Making the most of currently available bowel preparations for colonoscopy

ABSTRACT

Adequate bowel preparation is essential before colonoscopy. Choosing an agent can be confusing, since many are available. The authors review the available regimens, offer an algorithm for choosing an appropriate regimen, and provide bowel preparation instructions for patients.

KEY POINTS

Polyethylene glycol solutions are fast, effective, and preferred for cleansing the colon.

Use of split dosing, a low-volume solution, or both can increase patient acceptability without compromising efficacy.

Sodium phosphate can be prescribed for patients who cannot tolerate polyethylene glycol solutions, provided they are not at risk of electrolyte or fluid imbalances.

Enemas, bisacodyl, magnesium citrate, and metoclopramide (Reglan) can be useful as adjuncts to polyethylene glycol but by themselves are inadequate for cleansing the entire colon.

Educating patients about bowel preparation instructions, including correct dosing and adequate hydration, helps reduce the risk of adverse events and serious adverse events.

DURING COLONOSCOPY, the physician needs to inspect the entire mucosal surface. This can be done only if the bowel has been adequately prepared—ie, cleaned out (FIGURE 1). Inadequate bowel preparation reduces the quality of colonoscopy, raises the procedural risks, and increases the chance that polyps will go undetected.1–3 Furthermore, poor bowel preparation substantially increases costs by prolonging the procedure time and increasing the chance of an aborted examination, necessitating another procedure at an interval sooner than called for in the standard guidelines.3,4

Adequate bowel preparation depends on the right choice of bowel-cleansing agent. But with a myriad of products available, the right choice can be confusing to make.

This review discusses the currently recommended methods for bowel preparation before colonoscopy and suggests ways to solve common problems.

EARLY DETECTION IS KEY

Colorectal cancer is the third most common cancer in the United States and the second most common cause of cancer deaths. It largely can be prevented by detecting and removing adenomatous polyps, and survival rates are significantly better when it is diagnosed while still localized.3 Early detection, through widely applied screening programs that include colonoscopy, is thought to be playing a key role in the recent decline of colorectal cancer rates in developed countries.6
Bowel preparation agents, for the most part, can be classified into one of three categories:
• Polyethylene glycol solutions, which work as high-volume gut lavage solutions
• Osmotic agents, such as sodium phosphate, magnesium citrate, lactulose, and mannitol, which draw extracellular fluid across the bowel wall and into the lumen
• Stimulants (castor oil, senna, sodium picosulphate, and bisacodyl), which work by increasing smooth muscle activity within the wall of the colon.

Bowel preparation in the past consisted of dietary restriction, stimulant laxatives, and enemas. However, these were time-consuming (taking 48–72 hours), harsh, and not very effective for adequate visualization during colonoscopy.

In 1980, Davis et al developed an osmotically balanced, high-molecular weight, nonabsorbable polymer given in a dilute electrolyte solution. The osmotic effect of the polymer keeps the electrolyte solution in the colon. Since little fluid is exchanged across the colonic membrane, the potential for systemic electrolyte disturbance is limited.

FIGURE 1. Adequate bowel preparation is essential before colonoscopy. The preparation is excellent in the top two images, allowing optimal visualization of a polyp in the top right image (arrow). In contrast, the bottom two images show inadequate bowel preparation, with semisolid or solid debris that obscures the complete view of the mucosa in spite of extensive flushing and suction.
Since then, these solutions have become some of the preferred bowel cleansing agents worldwide.\textsuperscript{7,8} They work as an oral lavage and hence need to be taken in high volume (typically 4 L) for bowel cleansing.

Advantages and disadvantages of polyethylene glycol solutions
Polyethylene glycol solutions are more effective and better tolerated than regimens of diet combined with cathartic agents, or high-volume balanced electrolyte solutions, or mannitol-based solutions.\textsuperscript{7} Since they are osmotically balanced and do not induce substantial shifts in fluid and electrolytes, they are safe for patients who have electrolyte imbalances, advanced liver disease, poorly compensated congestive heart failure, or renal failure.

These preparations are, however, contraindicated in patients who have allergies to polyethylene glycol compounds, gastric outlet obstruction, high-grade small-bowel obstruction, significant colonic obstruction, perforation, diverticulitis, or hemodynamic instability. In addition, they are classified by the US Food and Drug Administration (FDA) as pregnancy category C and have been associated (albeit rarely) with Mallory-Weiss tear, toxic colitis, pulmonary aspiration, hypothermia, cardiac arrhythmias, pancreatitis, and inappropriate antidiuretic hormone secretion.\textsuperscript{10,11}

The main disadvantages of these solutions are the large volume of fluid (4 L) that patients must drink and their unpalatable taste, which

### TABLE 1
Commercially available polyethylene glycol solutions

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>VOLUME (ML)</th>
<th>PRICE ($)</th>
<th>GENERAL INSTRUCTIONS TO PATIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>GoLYTELY flavored</td>
<td>4,000</td>
<td>19.70</td>
<td>Take 240 mL or 8 oz (1 cup) every 10 minutes beginning around 6 PM the evening before colonoscopy. For split dosing, take half of the solution the evening before colonoscopy and half on the morning of colonoscopy.\textsuperscript{b}</td>
</tr>
<tr>
<td>GoLYTELY unflavored</td>
<td>4,000</td>
<td>18.45</td>
<td></td>
</tr>
<tr>
<td>Colyte flavored</td>
<td>4,000</td>
<td>25.63</td>
<td></td>
</tr>
<tr>
<td>Colyte unflavored</td>
<td>4,000</td>
<td>25.63</td>
<td></td>
</tr>
<tr>
<td>Nulytely (sulfate-free)</td>
<td>4,000</td>
<td>26.89</td>
<td></td>
</tr>
<tr>
<td>Trilyte flavored (sulfate-free)</td>
<td>4,000</td>
<td>27.98</td>
<td></td>
</tr>
<tr>
<td>Halflytely</td>
<td>2,000</td>
<td>51.01</td>
<td>Take two bisacodyl delayed-release tablets at 12 noon the day before colonoscopy and then 240 mL (8 oz) of Halflyte every 10 minutes beginning around 6 PM.</td>
</tr>
<tr>
<td>MoviPrep</td>
<td>2,000</td>
<td>50.08</td>
<td>Around 6 PM in the evening before the colonoscopy, take the first liter of MoviPrep solution over 1 hour (one 8-oz glass every 15 minutes); then about 1.5 hours later, take the second liter over 1 hour. In addition, take 1 L of additional clear liquid during the evening before the colonoscopy. For split dosing, take half of the solution the evening before colonoscopy and half on the morning of colonoscopy, each with 0.5 L of clear liquid.</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Average wholesale prices, based on Red Book 2008 and 2009 updates. The actual cost to a patient may vary, depending on insurance coverage.

\textsuperscript{b}For detailed instructions about split dosing, see TABLE 2.

\textsuperscript{c}MiraLAX has been used off-label for bowel preparation. Instruct patient to mix one bottle (238 g) in 64 oz of Gatorade or Crystal Light and keep in refrigerator, take four tablets of 5 mg bisacodyl at 4 PM, and start drinking the solution at a rate of 8 oz every 15 to 30 minutes. Price: $9.60.
is due to sodium sulfate. The large volume of ingestion is the main reason for nausea, bloating, cramping, and vomiting with these products, which affect patient compliance and the ultimate success of colonoscopy.

Commercially available polyethylene glycol solutions

Many polyethylene glycol preparations are available today. They can be divided into those that are full-volume solutions (typically 4 L, flavored or unflavored, with sulfate or sulfate-free) and low-volume solutions (typically 2 L) (TABLE 1).

Standard full-volume solutions (Colyte, GoLYTELY) have been widely studied and have the most evidence of safety and effectiveness. They are also inexpensive, and most insurance companies pay for them. However, about 5% to 15% of patients do not complete the preparation, because of poor palatability, large volume, or both.7

Sulfate-free and flavored solutions. To make polyethylene glycol solutions more tolerable, sulfate-free solutions have been developed. These are less salty, more palatable, and comparable to standard solutions in terms of effective colonic cleansing.12 Sulfate-free polyethylene glycol solutions commercially available in the United States are NuLytely (flavors: cherry, lemon-lime, orange, pineapple) and TriLyte (flavors: cherry, citrus-berry, lemon-lime, orange, pineapple).

Low-volume solutions have been developed in an attempt to increase acceptability and reduce volume-related adverse effects such as bloating. For example, HalfLytely (flavor: lemon-lime) consists of 2 L of polyethylene glycol solution packaged with two bisacodyl tablets. Stimulant laxatives such as bisacodyl and magnesium citrate effectively debulk the colon of solid stool and allow a lower volume of solution to be used.13,14

Also commercially available is a preparation that contains ascorbic acid (MoviPrep). Ascorbic acid acts as a flavoring and as a cathartic, also permitting a lower volume of fluid to be used.

Studies that compared full-volume and low-volume regimens (the latter including ascorbic acid, magnesium citrate, or bisacodyl) found the low-volume regimens to be as effective and more tolerable.14-18

Combining over-the-counter polyethylene glycol 3350 laxative powder (MiraLAX) and Gatorade or Crystal Light (or another clear liquid of choice) has also been shown to improve the taste and tolerability of the preparation. Although beneficial and commonly used in certain regions of the United States, this combination is not approved for bowel preparation and its use is considered off-label.

Increasing patient adherence to polyethylene glycol solutions

One way to increase tolerability and patient adherence is to split the dose so that the patient takes half the laxative prescription (polyethylene glycol or otherwise) the night before colonoscopy and the other half in the morning, usually about 4 to 5 hours before the scheduled time of the procedure.18,19

Split dosing not only improves patient acceptability, but also cleans the colon better.4 Traditional dosing, ie, drinking the entire volume of solution the night before, leaves a long interval between the end of the preparation process and the start of the procedure. Thick intestinal secretions empty out of the small intestine during that interval and obscure the cecum and ascending colon. With split dosing, the second dose is completed a few hours before the procedure, cleaning out the remaining intestinal secretions and obviating this problem.

Other measures that can make polyethylene glycol solutions more tolerable are:

- Chilling the solution
- Adding lemon slices or sugar-free flavor enhancers (such as Crystal Light) or lemon juice
- Giving the solution by nasogastric tube (at a rate of 1.2–1.8 L per hour) in patients with swallowing dysfunction or altered mental status
- Adding metoclopramide (Reglan) 5 to 10 mg orally to prevent or treat nausea
- Adding magnesium citrate (1 bottle, about 300 mL) in patients without renal insufficiency, or bisacodyl (two to four tablets of 5 mg each), so that the volume can be less
- Stopping further ingestion of solution once the stool is watery and clear on the morn-
ing of the procedure (for patients who can clearly understand and follow bowel preparation instructions).\textsuperscript{17}

\section*{SODIUM PHOSPHATE SOLUTIONS}

Sodium phosphate is an osmotic laxative that draws water into the bowel lumen to promote colonic cleansing. Retention of water in the lumen of the colon stimulates peristalsis and bowel movements.

\textbf{Advantages and disadvantages of sodium phosphate solutions}

Sodium phosphate is widely used worldwide and has been found to be a very acceptable and effective bowel cleansing agent. A recent systematic review of 25 studies\textsuperscript{18} found that sodium phosphate was superior to polyethylene glycol in 14 studies, that there was no significant difference in 10 studies, and that only one study found polyethylene glycol to be better tolerated than sodium phosphate.\textsuperscript{18} Similarly, a meta-analysis\textsuperscript{19} found sodium phosphate to be more effective than polyethylene glycol in bowel cleansing (odds ratio 0.75; $P = .0004$); more easily completed by patients (odds ratio 0.16; $P < .00001$); and comparable in terms of adverse events (odds ratio 0.98; $P = .81$).\textsuperscript{19}

However, most of the clinical trials excluded patients who had renal failure, ascites, or serious heart disease—the groups most at risk of significant adverse effects from sodium phosphate use. The main reasons sodium phosphate was better tolerated were better flavor and smaller volume (1.5–2 L compared with 4 L for polyethylene glycol).\textsuperscript{20-22}

The main disadvantage of sodium phosphate is its potential to cause large fluid and electrolyte shifts. Its use has been associated with a variety of electrolyte abnormalities, including hyperphosphatemia, hypocalcemia, hypokalemia, increased plasma osmolality, hyponatremia, and, conversely, hypernatremia.\textsuperscript{7,8,23} Asymptomatic hyperphosphatemia alone can be seen in as many as 40\% of healthy patients completing sodium phosphate preparations. It may be significant in patients with renal failure and can lead to acute phosphate nephropathy.

Rare adverse events such as nephrocalcinosis with acute renal failure also have been reported, especially in patients taking angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers.\textsuperscript{23}

The significant volume contraction and consequent dehydration seen in some patients using sodium phosphate may be decreased by encouraging patients to drink fluids liberally, especially before the day of the procedure and after the procedure.\textsuperscript{7}

Recently, renal failure due to hyperphosphatemia (acute phosphate nephropathy) has been reported even in patients with normal kidney function.\textsuperscript{24} Because of the risk of inappropriate use or overdose associated with over-the-counter sodium phosphate, the FDA recommended on December 11, 2008, that sodium phosphate products be available only by prescription when they are used for bowel cleansing.\textsuperscript{25} The C.B. Fleet Company voluntarily recalled its oral sodium phosphate products sold over the counter (Fleet Phospho-Soda and Fleet EZ-PREP). In addition, the FDA required a black box warning on the prescription oral sodium phosphate products Visicol and OsmoPrep, alerting consumers to the risk of acute phosphate nephropathy.\textsuperscript{25} According to the FDA, health professionals should use caution when prescribing Visicol or OsmoPrep for patients who may be at higher risk of kidney injury, such as:

- Patients over 55 years of age
- Patients who are dehydrated or who have kidney disease, acute colitis, or delayed bowel emptying
- Patients taking certain drugs that affect kidney function, such as diuretics, ACE inhibitors, angiotensin receptor blockers, and nonsteroidal anti-inflammatory drugs.\textsuperscript{16}

\textbf{Commercially available sodium phosphate products}

Sodium phosphate products can still be prescribed, but they are no longer available over the counter in the United States. Patients should be screened to make sure they can safely take these products, and the doses should not exceed the maximum recommended.

Currently, the only two sodium phosphate preparations available in the United States are in tablet form (Visicol and OsmoPrep). Oral sodium phosphate solution is no longer
The importance of patient education before bowel preparation cannot be overemphasized. The recommended dose is 20 tablets on the evening before the procedure and 12 tablets (OsmoPrep) to 20 tablets (Visicol) 3 to 5 hours before the procedure, given with clear liquids or ginger ale. Adverse effects are reduced with the tablet formulation; however, the large number of tablets required is the major drawback, reducing patient acceptability.

FIGURE 2 shows a simplified algorithm for selecting the optimal bowel preparation agent for an individual patient.

**OTHER BOWEL PREPARATION AGENTS AND ADJUNCTS**

**Magnesium citrate**

Like sodium phosphate, magnesium citrate is a hyperosmotic agent that promotes bowel cleansing by increasing intraluminal fluid volume. Since magnesium is eliminated solely by the kidney, it should be used with extreme caution in patients with renal insufficiency or renal failure.

Adding magnesium citrate as an adjunct to polyethylene glycol has been shown to reduce the amount of polyethylene glycol solution required (2 L) for the same result.\(^{17}\)

For patients who cannot tolerate polyethylene glycol, a reasonable alternative is magnesium citrate (1 bottle, around 300 mL) the evening before the procedure plus either bisacodyl tablets at the same time as the magnesium citrate or rectal pulsed irrigation immediately before the procedure.\(^{7}\)

Saline laxatives that include sodium picosulfate and magnesium citrate in combination are available primarily in the United Kingdom for bowel preparation for colonoscopy. Sodium picosulfate acts locally in the colon as a stimulant laxative and by increasing the force of laxatives, whereas magnesium citrate acts as an osmotic laxative by retaining fluids in the colon to clear the colon and rectum of fecal contents. The combination has been found to have similar efficacy and tolerability as sodium phosphate but is not currently available in the United States.\(^{26}\)
Enemas

Enemas are sufficient for flexible sigmoidoscopy, but when used alone they do not clean out the proximal colon enough for adequate visualization during colonoscopy. They are best used as adjuncts to other bowel preparation agents when patients present with poor distal colon preparation for colonoscopy.\(^7\) Enemas are also useful in washing out the distal segment of bowel in patients with a proximal stoma. The common types of enemas used are tap water, sodium biphosphate (Fleet), and mineral oil.

Tap water enemas distend the rectum and mimic the natural distention by the stool to allow the rectum to empty itself. Tap water (1 L) has fewer adverse effects than sodium biphosphate or mineral oil but is less effective.

Sodium biphosphate (Fleet) enemas draw fluid into the bowel by osmotic action, prompting contraction. One or two bottles are commonly used for bowel cleansing before sigmoidoscopy. However, as with oral sodium phosphate, sodium biphosphate enemas should be avoided in the elderly and in those with renal failure because of the risk of hyperphosphatemia and subsequent hypocalcemia.

In a head-to-head comparison,\(^28\) sodium biphosphate enema was found to provide significantly better bowel preparation than the sodium picosulfate-magnesium citrate combination (currently not available in the United States) for flexible sigmoidoscopy, being judged adequate or better in 93% of procedures as opposed to 74%.\(^28\)

Oil-based enemas such as cottonseed oil plus docusate (Colace) and diatrizoate sodium (Hypaque) are powerful lubricant laxatives that work by slowing the absorption of water from the bowel, so that the stool is softer. However, they have a number of adverse effects, such as severe allergic reactions (including angioedema and anaphylaxis), muscle cramps, and sporadic seepage that can soil the patient's undergarments for up to 24 hours. Also, their safety in children less than 2 years of age and in pregnant and breastfeeding mothers is not established.

Oil-based enemas are usually reserved for short-term use in refractory constipation, especially to soften feces that have become hardened within the rectum (as in fecal impaction).\(^27\)

Adjuncts

Diet. Dietary modifications alone, such as a clear liquid diet, are inadequate for colonoscopy, but they may be beneficial as adjuncts to other cleansing methods by decreasing the formation of solid residue. Clear liquids also help maintain adequate hydration during bowel preparation and are recommended with all bowel preparation regimens.

Hyperosmolar or stimulant laxatives. Bisacodyl (two to four tablets of 5 mg each), magnesium citrate (one bottle, about 300 mL), and low-dose senna (36 mg, about four 8.6-mg Sennakot tablets) have been used as adjuncts to low-volume polyethylene glycol solution, achieving results similar to those with full-volume polyethylene glycol. Depending on the type of study to be done, these agents are taken within 2 to 6 hours of starting the polyethylene glycol solution.

In contrast, the routine use of nonabsorbable carbohydrates such as mannitol and lactulose is not favored for bowel preparation, since the hydrogen gas produced by bacterial fermentation of the nonabsorbed carbohydrates increases the risk of explosion during electrosurgical procedures.\(^29\)

Antiemetic agents. Metoclopramide (5–10 mg), a dopamine antagonist gastroprokinetic that sensitizes tissues to the action of acetylcholine, is commonly used to prevent nausea or vomiting associated with bowel preparation agents.\(^7,30\)

Antifoaming agent. Simethicone (three tablets of 80 mg each, total dose 240 mg), an anti-flatulent, anti-gas agent, is prescribed by many gastroenterologists in an attempt to reduce bubbles during colonoscopy and improve visibility. It works by reducing the surface tension of air bubbles and causing small bubbles to coalesce into larger ones that pass more easily with belching or flatulence.

Nasogastric or orogastric tubes have been used to instill colonic preparations, especially for inpatients unable to drink polyethylene glycol solutions or for patients who are unresponsive or mechanically ventilated. This method can also be useful for rapid bowel cleansing (within 2 to 3 hours) for patients with lower gastrointestinal bleeding. However, routine use of a nasogastric tube solely for bowel preparation is

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A clear liquid diet may be beneficial as an adjunct to other cleansing methods

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**Instructions for patients:**
*Split-dose polyethylene glycol bowel preparation*

### Two weeks before colonoscopy
You must speak with your primary care physician or a specialist if you:
- Are taking blood thinners or antiplatelet agents such as warfarin (Coumadin), enoxaparin (Lovenox), fondaparinux (Arixtra), clopidogrel (Plavix), prasugrel (Effient), anagrelide (Agrylin), cilostazol (Pletal), pentoxyphilline (Trental), dipyridamole (Persantine), dipyridamole with aspirin (Aggrenox), or over-the-counter medications like aspirin or other anti-inflammatory drugs such as Motrin, Advil, or Aleve.
- Have diabetes and take insulin. You may need to have your insulin adjusted the day before and the day of the procedure; please bring your diabetes medication with you to take after the procedure, if needed.
- It is important to continue to take all other prescribed drugs.

### Five days before colonoscopy
- Do not take bulk-forming agents such as Metamucil or Citrucel.
- Do not take iron-containing preparations, such as a multivitamin with iron.
- Arrange for a driver to take you home after the procedure.
- Purchase your prescription 2 to 5 days before the procedure. Do not mix the solution until the day before the procedure.

### The day before colonoscopy
Instructions for preparing the solution are provided on the medication bottle. The solution should be mixed no sooner than 48 hours prior to its usage by adding tap water to the gallon level mark and then shaking or stirring the solution until it is well mixed. Do not add sugar or flavorings containing sugar to the solution. Refrigerating the solution, adding lemon juice or Crystal Light, and rapidly drinking 8-oz portions (instead of sipping) help make the solution more palatable.
- Do not eat solid foods for 24 hours before the colonoscopy appointment.
- Do not take red-colored drinks, Jell-O, or popsicles.
- It is essential to drink at least 8 oz of clear liquids (1 cup) every hour while awake to avoid dehydration. Clear liquids include apple or white grape juice, broth, coffee or tea (without milk or creamer), clear carbonated beverages such as ginger ale or lemon-lime soda, Gatorade or other sports drinks (not red), Kool-Aid or other flavored drinks (not red), plain Jell-O or other gelatins (not red), popsicles (not red), and water.
- At 6 PM the evening before the procedure, begin drinking 8 oz (240 mL, 1 cup) of the solution every 15 to 20 minutes until half of the solution is ingested. Continue drinking clear liquids until you go to bed.

### The day of colonoscopy
- If you have an afternoon appointment, begin drinking the remaining solution at 6 AM on the morning of the procedure, about 8 ounces every 10 minutes until finished, at approximately 8 AM. If your procedure is scheduled in the early morning, you will need to get up in the night to finish the second half of the solution at least 2 or 3 hours before the colonoscopy appointment or complete it all on the evening before the procedure.
- You should drink at least 8 oz of clear liquids every hour (no solids, alcohol, or red-colored drinks) until 2 hours before the colonoscopy appointment. You may take your morning medications.
- After the colonoscopy, you are encouraged to drink fluids to prevent dehydration. You can eat your usual diet and can resume most of your medications (unless instructed differently by your doctor) the same day.

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**TABLE 2**

**BOWEL PREPARATIONS FOR COLONOSCOPY**

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*Patients who have early-morning appointments or have to travel long distances for colonoscopy may decide to take the entire solution the night before, starting at 6 PM.*

*Patients scheduled for concomitant upper endoscopy or those with procedures requiring anesthesia may be told to complete the entire solution earlier than 2 hours before the procedure’s scheduled starting time.*
discouraged as it can lead to severe complications, such as aspiration and trauma during insertion.7

OTHER CONSIDERATIONS

Patient education

The importance of patient education for successful bowel preparation cannot be overemphasized. Patients need to be informed about why they need to undergo colonoscopy, the importance of bowel preparation, the side effects of agents used, and the exact preparation instructions. An interactive educational tutorial about colonoscopy for patients is available at Medline Plus at http://www.nlm.nih.gov/medlineplus/tutorials/colonoscopy/htm/index.htm.

In a prospective study, an education program reduced the rate of preparation failure from 26% to 5%.31 Many endoscopy centers provide education about colonoscopy and give patients clear, written instructions at the time an appointment for colonoscopy is made. TABLE 2 details bowel preparation instructions for split-dose polyethylene glycol regimens. Similar instructions for bowel preparation are also available online at http://clevelandclinic.org/bowelprep.

REFERENCES

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