and adherence may be challenging for chronically ill patients.

Pharmacologic Therapies In general, patients with regular opioid exposure will require pharmacologic therapy to appropriately manage OIC. Both stimulant and osmotic laxatives have shown to be effective in treating OIC and are considered the cornerstone of treatment. Failure of oral pharmacologic therapy usually requires more invasive rectal based interventions or one of the newer treatment modalities (see *Fast Fact #295).*

- **Stimulant Laxatives:** Senna and bisacodyl are the main stimulant laxatives available in the US and work by increasing enteric muscle contraction and GI motility. The onset of action for oral senna and bisacodyl is around 6-12 hours. Starting dose for senna is two 8.6 mg tabs; bisacodyl is one 10mg tab. However, higher doses are usually needed for OIC. Senna can be safely dosed up to 12 tabs daily and bisacodyl up to 30 mg (9). Both medications are relatively inexpensive. Because stimulant laxatives cause intestinal contractions their use can be limited by abdominal cramps and pain. This can sometimes be avoided by dividing the total dose into smaller more frequent doses (9).
- **Osmotic Laxatives:** These include non-absorbable sugar molecules such as polyethelyne glycol (PEG), lactulose, and sorbitol, as well as poorly absorbed salt-based molecules like milk of magnesia and magnesium citrate. Osmotic laxatives have limited intestinal absorption leading to an increase in colonic intraluminal water through oncotic pressure. With increased intraluminal volume and distension, reflex peristalsis subsequently occurs. Additionally, the increase in intraluminal water also leads to softer stool and allows for easier intestinal transit. The starting daily dose for PEG is 17 g, for lactulose is 15 ml, and 30 ml for 70% sorbitol solution. Osmotic laxatives will have a linear effect on bowel function with dose increases; the maximum effective daily dose of PEG is 68 g (10), lactulose is 60 ml, and for sorbitol is 150 ml. The onset of action for osmotic laxatives tends to be variable ranging from 12 to 48 hours, but when used regularly patients will have a more consistent effect. Osmotic laxatives generally do not lead to a loss of fluids or electrolytes as they only bind to orally taken fluid. With this, PEG requires 125 ml of fluid per 17 g dose (11) and similarly ~200 ml is recommended with every 30 ml of lactulose (12). Major side effects from osmotic laxatives include abdominal cramping, pain, and flatulence. Lactulose and sorbitol tend to have more of these side effects than PEG (11). While sorbitol and lactulose have shown similar efficacy, sorbitol tends to be more cost effective (13). Magnesium based compounds (milk of magnesia and magnesium citrate) are also effective, but the magnesium load can be dangerous for patients with renal insufficiency.

- **Rectal Based Laxatives:** Unfortunately, there is a lack of clinical research to support rectal based laxatives, but anecdotally they are often used for refractory constipation. Stimulant suppositories such as bisacodyl and rectal vault lubricants such as glycerin are inexpensive. Their onset is usually within 10-15 minutes and can be dosed daily (9). Warm tap water and milk of molasses enemas (12) can be dosed more frequently (up to every two hours). They work by causing rectal distension and reflex defecation. Other enema formulations, such as phosphate or saline enemas, should be used with caution in renal insufficiency due to concern for electrolyte shifts.
- **Manual Evacuation:** Digital stimulation and manual disimpaction may be necessary if fecal impaction is suspected. Due to the discomfort associated with manual evacuations, these are often interventions of last resort and may require pre-medication with pain medications and/or anxiolytics.
- **Ineffective Therapies:** Docusate sodium not demonstrated efficacy in randomized controlled studies for OIC compared with placebo (14). Bulk forming laxatives (psyllium or fiber) require at least 1.5 L of water to be effective and can actually lead to worsened constipation with inadequate fluid intake. Consequently, most guidelines do not routinely recommend their use (11,15,16).

Practical Advice A consistent bowel regimen is essential in preventing constipation in patients on chronic opioid therapy. Providers should educate their patients about the signs and symptoms of OIC and seek appropriate consultation in a timely manner. A scheduled stimulant laxative regimen such as Senna 2 tabs twice daily should be prescribed at the onset of regular opioid use regardless of opioid dosing. The goal for the bowel regimen should be an unforced bowel movement at least every other day. If a patient has not had a bowel movement in 48 hours, increasing stimulant laxative dose and/or adding an osmotic laxative is appropriate. Failure of oral laxative therapy usually requires rectal based interventions and/or one of the newer treatment modalities (see *Fast Fact #295).*

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #295
OPIOID INDUCED CONSTIPATION PART II: NEWER THERAPIES

Andrew Badke MD and Drew A Rosielle MD

Background *Fast Fact #294* introduces OIC and discusses well-established treatments. This *Fast Fact* discusses emerging management approaches. In general, these agents are used for refractory OIC, which implies persistent and distressing symptoms despite exposure to typically effective doses of stimulant and osmotic laxatives. When exactly to use these emerging therapies remains largely empiric.

Opioid Antagonists Since the majority of symptoms associated with OIC are secondary to stimulation of μ-opioid receptors in the gut, opioid antagonists offer an attractive pharmacologic rationale for OIC (1).

Naloxone: Until recently, naloxone was the only available opioid antagonist for OIC treatment. Typically, patients orally ingest the contents of IV ampules. Naloxone has a high first pass metabolism, so it is possible for patients who take it orally to have peripheral μ-opioid receptor antagonism *without* significant impact on central receptors which could lead to opioid withdrawal and loss of analgesia (2). In a small, non-controlled study, 80% of chronic opioid users had bowel evacuation in 1-4 hours after naloxone administration. Unfortunately, over two-thirds reported a 10-15% loss of analgesia and nearly one-third had withdrawal symptoms (3). Therefore, if used, it is recommended to start at a low dose of 0.8 mg twice daily. Effective doses typically need to be at least 10% of equivalent daily morphine dose, so naloxone usually requires slow up-titration with max dosing of 12 mg daily (2).

Methylnaltrexone bromide: Methylnaltrexone is a peripherally-acting μ-opioid receptor antagonist. It is a methylated form of naltrexone and formulated as a subcutaneous injection. It is less able to cross the blood brain barrier, reducing the risk of altering analgesia or inducing central opioid withdrawal. An industry-funded randomized controlled trial of chronic opioid users showed that weight based methylnatrexone dosing led to laxation in nearly half of subjects within 4 hours as opposed to 15% of placebo (4). A subsequent meta-analysis of 6 separate trials with methylnaltrexone demonstrated the number needed to treat (NNT) is 3 for OIC patients that have failed to respond to standard laxative therapy (5). Its use is limited by cost which averages $55 per dose, and it is also contraindicated when bowel obstruction is suspected or for patients with compromised bowel integrity. The most common side effects are nausea, diarrhea, and cramping – which can be severely painful.

Naloxegol: Two oral peripheral acting μ-opioid receptor antagonists are available in the US: alvimopam, which is only approved for post-operative ileus, and naloxegol (pegylated naloxone), which has recently been approved for OIC in non-cancer patients. Two separate phase-three clinical trials showed an increase from 1 to >3 bowel movements per week in non-cancer patients on chronic opioids with daily dosed naloxegol compared to placebo. There was also a significant improvement in a subset of patients who had failed traditional laxative therapy as well (7). Both 12.5 mg and 25 mg have been studied; the 25 mg dose has a higher success rate but is associated with more abdominal pain, nausea, vomiting and diarrhea (7). Its current price is approximately $300 for 30 pills.

Other Agents
Lubiprostone: Lubiprostone is a selective chloride channel-2 activator that acts locally on the small intestine to increase fluid secretion and GI motility. It is FDA approved for OIC. Two randomized controlled trials in non-cancer chronic opioid users demonstrated an increase in frequency of spontaneous bowel movements by week 8. Moreover, approximately 40% of subjects had a bowel movement at 24 hours, 60% within 48 hours, and 27% of subjects had > 3 bowel movements per week (8,9). The most studied dose is 24 mcg orally twice per day.

Common side effects included nausea, diarrhea and abdominal distension. Curiously, lubiprostone does not appear to be effective for methadone induced constipation (10).
Linactolide has a different mechanism than lubiprostone, but is also a small intestinal secretogogue. It currently is approved for irritable bowel syndrome. Though there is interest in its efficacy in OIC, it has yet to be specifically studied in this population.
Prucalopride is a serotonin receptor type-4 agonist which is available in Canada and parts of Europe and Asia to treat chronic constipation. It is a prokinetic agent which has shown promise for treating OIC in a phase 2 study (5). It is unclear if or when it will be released in the US.

Practical Advice Traditional oral and rectal laxatives have been the mainstay of treatment in OIC for many years. However, recent development of novel approaches to treat OIC show promise for the future. Of the pharmacologic interventions described above, methylnatrexone has been the best studied and shown to be the most efficacious. It is reasonable to give methylnaltrexone after failure of oral laxatives (see *Fast Facts* #294) in OIC, and potentially can be used prior to using more invasive rectal based interventions. With time and more clinical trials, other oral formulations targeting OIC may become more standard of care. Patient and caregiver education about the importance of adherence to recommended therapy and guidance about signs and symptoms of OIC is essential to ensure effective treatment.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #304
DYSGEUSIA
Rafael Bloise MD, Mellar P Davis MD FCCP FAAHPM

Background Taste warns us of danger and is a stimulus for appetite. The most common taste disorder is dysgeusia, commonly defined as a qualitative distortion of the sense of taste. Though taste acuity declines with age, many patients with age-related hypogeusia are not subjectively bothered by it. Rather patients are more often to report dysgeusia when they experience an abrupt alteration resulting in an overly strong/weak taste as occurs in many progressive illnesses frequently encountered by palliative care clinicians. Among the seriously ill, dysgeusia can adversely influence nutrition and quality of life as well as lead to food aversions, distorted smells, and loss of eating pleasure (1,2). This *Fast Fact* will assist clinicians caring for seriously ill patients better identify and care for patients with dysgeusia.

Etiologies Dysgeusia is more closely associated with medical illness than age. Much of the medical literature on dysgeusia has been focused on cancer patients, as cancer is a putative risk factor for dysgeusia. In cancer, dysguesia is most associated with chemotherapy and radiation; yet there is considerable intra-individual variability regarding the intensity of impact (3). Patients with head and neck cancer and those exposed to tyrosine kinase inhibitors or taxane based regimens are most at risk (4,5). Common non-malignancy causes of dysgeusia in the seriously ill include, infections, zinc deficiency, hypothyroidism, Cushing's Syndrome, liver disease, sequelae from ENT operations, and medications such as psychotropics, opioids, and antihypertensives.

Medical Evaluation Patients often fail to volunteer symptoms of dysguesia to their clinicians and when they do, the symptom is often ignored (6). Hence, patients with cancer or other described risk factors should be routinely asked about distorted smell and taste.

- *Do you have an altered sense of smell or taste which interferes with eating?*
- *Do you experience a metallic taste when eating?*
- *Have you developed aversions to certain foods?* (7)

In addition, clinicians should evaluate for:

- Recent ear or respiratory infections, Bell's palsy, cranial nerve deficits, or dental procedures.
- Cheilitis -- a painful inflammation and cracking of the corners of the mouth
- Mucositis or thrush
- Gastrointestinal symptoms such as dysphagia, weight loss, appetite changes, and early satiety
- Thyroid function testing if clinically appropriate
- The "3 drop test" is available to measure taste thresholds and identify hypogeusia by using sugar, citric acid, sodium chloride and caffeine or quinine; however, most experts believe such tests likely offer little guidance in the management of dysgeusia (8).

Impact on Quality of Life (QOL) Chemotherapy induced dysgeusia most often resolves within months. However, in that time, it can have a devastating effect. Because eating habits are shaped by life experiences and life experiences are shaped by eating habits, dysgeusia can alter customs within the family unit and lead to a reduction in socialization around meals (9,10).

Non-Pharmacological Management Strategies Many with dysguesia try home remedies such as lemon juice, candy before meals, sweet drinks, plastic utensils, drinking from a straw, brushing teeth and tongue before meals, and using salt, soda or antibacterial mouthwashes before eating even though there is little evidence to their use (11). There is weak evidence for flavor enhancers (e.g. salt, sugar, monosodium glutamate, monopotassium glutamate) during chemotherapy (12). Randomized trials of dietary counseling had mixed results (13). Acupuncture is likely ineffective (14).

Pharmacological Management Strategies First, clinicians should treat identified reversible causes if consistent with goals of care and the patient's overall medical situation. Once these are ruled out, clinicians may consider empiric therapies. There are a multitude of ineffective drugs which clinicians should be aware: corticosteroids, vitamin A, gabapentin, gingko biloba, glutamine, and amifostine have all been shown to be non-beneficial (15-17). Other medications may help, however the data are not fully convincing. A randomized trial demonstrated taste improvement with alpha lipoic acid (available over the counter); however, other studies did not reproduce this finding (18-20). Dronabinol at low doses such as 2.5 mg twice daily may improve dysguesia in advanced cancer without improving appetite; however, it is not always covered by insurance (21). Multiple randomized trials of zinc supplementation at doses between 30 to 50 mg three times a day demonstrated a modest improvement in taste acuity and taste quality among individuals undergoing chemotherapy and/or radiation (22,23). This benefit was not observed in a non-cancer population (24).

Summary Although there are no guidelines for the assessment and management of dysgeusia, clinicians should inquire about dysgeusia in at risk patients to better identify reversible causes such as thrush, mucositis, and hypothyroidism. Much like fatigue, anorexia, or other common constitutional symptoms in serious illness, inquiring about dysgeusia can better ennoble clinicians to the patient experience. Zinc at doses of 100-150 mg daily has modest benefits but it can cause adverse effects such as eczema and gastrointestinal distress. Those who do not tolerate zinc or fail to respond after 1-2 months may benefit from dronabinol 2.5 mg twice daily or alpha lipoic acid.

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FAST FACTS AND CONCEPTS #308
TUNNELED INDWELLING CATHETERS FOR MALIGNANT ASCITES
James Burleigh DO, Zankhana Mehta MD, Dr. Neil Ellison MD

Background Malignant ascites can develop in almost half of patients with certain cancers and may portend a survival of one to four months (1,2). When ascites recurs after a large volume paracentesis (LVP), physical symptoms along with the need for travel to an office for repeat procedures, can carry significant burden (3). Tunneled indwelling peritoneal catheters are an alternative, permanent drainage system that allows patients to control symptoms in the home setting. This *Fast Fact* will review the use of tunneled indwelling catheters, including indications, use, and associated risks. See *Fast Facts* 176 and 177 for further information on the diagnostic and treatment approaches for malignant ascites.

Indication As of 2015, the FDA has approved multiple tunneled indwelling catheter systems, such as PleurX®, Asept®, and Aspira®, for the management of malignant ascites requiring frequent therapeutic LVPs (4). Timing of placement for malignant ascites is empiric; though usually it is considered after a patient has had at least two prior LVPs (2,4). Placement may also be considered in patients for whom disease burden makes frequent clinic visits difficult, and when post-procedural symptoms, such as discomfort, fatigue, and dizziness, are troublesome (3,4). The same considerations are relevant for non-malignant ascites; however, due to survival and infection concerns many clinicians limit the off-label use for non-malignant ascites to patients with an anticipated survival of less than two months. Due to the cost of the initial procedure, catheter placement is often performed prior to hospice enrollment.

Contraindications Single or multifocal loculated pockets of ascites, peritonitis, and non-correctable coagulopathy (4). While the literature does not have set guidelines for platelet counts or safe INR levels, some experts caution against catheter placement with INR levels greater than 2.

Complications If obstruction or accidental removal occurs, replacement of a new catheter can be pursued (4,5). Insertion site erythema, bacterial peritonitis, and exudative drainage have been documented; associated superficial infections are often manageable with oral antibiotics (2,4). Recent studies have shown much lower complication rates with the tunneled indwelling catheters, with 0.12 events per 100 catheter-days, compared with non-tunneled catheter systems. Consequently, the use of non-tunneled catheter systems for malignant ascites is essentially archaic (3). Overall rate of procedural complications, including immediate and delayed infections, are similar to repeat LVPs (6).

Use Using radiographic guidance, a single cuff, 15.5 French silastic catheter is tunneled under the skin into the peritoneum (1). This is usually performed as an outpatient procedure by an Interventional Radiology clinician (2). Technical success rates for placement are near 100%. Catheters usually remain in place until death; a recent study found a mean length of retention of 113 days (4). Patients and their families can be trained to perform drainage at home or use home health staff (5). Most systems utilize low-vacuum drainage bottles or bags; other alternatives are wall or portable suction, or water seal. The one-way valve is opened with sterile technique and up to two liters can be drained daily (2). The drainage valve is closed when flow slows to a trickle, and fluid is disposed of in the toilet. During use, transient pain and cough may be experienced. Once completed, the catheter is coiled against the skin, and a cover dressing is replaced (2). Drainage frequency is determined by the rate of ascites recurrence and patient's symptoms, with some patients requiring daily drainage (1). Using a protective dressing, patients can shower; however product information recommends against bathing. If wet, the catheter should be dried immediately, and the dressing replaced. If required, sterile samples of peritoneal fluid can be drawn directly from the catheter (7).

Cost According to Medicare's 2015 Ambulatory Payment Classifications, including imaging guidance and equipment, the initial outpatient placement of a tunneled indwelling catheter can cost five to seven times that of a LVP. Even considering the cost of drainage containers plus placement cost, tunneled indwelling catheters can have a potential financial benefit over LVPs in as early as a week (8).

Conclusion Peritoneal indwelling tunneled catheters are safe and effective for the management of refractory malignant ascites. Patient satisfaction has been quite high, with a relatively low complication rate (5).

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PC NOW PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #317
PALLIATION OF NEUROGENIC BOWEL

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Background: Neurogenic bowel is the loss of normal bowel function that results from damage to the gastrointestinal innervation (1). It occurs in many diagnoses within the scope of hospice and

palliative care clinicians. This *Fast Fact* will focus on how to identify and manage neurogenic bowel in the palliative care and hospice patient population.

Pathophysiology:

- Upper motor neuron (UMN) lesions: occur above the conus medullaris and are associated with hyperreflexic bowel or an increase in tone of the intestinal wall and anal sphincter (2). Because peristalsis remains intact, the combination of propelling stool against a tight sphincter often presents as constipation with fecal retention and impaction. Evacuation depends on initiating the rectal-colon reflex by stimulating the bowel wall digitally or with a suppository.
- Lower motor neuron (LMN) lesions: are at or below the level of the conus medullaris and are associated with an areflexic bowel, characterized by a flaccid anal sphincter, and slow peristalsis (2). LMN lesions present as constipation with bowel incontinence. The major therapeutic distinction is to utilize stool bulking agents like fiber to prevent bowel accidents in LMN lesions.

Impact of Neurogenic Bowel: Neurogenic bowel rates as a significant cause of anxiety and distress, especially for those who require greater than 15 minutes to complete bowel routines (3,4). In the critically ill, neurogenic bowel can even be life threatening and associated with viscous perforation, delirium, or difficulty weaning from a ventilator (5-7). Patients with non-traumatic spinal cord injury (SCI) have shorter life expectancies whereas traumatic SCI patients, if getting excellent care and are not ventilator dependent, have near normal life expectancies (8).

Clinical Evaluation: While the presence of neurogenic bowel is usually evident in traumatic SCI, clinicians may overlook it in non-traumatic etiologies such as multiple sclerosis, stroke, or cancer (see *FFs* # 237 & 238). In patients with an insult to the spinal cord, a digital rectal exam should be performed to distinguish between UMN and LMN lesions. UMN lesions will result in a tight sphincter, while LMN lesions will result in a flaccid anal sphincter with no volitional contraction.

Management of Neurogenic Bowel: Despite data showing that patients with well-managed neurogenic bowel have a better quality of life, there is a paucity of controlled trials examining the best treatments (1,4,6). As a result, the following empiric recommendations arise from a consortium of SCI experts (9):

- Non-pharmacological measures: *Routine is critical*. At the same time every day, ideally about 30 minutes after a meal in order to utilize the gastro-colic reflex, the patient should sit on a commode while a clinician applies pressures to the abdomen in a clockwise manner for 5 minutes at a time. For terminally ill patients who cannot tolerate regular meals nor a commode, do the same with the patient on his or her side in the bed. Follow this with digital stimulation to the rectal wall in a circular motion for 20-30 seconds and if necessary, manual disimpaction.
- Pharmacological measures: Administer a 10 mg bisacodyl suppository at the same time daily. Make sure the suppository contacts the bowel wall, not just the stool itself. Once the patient is having regular bowel movements at least every other day, transition to a glycerin suppository or a mini-enema (a commercially available 5 mL enema of docusate, polyethylene glycol and glycerin). To time bowel movements for the morning, give 2-4 tabs of senna at bedtime.
- Next steps: if these measures are ineffective after 2-3 days, imaging with a KUB may be needed to evaluate for ileus or bowel obstruction. Otherwise consider lactulose 30 mL, magnesium citrate 300 mL or sorbitol 70% solution up to 150 mL PO, or an enema.

Special Considerations

- SCI patients are susceptible to autonomic dysreflexia (AD), an abnormal sympathetic nervous system response to a noxious stimulus below the level of the spinal cord lesion. Typical AD symptoms are diaphoresis and a rapid rise in blood pressure that can be life threatening. The definitive treatment is to remove the noxious stimulus (e.g. malfunctioning Foley, TED stockings or impacted stool).
- Patients already on opioids will likely require higher doses as well as more frequent use of cathartics. See *Fast Facts* #294 and 295.

- Transanal irrigation, a self-administered irrigation consisting of a soft inflatable balloon to hold a rectal catheter in place, has been shown to be effective for refractory cases in small studies (4).
- Though more invasive, colostomy placement and electrical stimulation to the bowel have been described in select patients with longer prognoses and refractory symptoms.

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