<table>
<thead>
<tr>
<th>Program Name:</th>
<th>Bowel Preparation for Colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Planning Committee:</strong></td>
<td></td>
</tr>
<tr>
<td>• Ron Pohar, BScPharm, APA</td>
<td></td>
</tr>
<tr>
<td>• Lola Joyce, RN, CGN(C)</td>
<td></td>
</tr>
<tr>
<td>• Peter Thomson, B.SC. (Pharm), PharmD</td>
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</tr>
<tr>
<td><strong>Accreditation Information:</strong></td>
<td>This version of the program is unaccredited and intended for informational purposes only. An accredited version is available online at <a href="http://www.rxBriefCase.com">www.rxBriefCase.com</a> until May 25, 2016</td>
</tr>
<tr>
<td><strong>Sponsor:</strong></td>
<td>This case study is supported by an educational grant from Ferring</td>
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</table>
Learning Objectives

Upon completion of this program, participants will be able to:

1. Describe the importance of adequate bowel cleansing prior to colonoscopy and factors associated with inadequate cleansing.
2. Describe the alternative bowel preparations and their administration requirements, comparative safety and efficacy, adverse effects, and considerations for use in specific populations.
3. Identify key considerations in selecting an appropriate bowel preparation.
4. Identify key patient counselling points for bowel preparations.

Pre/Post Survey

1. Please rate your familiarity with the following options for bowel preparation prior to colonoscopy (1 = unfamiliar, 5 = very familiar).
   a) Polyethylene glycol (PEG) 4 L
   b) Polyethylene glycol (PEG) 2 L plus ascorbic acid
   c) Polyethylene glycol (PEG) 2 L plus bisacodyl
   d) Sodium picosulfate/magnesium citrate
   e) Magnesium citrate

2. Please rate your knowledge of the clinical evidence of safety and efficacy for the following bowel preparations (1 = limited knowledge, 5 = extremely knowledgeable).
   a) Polyethylene glycol (PEG) 4 L
   b) Polyethylene glycol (PEG) 2 L plus ascorbic acid
   c) Polyethylene glycol (PEG) 2 L plus bisacodyl
   d) Sodium picosulfate/magnesium citrate
   e) Magnesium citrate

3. Please rate your familiarity with split dose regimens for bowel preparation prior to colonoscopy (1 = unfamiliar, 5 = very familiar).

4. Please rate your level of agreement with the following statements (1 = strongly disagree, 5 = strongly agree):
   a) Patient acceptability is an important consideration in the selection of a bowel cleansing preparation.
   b) Evidence of clinical efficacy is an important consideration in the selection of a bowel cleansing preparation.

5. How comfortable are you with selecting an appropriate bowel preparation for the following groups (1 = completely uncomfortable, 5 = completely comfortable)?
   a) Pediatric patients
   b) Elderly patients
Pre/Post Test

1. Which of the following are consequences of inadequate bowel cleansing prior to colonoscopy?
   a) Shorter procedure times
   b) Increased rates of cecal intubation
   c) Lower health care costs
   d) Delays in diagnosis and treatment

2. Inadequate bowel cleansing:
   a) Occurs in approximately 10% of patients undergoing colonoscopy
   b) Is associated with the use of opioids
   c) Is more common in patients with higher levels of education compared to lower
   d) Is more common in younger patients than the elderly

3. An ideal bowel preparation should:
   a) Be palatable and easy to tolerate
   b) Have minimal impact on fluids and electrolytes
   c) Alter the intestinal mucosa
   d) A and B
   e) All of the above

4. Which of the following is correct regarding the selection of a bowel preparation?
   a) Patient preference is an important consideration in selection
   b) Inability to tolerate a bowel preparation in the past may suggest that agent should be avoided if possible
   c) Safety, efficacy and tolerability are all inter-related considerations in the selection of a bowel preparation
   d) All of the above

5. Magnesium citrate is an iso-osmotic laxative.
   a) True
   b) False

6. Sodium picosulfate/magnesium citrate:
   a) Is contraindicated in pediatric patients
   b) Is contraindicated in patients with inflammatory bowel disease
   c) Is contraindicated in elderly patients
   d) None of the above are contraindications to sodium picosulfate/magnesium citrate

7. Polyethylene glycol solutions are contraindicated in elderly patients due to their tendency to cause electrolyte disturbances.
   a) True
   b) False
8. Split dose regimens for administration of bowel cleansing preparations are recommended in a number of clinical practice guidelines.
   a) True
   b) False

9. Which of the following is correct regarding bowel preparations and drug interactions?
   a) Bowel preparations do not affect the absorption of medications
   b) No adjustment of the timing of regularly scheduled medications is needed when undergoing bowel preparation.
   c) Drugs that may be chelated by magnesium should be taken at least 2 hours before or 6 hours after a magnesium containing bowel preparation
   d) None of the above are correct

10. Which of the following is correct regarding a clear liquid diet?
    a) Red or purple colored fluids should be avoided
    b) The only fluid that should be consumed is plain water
    c) A variety of clear fluids should be consumed which may include broth, sports drinks, gelatin, popsicles
    d) A and C are both correct

11. Which of the following points should be discussed when educating patients about bowel preparation?
    a) A balanced electrolyte solution is recommended, rather than only water to replace fluids
    b) Watch for signs of dehydration such as dizziness and headache
    c) The expected timing for administration of the bowel preparation
    d) All of the above

Introduction – Colonoscopy and Bowel Cleansing

Colonoscopy is the gold standard for visualization of the colon for diagnostic, screening and therapeutic purposes. Visualization of the mucosal lesions requires adequate cleansing of the bowel prior to the procedure, which is routinely defined as the ability to visualize polyps of 5 mm or greater. Unfortunately, inadequate cleansing of the bowel is common, with up to 23% of colonoscopies not being completed as a result of inadequate preparation. Inability to complete a colonoscopy due to inadequate bowel cleansing has numerous consequences. Targets for improving bowel cleansing include improving patient understanding about the preparation, using regimens that are acceptable and tolerable from the patient perspective, and selecting regimens that consider patient-specific factors that might be impacted from the preparation. This lesson will review the consequences of inadequate bowel cleansing prior to colonoscopy, the available bowel preparation regimens, the key considerations in selecting an appropriate bowel preparation and key patient counselling points for bowel preparations, which can improve patient adherence to the regimen and tolerability.
Indications for Colonoscopy

Colonoscopy is used for screening, diagnostic and therapeutic purposes and is the preferred procedure for investigating disease of the large bowel in adult and pediatric populations. Colonoscopy is an important diagnostic tool in conditions such as inflammatory bowel disease (IBD) and for investigating other causes of lower GI symptoms. One in 13 males and 1 in 16 females will develop colorectal cancer in their lifetimes, making it the second and third most common cancers in Canadian males and females, respectively. For colorectal cancer screening, colonoscopy is considered the ‘gold standard’ due to its high sensitivity and specificity, and the ability to obtain samples and remove polyps during the procedure when indicated.

Inadequate Bowel Cleansing

Consequences of Inadequate Bowel Cleansing

Patients reporting for colonoscopy frequently fail to achieve adequate bowel preparation, which impedes the ability to perform a quality colonoscopic examination. When a colonoscopy cannot be performed as planned, there are a number of consequences that create inefficiencies in patient care and utilization of health care resources, potentially leading to additional healthcare costs and a negative impact on the patient.

- For the patient, the need to reschedule the procedure can lead to delays in diagnosis and treatment if needed, the need to repeat the preparation, which may be burdensome, unpleasant and time consuming, requiring time away from work and disruption of usual activities, both social and work-related.
- Patients, particularly those who experienced difficulties adhering to the bowel preparation regimen or had difficulties tolerating it, may be unwilling to undergo the preparation again, which may necessitate using a different test than what was originally intended.
- Patients may experience anxiety while waiting for a repeat procedure, for example when cancer is suspected. For those who had a negative experience with the initial attempt, repeating the bowel preparation can also be a source of anxiety.
- Failure to complete the procedure can be a deterrent to future participation in colorectal cancer screening. There is evidence that fear of bowel preparation is a key reason why individuals avoid colonoscopy.
- For those who can undergo colonoscopy despite suboptimal cleansing, the time to complete the examination itself may be prolonged, possibly requiring additional sedation. As well, the exam may still remain incomplete, requiring a follow-up procedure.
- The risk complications (e.g. perforation) may be increased due to inadequate visualization, and due to the need for repeat procedures or a different procedure.
- Inadequate preparation can reduce the accuracy of the colonoscopy, leading to lower rates of polyp and adenoma detection, decreased detection of flat lesions and lower rates of cecal intubation (which is a quality indicator for colonoscopy).
- Frustration for both the physician and the patient are also consequences.
- Delays on the endoscopy unit due to need for increased washing of the bowel wall through the colonoscope, which prolongs the procedure.
Practice Tip

Failure to complete colonoscopies due to inadequate preparation creates inefficiencies in patient care and utilization of health care resources, potentially leading to additional healthcare costs and a negative impact on the patient.

Test Yourself

Which of the following factors has been associated with inadequate bowel cleansing?

   a) Use of constipating medications  
   b) Low health literacy  
   c) Excessive fluid consumption  
   d) A and B are both correct

Factors Associated with Inadequate Bowel Cleansing

A number of characteristics and factors have been associated with inadequate bowel cleansing. Being familiar with these characteristics can help healthcare providers to identify patients who may be at increased risk of inadequate bowel cleansing and tailor the selection of regimen to help meet their needs to ensure the most effective outcome of the preparation.

The predictors of inadequate bowel cleansing can be categorized as medical factors and socioeconomic factors (Table 1). Medical factors include comorbidities, patient characteristics and medications. Constipating medications such as opioids and tricyclic antidepressants and other agents with anticholinergic side effects increase the risk of inadequate bowel cleansing. Socioeconomic factors are generally those that increase the risk of the patient not following the instructions of the bowel preparation.

Table 1: Predictors of inadequate bowel cleansing⁵,⁶

<table>
<thead>
<tr>
<th>Medical Factors</th>
<th>Socioeconomic Factors</th>
<th>Adherence-related Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic constipation</td>
<td>Lower socioeconomic status</td>
<td>Inadequate instruction</td>
</tr>
<tr>
<td>Use of constipating medications</td>
<td>Less education</td>
<td>Lag time between instruction and procedure</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>Lower health literacy</td>
<td>Failure to adhere to dietary restrictions</td>
</tr>
<tr>
<td>Obesity</td>
<td>Lack of insurance coverage</td>
<td>Inadequate consumption of fluid</td>
</tr>
<tr>
<td>Comorbidities such as diabetes, stroke, dementia, and Parkinson’s disease</td>
<td>First language other than English</td>
<td>Failure to consume entire volume of the preparation</td>
</tr>
<tr>
<td>Prior inadequate preparation for colonoscopy</td>
<td>Low patient activation</td>
<td>Side effects</td>
</tr>
<tr>
<td>Prior resection of the colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older age</td>
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</tbody>
</table>
Overview of Bowel Cleansing Preparations

The Ideal Bowel Preparation

While no bowel preparation is clearly ideal, there are a number of characteristics that can help to optimize the outcome of cleansing and the quality of the examination. Ideal preparation would have optimal results, which would include:

1. The ability to identify significant lesions
2. Minimal need for repeat examinations
3. Adequate cleansing of the bowel without altering the mucosa or causing electrolyte or fluid balance disturbances and other untoward effects
4. Easy to administer and tolerate (i.e., low adverse event rate, minimal discomfort to the patient, palatable)
5. High rates of patient adherence
6. Rapid emptying of the colon

Other ideal characteristics would include being low in cost, free from significant adverse effects, and having minimal impact on special populations such as older adults, patients with heart, liver or renal disease, those who are pregnant and children. Having minimal impact on a patient’s lifestyle would also be a key characteristic of an ideal bowel preparation. This extends beyond the consuming the actual preparation and also includes:

1. Dietary modification
2. Adjustments in work and social schedules
3. Feelings of hunger and sleep disturbances
4. Restriction in long commute times or other activities
5. Need for easy access to restrooms
6. Consideration of the distance from home to the endoscopy suite, which can impact on timing of dosing

Test Yourself

Iso-osmotic laxatives draw extracellular fluid into the bowel lumen, which stimulates peristalsis.

a) True
b) False

Categories of Laxatives

Bowel preparation regimens typically incorporate dietary modifications along with oral agents that act as cathartics to accelerate evacuation of the bowel. Dietary modification generally consists of a clear liquid diet beginning the day before the procedure, which helps to improve visualization of the details of the mucosa. A low residue diet several days prior may also be recommended; however, dietary recommendations are often site-specific and are beyond the scope of this lesson. Adequate fluid consumption is also an important part of the regimen. Bowel preparations that are used prior to colonoscopy can be categorized into three major types: hyperosmotic, iso-osmotic and stimulant laxatives. The mechanism of each category is outlined in Table 2.
Table 2: Laxative categories used in bowel preparations

<table>
<thead>
<tr>
<th>Type of Laxative</th>
<th>Mechanism</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertonic osmotic</td>
<td>Draw extracellular fluid into the bowel lumen, causing distension, which</td>
<td>Magnesium citrate, Sodium phosphate</td>
</tr>
<tr>
<td>agents</td>
<td>stimulates peristalsis and evacuation</td>
<td></td>
</tr>
<tr>
<td>Iso-osmotic agents</td>
<td>High molecular weight, poorly absorbed iso-osmotic polymer in a dilute</td>
<td>Polyethylene glycol (PEG)</td>
</tr>
<tr>
<td></td>
<td>electrolyte solution, which is retained in the colon and acts as a lavage</td>
<td></td>
</tr>
<tr>
<td>Stimulant laxatives</td>
<td>Enhance intestinal motility. Some may also increase the water content of</td>
<td>Sodium picosulfate, bisacodyl</td>
</tr>
<tr>
<td></td>
<td>the bowel</td>
<td></td>
</tr>
</tbody>
</table>

Agents used in bowel preparation can further be categorized as high volume and low volume. High-volume preparations are typically defined as those that require the consumption of at least four litres of the cathartic itself. Low volume bowel preparations involve the consumption of smaller amounts of the cathartic. It should be noted, however, that low volume preparations require that the patient consume additional everyday clear fluids, which may make the total volume consumed with the low volume preparation similar to that of the high-volume preparation. The difference then is in the amount of bowel preparation needed to be consumed by the patient and not the total volume of liquid prior to the procedure.

Meet Our Patient - John

John is 43 years old and has an 18-year history of ulcerative colitis, for which he takes 2 grams of 5-ASA on a daily basis. Currently John’s ulcerative colitis is well controlled and is having minimal impact on his quality of life. He was recently scheduled for a colonoscopy for colorectal cancer screening; however, the procedure could not be completed due to inadequate cleansing. John is now scheduled for a repeat colonoscopy and says that he is somewhat reluctant to “suffer through” the bowel preparation again. He would like to discuss what he can do differently this time around to ensure that he will be able to have the procedure carried out as scheduled.

Test Yourself

What information should you obtain from John to assess the reasons why his bowel preparation was ineffective?

a) The preparation that was used
b) When he started the preparation and how he took it
c) Whether he consumed the entire amount
d) What dietary modifications he followed
e) Whether or not he consumed adequate fluids with the preparation
f) All of the above

Upon further questioning, John lets you know that his bowel preparation consisted of four litres of polyethylene glycol solution and that he “could not stomach” the taste of it. He says that he could not finish the last litre or so of the solution.
Options for Bowel Preparation

Sodium Picosulfate/Magnesium Citrate

The combination of sodium picosulfate and magnesium citrate (formed from citric acid and magnesium oxide in the product) is used in a bowel cleansing regimen, causing evacuation of the bowel via two mechanisms of action, with sodium picosulfate acting as a stimulant laxative (increasing peristalsis) and magnesium citrate working via an osmotic effect.

Advantages

- Requires a smaller volume of bowel preparation to ingest, which improves patient completion and may improve tolerability
- Can be used in the elderly and children
- The additional 3-4 litres to be consumed are everyday clear fluids
- Well-studied, is better tolerated than PEG solutions in head to head comparative clinical studies, and was considered easier to use or had a better taste than PEG
- Relatively inexpensive

Disadvantages

- Requires consumption of 3 to 4 litres of everyday fluid along with it, which makes the total volume to consume similar to PEG. However, with sodium picosulfate/magnesium citrate there is a longer time frame for consumption permitted.

Test Yourself

Approximately what percentage of patients is unable to consume the entire quantity of bowel preparation with high volume (4 L) polyethylene glycol (PEG) solution using a standard dosing regimen?

a) 1% to 2%
b) 5% to 15%
c) 25%
d) 50%

Polyethylene Glycol (PEG) Solution – High Volume (4 L)

Polyethylene glycol (PEG) solutions belong to the iso-osmotic category of laxatives. PEG is a nonabsorbable, nonfermentable electrolyte solution that act as a lavage in the bowel, producing bowel cleansing.

Advantages

- The evidence of clinical efficacy of PEG solutions has been demonstrated in a number of clinical trials
- Risk of electrolyte disturbances may be lower than with some other preparations
- Relatively safer for patient with electrolyte imbalances, advanced liver disease, poorly compensated heart failure and renal failure
- Can be used in the elderly
• Does not alter the histological features of the mucosa and can be used in patients with suspected IBD without interfering with the diagnostic ability of colonoscopy or impeding the ability to take tissue samples.

Disadvantages

• The patient is required to consume four litres of the PEG solution, which may be challenging. Inability to consume the entire quantity is relatively common (5% to 15% of patients).
• The taste of PEG solutions contributes to the difficulty that patients experience in consuming the entire quantity. Flavouring agents have been added to make these products more palatable.

Polyethylene Glycol (PEG) Solution – Low Volume

Polyethylene glycol solutions can be combined with other laxative agents, permitting effective bowel cleansing with a smaller volume, such as two litres. The combination of PEG with a mega dose of ascorbic acid (4.7 grams) is one such option which has been shown to have equal effectiveness in bowel cleansing compared to PEG four litres. The ascorbic acid component is incompletely absorbed, exerting an osmotic effect. PEG 2 L has also been used in combination with bisacodyl, a stimulant laxative.

Advantages

• Requires a smaller volume than standard high volume PEG solutions, which may improve tolerability
• As with other PEG solutions, with smaller shifts in fluid and electrolytes, the risk of electrolyte disturbances may be lower than with some other preparations
• Offered in commercially available preparations (with ascorbic acid)

Disadvantages

• Low volume PEG still requires the intake of 500 mL of clear fluid per 1 L of preparation to prevent dehydration.
• The addition of ascorbic acid increases the potential for some drug interactions and may reduce palatability of the product
• Bisacodyl can cause ischemic colitis
• Higher cost

Magnesium Citrate

Magnesium citrate is a hyperosmotic laxative that draws fluid into the lumen. It has been used alone, in combination with bisacodyl or as an adjunct to PEG to reduce the volume required.

Advantages

• Requires a lower volume of bowel preparation consumption than with PEG

Disadvantages

• Magnesium citrate is eliminated entirely by the kidneys, requiring precaution in patients with known kidney disease and the elderly
• Risk of magnesium toxicity, leading to drowsiness, bradycardia, hypotension and nausea\textsuperscript{6}
• Magnesium citrate may be unpalatable

**Comparative Clinical Efficacy of Bowel Preparations**

**High Volume versus Low Volume PEG Solutions**

The clinical efficacy of large volume PEG solutions has been evaluated through systematic literature reviews. Pooled analyses suggest similar efficacy in terms of cleansing of the colon overall with high volume and a low volume PEG solution combined with ascorbic acid;\textsuperscript{10} however, cleansing in the right colon was greater with the high volume preparation in the one study that assessed this outcome. When 2 L PEG was combined with an additional agent other than ascorbic acid (e.g. bisacodyl, senna), it was less effective than with the high volume (4 L) preparation.\textsuperscript{10}

**Test Yourself**

The tolerability of sodium picosulfate/magnesium citrate is superior to that of PEG solutions.

a) True

b) False

**Sodium Picosulfate/Magnesium Citrate versus Low Volume PEG**

The efficacy, safety, and tolerability of a split dose regimen of sodium picosulfate/magnesium citrate was compared to a combination of low volume PEG (2 L) in combination with 10 mg of bisacodyl in two randomized controlled trials (SEE CLEAR I and SEE CLEAR II).\textsuperscript{11, 12} In the SEE CLEAR I study (n=601 participants) efficacy of bowel cleansing was evaluated by using standardized scales and tolerability was measured using a patient questionnaire. Sodium picosulfate/magnesium citrate was found to be superior in achieving excellent or good bowel cleansing overall compared to 2 L of PEG 3350 (84.2% vs 74.4%) and in cleansing of the ascending, mid, and rectosigmoid segments of the colon. Results were similar in the SEE CLEAR II study (n=603) where excellent or good bowel cleansing overall was 83% in the sodium picosulfate/magnesium citrate group and 79.7% in the 2 L of PEG 3350 group. Cleansing in the ascending, mid, and rectosigmoid segments of the colon was also similar. The most commonly reported adverse effects in both studies were nausea, vomiting, and headache, the rates of which were similar between groups. In both the SEE CLEAR I and II studies, the tolerability of sodium picosulfate/magnesium citrate was superior to that of the low volume PEG, details of which are provided in the section on Patient Preference and Tolerability.

**Patient Preference and Tolerability**

The tolerability of a bowel preparation is important as it affects the patient’s ability to complete the bowel preparation as instructed and affects willingness to undergo future bowel preparations. The need to consume four litres of PEG, for example, has presented challenges.\textsuperscript{4} Ease of use and taste are important considerations that have been assessed in numerous studies and in systematic literature reviews. The various products have different flavourings, which may affect palatability from a patient perspective. For example, Pico-Salax is cranberry or orange flavoured, while PegLyte and MoviPrep are fruit and lemon flavoured, respectively.
A systematic review included 19 studies in which the tolerability and/or acceptability of commonly used bowel preparations was assessed. The following observations were made:

- Sodium picosulfate/magnesium citrate was at least as acceptable as the regimens to which it was compared:
  - There was less abdominal pain compared to magnesium citrate alone, with less interruption of sleep and better bowel cleansing.
  - Patients had a preference for sodium picosulfate/magnesium citrate over PEG based upon taste, ease of taking and volume (Figures 1a and 1b).

Another systematic review also identified difficulties with the completion of PEG solutions. When looking at the comparison between high volume PEG and sodium picosulfate/magnesium citrate, the completion rate was 78% versus 88% when data were pooled across three studies.
A pooled analysis of two studies in which the tolerability of low volume PEG was compared with high volume PEG (65%) found that the willingness to repeat the bowel preparation was greater with the low volume PEG (73%).

### Split Dose Regimens

Split dose regimens for bowel preparation involve giving a portion of the bowel preparation (typically one-half of the bowel preparation) on the same day as the procedure. The standard dose is used and split between two administration times, the day before and the morning of the procedure. The second dose is usually 4 to 6 hours prior to the procedure to allow for the agent to have its effect, and the patient to travel to the location of the procedure. For patients who have their procedure in the early morning, it is often necessary to take the second dose early in the morning (e.g., 2 or 3 AM). Generally, the second dose needs to be completed a minimum of 2 hours prior to the sedation to reduce the risk of aspiration during the procedure, according to guidance from the American Society of Anesthesiologists and will be determined by institutional policies. Guidelines from the American Society for Gastrointestinal Endoscopy and the United States Multi-Society Task Force on Colorectal Cancer recommend the use of split dose regimens, based upon systematic reviews of the literature which demonstrated consistent and favorable efficacy outcomes with the split dose regimens. Studies in which split dose regimens have been compared to traditional administration show superior bowel cleansing with fewer adverse events and greater patient preference with the split dose administration. A randomized controlled trial (RCT) that evaluated traditional versus split dose administration of sodium picosulfate/magnesium citrate demonstrated superior bowel cleansing (mainly in the right-sided colon) with the split dose regimen. There were no differences noted in common adverse effects (nausea, vomiting, bloating, abdominal pain) and patient tolerability was high in both groups, with the majority of patients rating the preparation as very easy or easy to tolerate. Finally, patients who undergo bowel cleansing with split dose regimens are more willing to undergo the bowel preparation again in the future.

### Considerations in Bowel Preparation Selection

Bowel preparation should be individualized to help ensure safe and effective bowel cleansing. Evidence of efficacy and safety are key considerations in choosing amongst the available options for bowel preparation. As previously reviewed, the efficacy of high-volume PEG solutions, low volume PEG solutions, and sodium picosulfate/magnesium citrate is similar when administered appropriately. Thus, safety in specific patient populations and the patient’s preference as it relates to bowel preparation success are important considerations in choosing a bowel preparation.

### Comorbid Medical Conditions

The safety of a bowel preparation may be affected by comorbid medical conditions (Table 3), concurrent medications (Table 4) and patient demographics such as age. Selecting a bowel preparation that will be safe based upon these considerations is important. Any fluid or electrolyte disturbances should be corrected prior to administering a bowel preparation. Failure to do so can result in cardiac arrhythmias, seizures and renal impairment. Importantly, all preparations can cause clinically significant hyponatremia.

**Table 3: Contraindications and adverse effects of bowel cleansing preparations available in Canada**
<table>
<thead>
<tr>
<th>Product</th>
<th>Approved Indications</th>
<th>Cautions/Contraindications</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Picosulfate/Magnesium citrate</td>
<td>In adults and children:</td>
<td>Contraindications:</td>
<td>Nausea, vomiting, headache</td>
</tr>
<tr>
<td></td>
<td>• Clearance of the bowel prior to x-ray examination, endoscopy or surgery</td>
<td>• Congestive heart failure, severely reduced renal function</td>
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<tr>
<td></td>
<td></td>
<td>• Ileus, gastric retention, bowel perforation, gastrointestinal obstruction, toxic colitis, toxic megacolon</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Precautions:</td>
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<td></td>
<td></td>
<td>• Renal impairment, heart disease and inflammatory bowel disease</td>
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<td></td>
<td></td>
<td>• History of seizures or patients at risk of seizures due to medications that lower the seizure threshold</td>
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<tr>
<td></td>
<td></td>
<td>• Medications that affect fluid or electrolyte balance</td>
<td></td>
</tr>
<tr>
<td>Polyethylene Glycol (PEG) 3350 Solution – High volume (4 L)</td>
<td>In adults*:</td>
<td>Contraindications:</td>
<td>Abdominal fullness, abdominal pain, nausea, vomiting</td>
</tr>
<tr>
<td></td>
<td>• Bowel cleansing prior to colonoscopy or barium enema x-ray examination or surgical procedures requiring a clean colon</td>
<td>• Ileus, gastric retention, bowel perforation, gastrointestinal obstruction, toxic colitis, toxic megacolon</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• The treatment of constipation</td>
<td>Precautions:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ulcerative colitis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Patients with known or suspected hyponatremia, or in patients using concomitant medications that increase the risk of electrolyte abnormalities (due to increased seizure risk)</td>
<td></td>
</tr>
<tr>
<td>PEG-3350 – Small Volume (2 L)</td>
<td>In adults:</td>
<td>Contraindications:</td>
<td>Nausea, vomiting, abdominal pain</td>
</tr>
<tr>
<td>(with ascorbic acid)</td>
<td>• Indicated for cleansing of the colon as a preparation for</td>
<td>• Ileus, gastric retention, bowel perforation, gastrointestinal obstruction, toxic colitis,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Precautions:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ulcerative colitis</td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>Contraindications</td>
<td>Precautions</td>
<td></td>
</tr>
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<td>-------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Magnesium Citrate</td>
<td>Acute abdominal pain, nausea, vomiting or other symptoms of appendicitis or undiagnosed abdominal pain</td>
<td>Myasthenia gravis or other neuromuscular diseases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients with serious renal impairment (Creatinine clearance &lt; 30 mL/min)</td>
<td>Patients with reduced kidney function</td>
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</tr>
<tr>
<td></td>
<td>Patients with heart block</td>
<td>Patients on a low-sodium diet</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Drug interactions with bowel preparations

<table>
<thead>
<tr>
<th>Product</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Picosulfate/Magnesium citrate</td>
<td>Drugs that affect fluid or electrolyte balance</td>
</tr>
<tr>
<td></td>
<td>• Diuretics, Corticosteroids, Lithium</td>
</tr>
<tr>
<td></td>
<td>Drugs that induce SIADH</td>
</tr>
<tr>
<td></td>
<td>• TCAs, SSRIs, Antipsychotics</td>
</tr>
<tr>
<td></td>
<td>Drugs that may be chelated by magnesium (take at least 2 hours before or 6 hours after)</td>
</tr>
<tr>
<td></td>
<td>• Tetracyclines, fluoroquinolones, digoxin</td>
</tr>
<tr>
<td>Polyethylene Glycol (PEG) 3350 Solution – High volume (4 L)</td>
<td>Should not be taken within 2 hours of another drug as</td>
</tr>
</tbody>
</table>
the efficacy of the other drug may be reduced

| PEG-3350 – Small Volume (2 L) | • Caution in patients using concomitant medications that increase the risk of electrolyte abnormalities  
• Oral medication should not be taken within one hour of administration as absorption may be decreased  
• Large doses of ascorbic acid may increase the plasma concentration of ethinylestradiol in women taking oral contraceptives  
• Acidification of the urine following administration of ascorbic acid may result in altered excretion of other drugs (e.g. memantine, acetaminophen, salicylate, phenobarbital, methenamine). Renal tubular reabsorption of acidic medications may be increased (e.g., acetaminophen) and alkaline medications may be decreased. |
| Magnesium Citrate | Drugs that may be chelated by magnesium (take at least 2 hours before or 6 hours after)  
• Tetracyclines, fluoroquinolones, digoxin  
Laxative products potentially decrease transit time of concomitantly administered oral medications, and can, therefore, decrease absorption. Separate administration by 2 hours.  
May alter gastric and urinary pH, affecting dissolution, absorption, bioavailability and renal elimination of some drugs (e.g. memantine, acetaminophen, salicylate, phenobarbital, methenamine). |

**Patient Preference and Tolerability**

The patient’s experience with a bowel preparation is important, given that a negative experience can disrupt preparation for the procedure and deter the patient from future exams (such as colorectal cancer screening). Tolerability can relate to the volume of solution that needs to be consumed, as well as the solution’s palatability. It should be emphasized that in order for an agent to be effective and safe, it must be consumed in accordance with its instructions and in its entirety. Thus, tolerability is important because it can impact efficacy; if an individual cannot tolerate the bowel preparation, the full quantity will not be ingested, which will have a negative impact on efficacy. The patient’s past experience with bowel preparations should be considered when selecting an agent. Inability to tolerate a bowel preparation in the past may suggest that agent should be avoided if possible, as the individual may be unable to complete the full dosage or may simply refuse the procedure based upon fear of adverse events.

**Revisit Our Patient - John**

Given that John was unable to consume the 4 L of PEG solution for his initial colonoscopy, what might be a reasonable alternative for him?

a) Repeat with PEG 4 L but using a split dose regimen
b) PEG 2L with ascorbic acid  
c) Sodium picosulfate/magnesium citrate  
d) All of the above

Test Yourself
Bowel preparations can decrease transit rate of medications through the gastrointestinal tract.

a) True  
b) False

Concurrent Medications
Concurrent medications and the timing of their administration should be considered in selecting and while taking bowel preparations (Table 4).

Generally, sodium picosulfate/magnesium citrate and PEG solutions can increase the gastrointestinal transit rate of medications and can potentially reduce the absorption of orally administered medications. As such, some medications may require dosage modifications. This might be particularly relevant for anti-epileptics, contraceptives, antidiabetic agents, and antibiotics. Absorption may be altered when these drugs are taken within one hour of starting the bowel preparation. When selecting a bowel preparation, consideration should also be given to medications that affect fluid and electrolyte balance. Concurrent use of these medications can increase the risk of related adverse effects such as seizures and arrhythmias. Corticosteroids and diuretics, for example, may be associated with hypokalemia. Drugs that cause hyponatremia (for example SSRIs and tramadol) are also a potential concern.

Practice Tip
Bowel preparations and concurrent medications can interact via a number of mechanisms, including alteration in absorption from the bowel, potentiation of fluid and electrolyte disturbances and changes in reabsorption from the renal tubule.

Special Populations
Elderly Patients
Older age is a predictor of failure to achieve adequate bowel cleansing, but this is not necessarily related to overall tolerance to the bowel preparation. Adequate fluid intake before, during and after the use of bowel preparations is essential to minimize the risk of adverse effects with bowel cleansing regimens in at risk or frail populations. Evidence suggests that bowel preparations can be used safely in the elderly when administered in accordance with directions and adequate fluid intake. In a study of sodium picosulfate/magnesium citrate carried out in the frail elderly, no evidence of renal toxicity was observed. In another population-based study of elderly patients in Ontario, of the 50 660 outpatients who took bowel preparations, the risk of serious adverse events was slightly higher (2.8%) in patients categorized as high-risk (pre-existing renal or cardiac disease, those on diuretics and patients residing in...
nursing homes). Overall, the risk of serious adverse effects with sodium picosulfate/magnesium citrate and PEG-based regimens was relatively low (2.4%). Tolerance, however, of high volume PEG solutions may be poor in the elderly, with up to 40% having poor tolerance. Further, in elderly patients with difficulties swallowing, such as those with Parkinson disease, dementia or stroke, high volume PEG may be inappropriate due to administration difficulties. 

**Test Yourself**

In general, magnesium-containing bowel preparations are contraindicated in patients with severely reduced renal function (creatinine clearance of < 30 mL/minute).

a) True  
b) False

**Renal Impairment**

Magnesium-containing formulations (magnesium citrate and sodium picosulfate/magnesium citrate) require caution when using in patients with renal impairment or in patients taking medications that can adversely affect renal function, such as diuretics, angiotensin enzyme converting inhibitors, ARBs and NSAIDs). The risk to these patients can be reduced by ensuring adequate hydration before, during and after the use of the bowel cleansing regimen. In patients with creatinine clearance of less than 30 mL per minute, magnesium can accumulate and, as such, preparations containing magnesium are contraindicated. PEG solutions also carry a contraindication in this population.

**Patients with Inflammatory Bowel Disease (IBD)**

There are limited studies of bowel preparation in patients with inflammatory bowel disease (IBD). According to the manufacturers’ product monographs, precaution is generally recommended when using bowel preparations in patients with inflammatory bowel disease. PEG solutions have been shown to produce adequate cleansing prior to colonoscopy for colorectal cancer screening and for the assessment of symptoms suggestive of IBD, and have the advantage of not altering the intestinal mucosa. One concern with sodium phosphate and sodium picosulfate for bowel preparation in patients with IBD is their ability to cause superficial mucosal lesions, which can mimic those that are seen in patients with Crohn’s disease. However, the lesions attributed to these agents are distinctive and can be distinguished from those seen with IBD. This does not, however, preclude the use of sodium picosulfate for future colonoscopies for patients diagnosed with IBD or prior to colonoscopy for the purpose of colorectal cancer screening.

**Pediatric Patients**

Bowel preparation in pediatric populations is needed for the diagnosis and management of gastrointestinal diseases. The selection of a bowel preparation in pediatric patients requires individualization according to age, comorbidities and potential willingness or ability to adhere to the regimen. Hydration is extremely important in pediatric patients prior to, during and after bowel preparation to reduce the risk of adverse effects. Few studies of bowel preparations have been carried out in pediatric patients. Randomized controlled trials support the efficacy of PEG solutions, but the high volume required and palatability may be problematic for some patients.
compared sodium picosulfate/magnesium citrate with PEG solution found it to be better tolerated with similar efficacy in terms of cleansing in pediatric patients and in another randomized study sodium picosulfate/magnesium citrate was superior to bisacodyl tablets combined with phosphate enemas. Small volume PEGs have not been studied in the pediatric population and are not approved for use in this population.

Guidelines for Bowel Preparation

In 2014 and 2015, US guidelines addressing bowel preparation prior to colonoscopy were issued. The 2015 Guidelines from the ASGE did not explicitly recommend one bowel cleansing regimen over the others but focussed on the need to individualize the selection of agent. Key points from the ASGE (American Society for Gastrointestinal Endoscopy) 2015 guidelines are as follows:

- Bowel preparations should be individualized by the prescribing provider for each patient based on efficacy, cost, safety, and tolerability considerations balanced with the patient’s overall health, comorbid conditions, and preferences
- Verbal counseling regarding preparation administration should be provided to patients along with written instructions that are simple and easy to follow and in their native language
- Split-dose regimens for all patients and/or same day preparations for afternoon colonoscopies are recommended
- Sodium phosphate (no longer available approved for use in Canada) and magnesium citrate preparations should not be used in the elderly or patients with renal disease or patients taking medications that alter renal blood flow or electrolyte excretion

The United States Multi-Society Task Force on Colorectal Cancer issued a consensus document on Optimizing Adequacy of Bowel Cleansing for Colonoscopy in 2014 to help optimize the quality of preparation for colonoscopy and ensure patient safety. Key recommendations relevant to this continuing education lesson are summarized here:

**Dosing and Timing**

- Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy.
- A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination.
- The second dose of split preparation ideally should begin 4 to 6 hours before the time of colonoscopy with completion of the last dose at least 2 hours before the procedure time.
- Health care professionals should provide both oral and written patient education instructions for all components of the colonoscopy preparation and emphasize the importance of compliance.
- The physician performing the colonoscopy should ensure that appropriate support and process measures are in place for patients to achieve adequate colonoscopy preparation quality.
- Selection of a bowel-cleansing regimen should take into consideration the patient’s medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies.
Practice Tip

Practice guidelines emphasize the need to individualize bowel preparation based upon a number of factors, including patient preference. The use of split-dose regimens is endorsed.

Key Patient Counselling Points

Appropriate education prior to bowel preparation can make an important contribution to achieving adequate cleansing and ensuring patient safety. Here are some key points to review with patients prior to bowel preparation:

- It is important that patients understand the ramifications of nonadherence to instructions related to dietary modification and administration of the bowel preparation. Emphasize that failure to adhere often results in inadequate bowel cleansing and inability to perform the procedure. This will require rescheduling of the procedure, which may lead to delays in diagnosis, and will require repeating the bowel preparation.
- Patients often do not understand that preparation will begin several days prior to the procedure and frequently pick up their instructions and bowel preparation late. Initial education should emphasize the expected timing and the need to adhere to the recommended timing in order to achieve optimal cleansing.
- Adequate fluid consumption (i.e., 250 mL every hour while awake) is critical to prevent dehydration and electrolyte disturbances and also to ensure a high quality cleansing. Consuming a balanced electrolyte solution is recommended as drinking only water to replace fluids can result in electrolyte imbalances, including hyponatremia, and may result in seizures. Watch for signs of dehydration, which may include dizziness, decreased urine output, headache and orthostatic hypotension.
- Provide detailed instruction on how to reconstitute the bowel preparation for those that require reconstitution to avoid errors (Table 5).
- Provide suggestions for making PEG solutions more palatable.
- Be clear as to what is meant by a clear liquid diet (Table 6).
- Supplement verbal counselling with print materials in the patient’s first language, online resources, and smart phone applications. More information on this can be found in the resources section of this lesson.
- Three days prior do not consume seeds or nuts due to the potential for digestive residue or raw fruits or vegetables. Multigrain bread should also be avoided.
- Provide counselling on the adjustment of timing of concurrent medications if necessary.
- Educate patients as to what the stool should look like at the end of bowel preparation (clear, like water or at most lightly coloured).
PEG solutions can be made more palatable by chilling the solution up to 24 to 48 hours or by adding lemon slices, lemon juice or sugar-free flavor enhancer (e.g. Crystal Light).\textsuperscript{3,8} Rinsing the mouth after (swish and swallow with a clear soda (ginger ale, sprite) may also help.

### Table 5: Administration Instructions for Commercially Available Bowel Preparations

<table>
<thead>
<tr>
<th>Sodium Picosulfate/Magnesium citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fill a mug with 150 mL of cold water.</td>
</tr>
<tr>
<td>Empty one sachet into the mug and stir until dissolved.</td>
</tr>
<tr>
<td>After the first dose, consume 1.5 to 2 L of a variety of clear fluids over 4 hours, not just water alone, and 1.5 to 2 L after the second dose.</td>
</tr>
<tr>
<td>Also drink a balanced electrolyte solution (for example: Gatorade, Powerade).</td>
</tr>
<tr>
<td>Two dosages are taken, with the timing of administration being determined by the time of the procedure (Figure 1).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Polyethylene Glycol (PEG) 3350 Solution – High Volume (4 L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add tap water to the fill line (total volume 4 L). Replace cap tightly and mix well until all ingredients have dissolved.</td>
</tr>
<tr>
<td>240 mL of solution should be consumed every 10 minutes.</td>
</tr>
<tr>
<td>Rapid drinking of each portion is preferred rather than drinking small amounts continuously.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Polyethylene Glycol (PEG) 3350 Solution – Low Volume (2 L) with ascorbic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>A litre of the preparation consists of one ‘Sachet A’ and one ‘Sachet B’ dissolved together in one litre of water. This reconstituted solution should be drunk over a period of one to two hours. This should be repeated with a second litre of the solution.</td>
</tr>
<tr>
<td>There should be at least two hours between the end of intake of fluid (bowel preparation solution or clear liquid) and the start of colonoscopy.</td>
</tr>
<tr>
<td>Split-dose regimen: The evening before the colonoscopy, the first litre of solution over one hour (one 8 ounce glass every 15 minutes) is taken, followed by 500 mL of clear fluid. Then, on the morning of the colonoscopy, the second litre of solution is taken over one hour, followed by 500 mL of clear liquid at least two hours prior to the start of the colonoscopy.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Magnesium Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mL the evening before the procedure, often in combination with bisacodyl 20 mg orally.*</td>
</tr>
</tbody>
</table>

* 2 x 300mL and 2x 450 mL have also been used

**Figure 1: Dosage timing for sodium picosulfate/magnesium citrate**

<table>
<thead>
<tr>
<th>Split Dose Regimen: Preferred Method</th>
<th>Day Before Dosing: Alternative method</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Split-Dose regimen is the preferred dosing method. Instruct patients to take two separate doses in conjunction with fluids, as follows:</td>
<td>The Day-Before regimen is the alternative dosing method for patients for whom the Split-Dosing is inappropriate. Instruct patients to take two separate doses in conjunction with fluids, as follows:</td>
</tr>
<tr>
<td>Take the first dose during the evening before the</td>
<td></td>
</tr>
</tbody>
</table>

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colonoscopy (e.g., 5:00 to 9:00 PM) followed by 1.5 to 2 Litres of a variety of clear fluids. Consume clear liquids within 5 hours.

Take second dose the next day approximately 5 hours before the colonoscopy followed by 1.5 to 2 Litres of a variety of clear fluids. Consume clear liquids within 5 hours up to 2 hours before the time of colonoscopy.

Take the first dose in the afternoon or early evening (e.g., 4:00 to 6:00 PM) before the colonoscopy followed by 1.5 to 2 Litres of a variety of clear fluids. Consume clear liquids within 5 hours.

Take the second dose approximately 6 hours later in the late evening (e.g., 10:00 PM to 12:00 AM), the night before the colonoscopy followed by 1.5 to 2 Litres of a variety of clear fluids. Consume clear liquids within 5 hours up until 2 hours before the time of the colonoscopy.

Table 6: Constituents of a clear liquid diet

<table>
<thead>
<tr>
<th>Clear Liquid Diet *** (No red or purple colours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain water</td>
</tr>
<tr>
<td>Fruit juices without pulp, such as apple juice</td>
</tr>
<tr>
<td>Soup broth (bouillon)</td>
</tr>
<tr>
<td>Clear sodas, such as ginger ale and Sprite</td>
</tr>
<tr>
<td>Gelatin (Jell-O) (avoid red or purple)</td>
</tr>
<tr>
<td>Popsicles that do not have bits of fruit or fruit pulp in them (avoid red or purple)</td>
</tr>
<tr>
<td>Sports drinks that are not red, purple or blue</td>
</tr>
<tr>
<td>Tea or coffee with no cream or milk added</td>
</tr>
</tbody>
</table>

Meet Our Patient – Mary

Mary is 76 years old and has a history of osteoarthritis and osteoporosis. She is currently taking acetaminophen, calcium, vitamin D and risendronate. Several months ago Mary began experiencing fatigue and nonspecific abdominal pain. Bloodwork was ordered, which showed low hemoglobin and was then followed up with a fecal occult blood test. After having found that the fecal occult blood test was positive, she was then referred for colonoscopy. Mary has no past experience with bowel preparation.

Test Yourself
Which of the following bowel preparations may be appropriate options for Mary?

a) PEG 4 L
b) PEG 2L with ascorbic acid
c) Sodium picosulfate/magnesium citrate
d) All of the above
Case Resolution

Based upon systematic literature reviews, guidelines for bowel preparation state that there is insufficient evidence of efficacy to recommend a specific agent in the elderly.\(^{14}\) However, the contraindications and precautions of the individual agents should be considered in making a selection. Of key importance is to ensure that any fluid or electrolyte disturbances are corrected prior to beginning the bowel preparation and renal function be assessed. While PEG solutions have an advantage of having minimal effects in terms of fluid shifts and electrolyte balances, their use has been associated with hypokalemia and difficulties in consuming the entire preparation in some patients.\(^{14}\) Similarly, sodium picosulphate/magnesium citrate has also been associated with changes in fluid and electrolyte status, but overall the risk of serious adverse effects with this preparation was found to be low in a population-based study and similar to that of PEG.

Summary of Key Learning Points

- Failure to achieve adequate bowel cleansing prior to colonoscopy is common and can be affected by a number of factors, one of which is failure to adhere to the bowel preparation regimen.
- A number of bowel cleansing regimens have been shown to produce adequate bowel cleansing prior to colonoscopy provided that they are used according to the preparation instructions.
- Tolerability and palatability of a bowel preparation are important determinants of whether a bowel preparation is taken in its entirety and as instructed. Split-dose regimens can improve patient tolerance of bowel preparations with similar or better efficacy in terms of bowel cleansing.
- The volume of the preparation that the patient is required to take can limit the ability to complete the entire amount and achieve adequate cleansing. Lower volume preparations may help to overcome this barrier.
- Many different factors affect the choice of bowel preparation and include patient preference, past experience, comorbid medical conditions, and concurrent medications.

Resources

Smart Phone Applications

- Smart phone applications are available that provide information about colonoscopy and help guide the patient through the preparation process by providing reminders and information. These applications are available at [www.itunes.com](http://www.itunes.com) and/or [www.play.google.com](http://www.play.google.com).
  - Colonoscopy Prep Assistant
  - Colonoscopy Helper
  - ADH (http://www.arizonadigestivehealth.com/procedures-services/adh-mobile-app/)
  - DDC

Guidelines

- Canadian Association for Gastroenterology
Patient Resources

Colonoscopy


Bowel Preparation


Discussion Forum

1. What are the most significant barriers to patient adherence with bowel preparation that you encounter in your practice?
2. What are the key factors that you consider in selecting a bowel preparation for your patients?

References

16. E-cps (www.e-therapeutics.ca)