Enemas: A "Purge" Atory
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Citation


Abstract

Enemas have been used, since time immemorial as a method of alleviating a variety of disorders as well as to administer fluids and drugs. Though mainly seen as a way to relieve constipation by the general population, its has application in the administration of analgesia and anesthesia in children, control of fever and seizures, pre-operative bowel preparation, post-operative analgesia, and the treatment of hepatic encephalopathy, acute pancreatitis and hyperkalemia. Contrast enemas play an integral role in both diagnosis and treatment of a wide variety of acute abdominal problems in children and adults. The past few decades has seen it used increasingly in treating inflammatory bowel diseases involving the colon, as well as radiation proctitis and solitary rectal ulcer. It has also been gaining acceptance as a safe and cost-effective method of hydrating terminally ill individuals.

However, administering enemas can result in complications both due to the mechanical trauma and by the fluid and electrolyte imbalances, induced in susceptible individuals. As they are largely self-administered with little oversight, physicians need to educate their patients of these potential drawbacks.

INTRODUCTION

Purgatory has traditionally been viewed as a place of torment, the purpose of which is to purify the individual. Eventually, the person will be cleansed and is eligible to enter paradise. The commonly administered enema and purgatory are both unpleasant but serve similar purposes, one cleansing the body and the other the soul. Though enemas have been regarded with some distaste both by the medical profession and by patients, they are freely available and are largely self-administered, with no or little oversight. In recent years the increasing popularity of disposable hypertonic phosphate enemas as a method of catharsis, has highlighted the problems created in some sections of patients, both through the trauma of introduction and the electrolyte and metabolic imbalances induced. Primary care physicians frequently prescribe and utilize enemas in diagnosing and treating disorders, and sometimes must deal with the consequences of their administration. By addressing the role of enemas in managing patient problems, we hope to provide physicians with a better understanding of their potential, limitations and complications, enabling them to exercise greater restraint and judgment, when considering their use.

The benefits of “colon therapy” were recorded as early as 1500 B.C., in an Egyptian medical document called the “Eber Papyrus” and were extolled by Hippocrates, Pare’ and Galen. The first enemas were administered in a river by using a hollow reed to induce water to flow into the rectum.\[1\]

“Basti” is described in the Ayurveda (science of longevity-600 B.C.), as a process used to clean the body of toxic materials left by disease and poor nutrition, and involves introducing medicinal substances such as medicated oils or other herbal decoctions in a liquid medium into the rectum. It is claimed to alleviate a variety of gastrointestinal disorders, arthritis, obesity, acne, hypertension, fevers, common cold, sexual disorders, kidney stones and angina.\[2\]

The rectum has also been recognized as an alternate pathway for the ingestion and administration of drugs, food and fluids.\[3\] Dioscorides, in the first century A.D. recommended giving “wine of mandragora,” per rectum to ease the pain of spear and lance wounds.\[4\] Rectal administration of opioids was practiced in the middle ages and rectal infusion of tobacco smoke or clysters of tobacco leaves and juice was employed in the resuscitation of drowning victims.\[5\] In the 19th century, Piragoff and others reported on the rapid absorption and utility of liquid ether and vapor given per rectum for surgical procedures.\[6\] Complications such as abdominal cramping and especially bloody diarrhea were
Enemas gained in popularity in the early 1900s when colon irrigation machines were introduced in hospitals and physician's offices. Colon irrigation, which continues to be used, takes about 45 minutes and involves the infusion of warm, filtered water that cleans out the entire colon. Water temperature and pressure are closely monitored and regulated during a series of fills and releases to aid peristaltic action. It is claimed to be effective in resolving headaches, backaches, fatigue, bad breath, body odor, irritability, confusion, skin and gastrointestinal problems.[6]

Post, Cunningham and Gwathney, in the early 1900s popularized the rectal administration of ether analgesia and anesthesia, modified the procedure and made it much safer.[4] Avertin introduced in 1929 produced a quiet, trouble-free, cooperative patient with few problems.

**ROLE IN ANESTHESIA**

A number of barbiturates (e.g., Amytal, Surital, sodium Pentothal and most recently methohexital) have been administered rectally to produce preoperative analgesia and hypnosis in children.[4] Conscious sedation by rectal administration of midazolam or midazolam plus ketamine is an effective alternative to general anesthesia for dental treatment of uncooperative children.[4] Addition of ketamine to midazolam increased amnesia and drowsiness significantly and this combination is more effective in relieving anxiety and pain. Children sedated with this combination were significantly less anxious when they arrived for a second session.

Rectal pre-medication with atropine and diazepam in children results in a smoother induction of anesthesia with ketamine. No adverse circulatory, respiratory or psychomimetic side effects are seen, and analgesia persists into the recovery period.[8]

Thiopental administered rectally before pediatric computed tomographic scans produces sedation of rapid onset and short duration, with no complications.[4] Methohexitone 1% administered rectally in a dose of 20 mg/kg to children results in adequate sedation within 15 minutes, with no significant cardiovascular or respiratory depression. Minor complications include fecal soiling and hiccough.[10]

**CONTROL OF SEIZURES AND FEVER**

Paraldehyde 0.2-0.3 ml/kg in a syringe mixed in 50% olive oil or injectable diazepam at 0.5 mg/kg (maximum 10 mg), undiluted or diluted with a 50% propylene glycol solution administered rectally produces peak levels in 10-20 minutes, controlling seizures in 80% of children.[11,12]

In febrile children, lowering core body temperature is most simply achieved by giving an antipyretic, such as acetaminophen (orally or rectally) or ibuprofen. Rectal acetaminophen is administered at 20 mg/kg every 4-6 hours (maximum 90 mg/kg or 4 G in 24 hours)[13]

**ENEMAS AND CHILDBIRTH**

Enemas were routinely administered to women admitted for hospital delivery in the early stages of labor on the assumption that they decreased the length of labor, kept the delivery field free of fecal matter, decreased the incidence of perineal infection and dehiscence and prevented neonatal postpartum infections.[14,15] Both mothers and midwives considered this to be aesthetically acceptable. Soap-sud enemas were also used to induce labor, in post-dates or if immediate delivery was otherwise considered desirable. Controlled trials using small-volume, disposable phosphate enemas, apart from reducing the incidence of soiling during labor, did not shorten labor, irrespective of parity.[16,17] There was no correlation between use of enemas and subsequent postpartum infections. A Cochrane review concluded that there is not enough evidence to recommend the use of routine enemas during the first stage of labor.[14]
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Figure 1

Table 1: Role of contrast enemas in treatment of abdominal problems

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium Sulfate</td>
<td>-Lower abdominal pain, weight loss, constipation, rectal bleed</td>
</tr>
<tr>
<td></td>
<td>-Suspected sigmoid volvulus, Hirschsprung’s disease</td>
</tr>
<tr>
<td></td>
<td>-Intussusception, Meconium ileus, Meconium Plug syndrome</td>
</tr>
<tr>
<td></td>
<td>-Management of pseudointussusception</td>
</tr>
<tr>
<td>Gastrografin</td>
<td>-Management of incomplete/complete large bowel obstruction</td>
</tr>
<tr>
<td></td>
<td>-Hematochezia</td>
</tr>
<tr>
<td></td>
<td>-Suspected acute diverticulitis</td>
</tr>
<tr>
<td></td>
<td>-Contrast medium of choice in CT scans of abdomen and pelvis</td>
</tr>
<tr>
<td></td>
<td>-Therapeutic in Volvulus, Intussusception, Meconium ileus, Meconium Plug syndrome</td>
</tr>
<tr>
<td>Tap water</td>
<td>Diagnostic and therapeutic in intussusception (Ultrasound-guided reduction of intussusception)</td>
</tr>
<tr>
<td>Tap water mixed with</td>
<td></td>
</tr>
<tr>
<td>Iodine contrast</td>
<td>Contrast for CT study (Better definition of mucosal abnormality)</td>
</tr>
</tbody>
</table>

Figure 2

In 1808, Sir Humphrey Davy discovered barium, a soft silvery metal that rapidly tarnishes in air and reacts with water. Its radio-opaque character established its utility in outlining the bowel; the low cost, safety, and accuracy in diagnosis, its value in management. In 1969, Noblett introduced Gastrografin, allowing non-operative management of many neonates with uncomplicated meconium ileus.[31] The contrast-giving substances in Gastrografin are salts of amidotrizoic acid in which the X-ray absorbing iodine is present in stable chemical bond.

Later, other agents including air, water, saline and Hartmann’s solution were also found to be of value in the management of abdominal emergencies.

Barium, water-soluble contrast media, water, electrolyte solutions, or air may be used with radiographic or ultrasound guidance to diagnose and reduce intussusception. Barium enema is the gold standard study in management, and rectal instillation of barium under fluoroscopy is a time-tested method.[32] Success rate with barium ranges from 55-90% and the risk of perforation is <1%.[33] Dehydration, small-bowel obstruction, and presence of symptoms and signs longer than 12 hours were significant predictors of unsuccessful reduction.[33] Air insufflation at a pressure of 125-150 mm. Hg (pneumoreduction) has the same success as barium with more perforations.[23,24] A measuring device capable of recording rapid intracolonic pressure changes, found that pressures remained low during hydrostatic barium enema reductions, but sharp pressure increases with rapid swings occurred with air insufflation, accounting for the increased perforation.[32] However, without the problems associated with barium (allergic reactions, barium impaction, extravasation causing chemical and bacterial peritonitis, scarring and granuloma formation)[33], the overall risk of complications is the same or less than that with barium.[33]

Water-soluble contrast agents (saline, Hartmann’s solution with iodine) under ultrasound are also highly successful in reducing intussusceptions (76-95.5%), with the ability to view all components of the intussusception and a low complication rate (<1% perforation).[33] Filling of the terminal ileum with contrast indicates successful reduction of intussusception. Ultrasound guided water enema at a pressure of 90-110 mm Hg has also been successfully used.[32] Potential advantages of using these fluids and ultrasound include rapid re-absorption, the absence of radiation, easier assessment of the reduction process, cost-effectiveness and simpler and safer management of any complications, such as perforation.[33]

Meconium ileus, associated with cystic fibrosis, comprises 20% of neonatal intestinal obstruction.[29] Approximately 15% of patients with cystic fibrosis present with meconium ileus.[34] Contrast enema is administered to those patients in whom clinical features and x-rays suggest distal small bowel obstruction. Barium is not ideal in meconium ileus with impacted meconium pellets.[35] An isosmolar, water-soluble contrast medium, such as iothalamate meglumine 30% at 1:1 dilution with water is preferable.[33] Gastrografin is also effective in uncomplicated meconium ileus; advantage is
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taken of its high osmotic pressure and the surrounding tissue
is forced to release considerable amounts of fluid, which
then flows into the gut dissolving the hardened meconium.[26]

Meconium plug syndrome, the mildest and most common
form of functional transient distal colonic obstruction in the
newborn of unclear etiology, is caused by inspissated,
immobile meconium and ranges in incidence from 1 in 500-
1000 neonates.[32,33] Barium enema shows a normal colon
caliber with an obstruction representing the meconium plug,
which may be mobilized during the enema, providing
immediate relief of the obstruction. This syndrome may also
be the presenting sign in Hirschprung disease, and has been
associated with prematurity and maternal treatment with
magnesium sulfate.[34,35]

Gastrografin is preferred in suspected partial or complete
stenosis, acute hemorrhage, megacolon and computerized
tomography of the abdomen.[36] In suspected high impaction
or volvulus, gastrografin enema may be diagnostic and
therapeutic because it stimulates emptying of stool. Unlike
barium, Gastrografin does not elicit an inflammatory
response, can be used without prejudice in suspected acute
diverticulitis, and is a cost-effective method of elucidating
the cause of left lower quadrant peritonitis.[37]

ROLE IN ABDOMINAL SURGERY

Although surgery has attained a high degree of technical
sophistication, time-honored methods of pre-operative
preparation still continue to be religiously observed, with
little attempts to test their value scientifically. Enemas have
traditionally been used as a mechanical bowel cleanser prior
to abdominal surgery. Proponents of this procedure
improperly assumed that it shortened the duration of ileus. A
randomized trial designed to assess effect of enemas on
return of peristalsis after non-colonic surgery found that
enemas delayed rather than improved the return of normal
peristalsis, calling its utility into question.[38] A more
scientific rationale for mechanical preparation of the large
bowel before colorectal surgery exists, as reducing the
microbial load of the luminal contents should help to
decrease post-operative wound infections.[39] A meta-
analysis of clinical trials, however, showed that bowel
cleansing before colorectal surgery increased both wound
infections and anastomotic leakage.[40]

A double blind randomized controlled trial showed that
rectal diclofenac 75 mg twice-daily reduced morphine
consumption, improved postoperative analgesia, and reduced
the incidence of adverse effects such as sedation and
nausea.[41] Rectal paracetamol at a dose of 40-60 mg/kg
followed by 14-20 mg/kg, also produced significant
postoperative pain relief.[42]

TREATMENT OF CONSTIPATION

Constipation is defined as a frequency of defecation of twice
weekly or less. Most individuals complain of excessive
straining or discomfort at defecation or the passage of hard
or pellet stools.

Enema preparations are readily available without
prescription for relief of constipation (Table 2). Patients not
responding to oral laxatives can self-administer tap water
enemas every 3 to 4 days. Small-volume prepackaged
sodium phosphate-biphosphate enema kits (Fleet's enema)
are inexpensive, safe, easy to administer, well tolerated, and
provide adequate emptying of the lower colon.[43] Hot water,
peroxide, household detergents, and strong hypertonic salt
solutions are irritants, and should not be used.

Figure 3

Table 2: Various agents used as enemas

<table>
<thead>
<tr>
<th>Agent</th>
<th>Time kg before bowel movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Phosphate (Fleet’s)</td>
<td>5-30 minutes</td>
</tr>
<tr>
<td>Bisacodyl (Dulcolax)</td>
<td>15-60 minutes</td>
</tr>
<tr>
<td>Docusate sodium</td>
<td>2-15 minutes</td>
</tr>
<tr>
<td>Glycerine</td>
<td>15-60 minutes</td>
</tr>
<tr>
<td>Mineral oil</td>
<td>15-20 minutes</td>
</tr>
<tr>
<td>Senna</td>
<td>5-30 minutes</td>
</tr>
<tr>
<td>Castille soap (Soap water)</td>
<td>Variable</td>
</tr>
<tr>
<td>Saline</td>
<td>Variable</td>
</tr>
<tr>
<td>Milk and Molasses</td>
<td>Variable</td>
</tr>
<tr>
<td>Tap water</td>
<td>Variable</td>
</tr>
<tr>
<td>Carnomol</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Fecal impaction is a severe form of constipation
characterized by the presence of large fecal masses in the
rectum. Contributing factors include opioid pain
medications, inactivity over long periods, mental illness, and
long-term use of laxatives. Impaction may complicate other
illnesses, especially those that lead to dehydration or
gastrointestinal dysfunction. Patients experience paradoxical explosive diarrhea, fecal incontinence, abdominal distention and pain. Impactions are usually treated by moistening and softening the stool with enemas or with mineral oil, which because of its emollient action is particularly effective. The pulsed irrigation enhanced evacuation is a new method of clearing fecal impactions using pulses of small amounts of warm water to rehydrate stool and improve peristalsis. A preliminary study on 28 adult patients found the procedure to be safe and effective.\cite{51} A similar study in children with fecal impaction demonstrated effective disimpaction in all with no complications.\cite{52}

Antegrade enemas through a cecostomy, initially successful in children with spina bifida, are a safe and satisfactory option for children and adults, who are neurologically intact with severe constipation and fecal incontinence/impaction, not responding to other measures.\cite{45,53} In the Malone antegrade continence enema (MACE) the cecostomy is intubated through the stump of the appendix by a catheter.\cite{46}

Physicians should be aware of possible injury from enemas administered in treating constipation. A high degree of suspicion by the attending physician ensures prompt diagnosis and early intervention. Although generally safe and well tolerated in adults, serious metabolic complications and fatalities have been described. Perforation of the rectum and sigmoid colon have been caused by cleansing enemas.\cite{58} Children, the elderly, and patients with megacolon, who are given large tap water enemas may develop water intoxication and dilutional hyponatremia, which presents as weakness, shock, convulsions, and coma. Metabolic derangements resulting from sodium phosphate enema overdose in infants and small children include hypernatremia, hypocalcemia, hyperphosphatemia, and metabolic acidosis.\cite{59} Elderly patients with known impaired renal function, patients with impaired bowel motility or bowel obstruction with potential for prolonged intraluminal retention, should not receive sodium phosphate-based enema preparations under most circumstances, because of its propensity to induce these metabolic derangements.\cite{60}

Camomile, known for its spasmylytic, antiphlogistic, and laxative benefits, became of interest with the increasing demand for medications from natural sources during recent years. Immediate-type hypersensitivity causing life-threatening anaphylactic reactions to camomile or other members of the Compositae have occurred.\cite{61,62}

### ACUTE HEPATIC ENCEPHALOPATHY
Lactulose has become the standard drug for treatment of acute hepatic encephalopathy and patients in coma or with small bowel ileus can receive lactulose enemas (300 ml of lactulose in 1 liter of water, repeated every 6-8 hours).\cite{63} Though only one placebo controlled trial has shown it to be effective, until more clinical trials confirm this, its safety profile and large clinical experience justifies its continued use. Lactitol or lactose have comparable efficacy and can be used as a substitute.\cite{64,65}

### ACUTE PANCREATITIS
The development of peri-pancreatic infection can trigger serious complications such as systemic sepsis, ARDS and multi-organ failure, increasing morbidity and mortality.\cite{66} Bacterial translocation from the gut has been accepted as the main source of pancreatic or peri-pancreatic infection. Sahin et al designed an animal model, inducing pancreatitis through biliopancreatic duct ligation, and studied the effect of enemas on resultant regional and distant infectious complications.\cite{67} Significant reductions in infections were noticed in the animals, who had received enemas. Another study on pancreatitis induced by intrabiliary injection of a trypsin/enterokinase mixture found that all severe pancreatic lesions were associated with bacterial infection in ascitic fluid and peripancreatic lymph nodes. In the study, enemas without or without antibiotics decreased endotoxin level and histological pancreatic damage, and improved survival.\cite{68} In conclusion, large bowel enema reduces the frequency of septic complications in acute pancreatitis by reducing bacterial translocation.

### TREATMENT OF HYPERKALEMIA
Hyperkalemia is treated by the rectal administration of the sodium-potassium ion-exchange resin sodium polystyrene sulfonate (SPS, Kayexalate 30-60 gm in 100 ml of 20% sorbitol). SPS was originally administered in a simple suspension exchanging potassium ions for hydrogen, which was then excreted in the stool. SPS, however, also binds intraluminal calcium, causing constipation and fecal impaction, which may result in bowel obstruction and perforation. Sorbitol solution is used to dissolve SPS, reducing these sequelae. Significant complications including colonic necrosis can still occur.\cite{69}

### INFLAMMATORY BOWEL DISEASE
Topical aminosalicylates, available in the form of mesalamine enemas or suppositories are the first line of
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treatment of ulcerative colitis, with few associated side effects. (Table 3) A recent meta-analysis reviewing 17 randomized, double-blind controlled trials concluded that topical mesalamine is useful for treatment and maintenance of remission in left-sided ulcerative colitis and proctitis.[61] Mesalamine enemas reach the splenic flexure in 92% of patients.[62] Approximately 80% of patients with left-sided colitis respond within 3 to 21 days,[63] and should be treated for 3 to 6 weeks. Of patients with distal colitis who are initially refractory to mesalamine, 50 to 75% respond after 4 to 6 months of additional treatment. There is, however, a high relapse rate once the drug is discontinued. The data are less compelling for management of active Crohn's disease with aminosalicylates, and those who benefit most have colonic involvement.

Figure 4
Table 3: Role of enemas in Colitis

Retention enemas and foam preparations of hydrocortisone and prednisolone were the first topical steroids used in treatment of active distal ulcerative colitis and proctitis. Though effective, systemic absorption induces many side effects.[64] Budesonide enemas in doses of 2g/100 ml, Tixocortol pivalate and Prednisolone metasulfobenzoate are no more effective as other steroids or mesalamine in active distal disease but an extensive first-pass hepatic metabolism diminishes systemic effects.[65,66] Cyclosporine A enema at a daily dose of 350 mg is not effective in refractory mild to moderately active left sided ulcerative colitis.[69]

RADIATION PROCTITIS

Acute and chronic injury to rectal and colonic mucosa is a sequel of abdominal and pelvic radiation.[70] The overall frequency following irradiation of the pelvic organs is about 5%. Radiation proctitis results from ischemia and fibrosis induced by radiation on blood vessels and connective tissue. Clinical manifestations include rectal bleeding, tenesmus and diarrhea. Enemas containing 5-ASA have been tried without much success.[71] Sucralfate retention enemas 2 grams administered every 12 hours are effective in most patients, resulting in both clinical and endoscopic response (94.1% and 70.5% respectively).[72] The cytoprotective effect of Sucralfate is considered responsible for this favorable effect. In contrast, oral sulfasalazine in combination with rectal steroids proves far inferior, with less than 50% response.[72]. Short chain fatty acid (SCFA) enemas 60 ml. twice daily for 4 weeks also reduces inflammatory changes and bleeding.[73] SCFA may be beneficial in radiation proctitis by providing additional energy source, improving regional blood flow, accelerating wound healing, or providing a general trophic effect.

SOLITARY RECTAL ULCER SYNDROME (SRUS)

SRUS is a disorder of rectal evacuation, associated with prolonged straining at stool, tenesmus, bleeding, deep-seated pelvicrectal ache, frequent desire to defecate and a sense of incomplete evacuation. Steroid retention enemas, sulfasalazine and local excision have not proved to be consistently effective.[74] Sucralfate retention enemas 2 grams twice a day for 6 weeks shows both clinical improvement by 2 weeks and endoscopic healing by 4-6 weeks of treatment.[75]

PROCTOCLYSIS

Proctoclysis refers to the rectal administration of fluids developed for patients who require parenteral hydration, but who are unable to receive it by another route, because of contraindications or lack of technical resources. Decreased oral intake is an consequence of cancer associated anorexia, lassitude, depression, gastrointestinal symptoms or mass effect of the tumor that precludes oral intake. Absorption of fluids has been noticed after enemas. It is a safe, effective and low-cost technique for the delivery of hydration in
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terminally ill cancer patients, who do not have tumor involvement of the colon.[5-8] It does not need any sterile device or manipulation and can be delivered by family members or other non-professionals, with minimal training and oversight. Potential applications may lie in rural areas or developing countries with minimal access to health care professionals.

A #22 French nasogastric catheter is inserted approximately 40 cm into the rectum and normal saline or tap water is infused at a rate of 250 cc/hr. Hydration is well maintained at minimal cost and discomfort. In patients with severely restricted oral intake or dehydration, the decision to administer fluids should be individualized and made on the basis of a careful assessment that considers problems related to dehydration, potential risks and benefits of fluid replacement, and patients' and families' wishes.[7-9]

CONCLUSION

It is indeed astonishing that intubating an easily accessible orifice has such protean clinical value. Though most commonly used to relieve constipation, rectal administration of a variety of medications (steroids, analgesic and anesthetic agents, IV fluids) has eased the delivery of effective therapy in many illnesses. The role of contrast enemas in assessment and treatment of much abdominal pathology in both adults and children needs to be emphasized. Awareness of the potential risks of enemas needs to be increased, as enemas are used freely, with little medical supervision. The utility in preoperative bowel preparation continues to remain in question. In spite of the antipathy it creates in some patients, enemas should continue to find increasing acceptance and greater application in clinical situations.

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References

17. Drayton, S., Rees, C. "They know what they are doing." Nursing Mirror, 1984; 159: 4-8 (Abstract).
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44. Puet TA, Pfen L, Hurst DL. Pulsed irrigation enhanced evacuation:
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