

## Gastroenteric tube feeding: Techniques, problems and solutions

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### Abstract

Gastroenteric tube feeding plays a major role in the management of patients with poor voluntary intake, chronic neurological or mechanical dysphagia or gut dysfunction, and patients who are critically ill. However, despite the benefits and widespread use of enteral tube feeding, some patients experience complications. This review aims to discuss and compare current knowledge regarding the clinical application of enteral tube feeding, together with associated complications and special aspects. We conducted an extensive literature search on PubMed, Embase and Medline using index terms relating to enteral access, enteral feeding/nutrition, tube feeding, percutaneous endoscopic gastrostomy/jejunostomy, endoscopic nasoenteric tube, nasogastric tube, and refeeding syndrome. The literature showed common routes of enteral access to include nasoenteral tube, gastrostomy and jejunostomy, while complications fall into four major categories: mechanical, *e.g.*, tube blockage or removal; gastrointesti-

nal, *e.g.*, diarrhea; infectious *e.g.*, aspiration pneumonia, tube site infection; and metabolic, *e.g.*, refeeding syndrome, hyperglycemia. Although the type and frequency of complications arising from tube feeding vary considerably according to the chosen access route, gastrointestinal complications are without doubt the most common. Complications associated with enteral tube feeding can be reduced by careful observance of guidelines, including those related to food composition, administration rate, portion size, food temperature and patient supervision.

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**Key words:** Enteral tube feeding; Percutaneous endoscopic gastrostomy; Refeeding syndrome; Enteral nutrition; Buried bumper syndrome; Nasoenteral tubes; Colocutaneous fistulae

**Core tip:** Keeping up with new developments in the fast-moving field of enteral nutrition is a challenge for any gastroenterologist. While enteral tube feeding plays a major role in the care of critically ill patients and those with poor voluntary intake, chronic neurological or mechanical dysphagia or gut dysfunction, mechanical, gastrointestinal, infectious and metabolic complications can lead to serious conditions or death. We have undertaken a comprehensive review of current literature assessing the safety and effectiveness of various endoscopic, sonographic, radiologic, electromagnetic and fluoroscopic application techniques. In addition, we address prophylactic measures to prevent complications, problem solutions and special aspects.

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## INTRODUCTION

Enteral nutritional support plays a very significant part in the management of patients with poor voluntary oral intake<sup>[1,2]</sup>, chronic neurological or mechanical dysphagia<sup>[3-5]</sup>, or intestinal failure<sup>[6,7]</sup>, and in the critically ill<sup>[8,9]</sup>. Enteral feeding is not only more physiological than parenteral nutrition (PN), but has also been shown to improve patient outcomes, decrease costs<sup>[10]</sup> and reduce septic complications<sup>[11,12]</sup> in comparison to PN. In a meta-analysis of 82 randomized controlled trials (RCTs), PN was associated with a significantly increased risk of infectious complications, especially in patients receiving therapy for malignancy<sup>[13]</sup>. In patients who cannot be fed using routine bedside methods, endoscopically or radiologically-aided methods must be employed to achieve enteral access. Complicated access situations require the additional expertise of a gastroenterologist, who is an integral part of the nutrition support team<sup>[14]</sup>. While the range and ease of enteral access procedures has been greatly enhanced in recent years by the introduction of new techniques and improved equipment and accessories, many studies have nonetheless demonstrated a high prevalence of tube- and/or feeding-related complications in patients receiving long-term enteral nutrition<sup>[15-19]</sup>.

The purpose of this review is to provide an overview of current knowledge and practice in the rapidly changing and developing field of endoscopic enteral tube feeding (ETF), covering routes of access as well as problems associated with enteral feeding and their solutions.

In principle, tube systems for gastric or jejunal nutrition can be placed by nasal insertion (nasogastric tubes; NETs), guided percutaneous application, or surgical techniques. Nasal tubes are mainly used for short-term enteral feeding (4-6 wk) and in situations where other methods of enteral feeding are contraindicated. In the long term, however, NETs are often poorly tolerated by the conscious patient, since they not only elicit a foreign body sensation in the pharynx, but may also cause reflux esophagitis and pressure ulcers, and have a tendency to dislocate. NETs can also be a source of psychological stress to the patient, the presence of the tube being a visible sign of his/her illness. Enteral feeding *via* transnasal tubes is often poorly tolerated by geriatric patients with an acute confusional state, and the need for repeated insertion of tubes following voluntary removal by the patient is demanding and time-consuming for nursing staff. Nasal tubes are not suitable for patients who are to undergo orofacial therapy for potentially reversible dysphagia (in most cases due to cerebrovascular accident). Furthermore, the presence of a nasal tube significantly interferes with swallowing training<sup>[20]</sup>.

Techniques for achieving NET placement include unguided bedside insertion or placement under fluoroscopic, endoscopic, electromagnetic or direct surgical guidance. Depending on experience, the success rate of endoscopic transnasal and transoral NET feeding tube placement has been described to range from 86% to 97%<sup>[21]</sup>.

Blind insertion, the most common technique for nasogastric intubation, results in malposition in 0.5%-16% of cases, with tracheal, pulmonary, or pleural malposition in 0.3%-15%. This may result in pulmonary or pleural formula infusion, pneumothorax or pulmonary abscess<sup>[22]</sup>. A study by de Aguilar-Nascimento and Kudsk<sup>[23]</sup> demonstrated that of 932 blind postpyloric tube placement attempts, 433 (46%) failed and 20 (1.6%) were airway misplacements. Air instillation and auscultation are inaccurate methods for validating the position, and misplacement is often not suspected unless a radiograph is obtained<sup>[24,25]</sup>.

After gastric positioning, spontaneous or prokinetically-assisted transpyloric tube migration occurs only in 5%-15% of patients, compared to 14%-60% using guided assistance. Duodenal intubation can successfully be achieved in 70%-93% of patients using right lateral positioning, gastric insufflation, tube tip angulation, and clockwise rotation during insertion. However, such tube placements require experience and an average of 28-40 min to perform<sup>[26]</sup>. In a recent study of 616 patients in an intensive care unit (ICU), Rivera *et al.*<sup>[27]</sup> demonstrated that the use of an electromagnetic tube placement device (ETPD) to monitor tip position of the feeding tube resulted in no adverse events, reduced costs, and earlier initiation of EN.

Failure of bedside NET placement is an indication for the use of fluoroscopy or endoscopy. Enteral intubation under fluoroscopic guidance is successful in 90% of cases, achieving jejunal positioning in 53%, but requires on average 22 min of fluoroscopy room time<sup>[28]</sup>. While endoscopically-guided (ENET) nasogastric access techniques have been in use since 1984<sup>[29]</sup>, ENET placement can be very tedious and unrewarding for the endoscopist when compared to other procedures such as polypectomies, PEG or endoscopic retrograde cholangiopancreatography (ERCP). Most endoscopy training programs do not adequately teach techniques for ENET placement. However, a lack of perseverance on the part of the endoscopist may result in unnecessary administration of total parenteral nutrition (TPN) in patients who are in fact suited for enteral feeding. The positioning of feeding tubes distal of the ligament of Treitz may cause some uncertainty even amongst experienced endoscopists<sup>[30]</sup>. A new, recently-described nasoendoscopic placement method shows promise as a more successful technique for tube placement beyond the duodenal flexure<sup>[31-33]</sup>.

One in ten patients experiences procedure-related complications following NET<sup>[34]</sup>, either at the time of insertion or subsequently. Reported complications of nasal tube feeding include nasopharyngeal lesions, sinusitis, aspiration, diarrhea, intestinal ischemia and metabolic derangements. Aspiration is reported in up to 89% of patients, with no clear advantage of nasogastric over gastroenteric feeding. Distal duodenal or jejunal feeding may prevent regurgitation of feeding formula<sup>[24]</sup>. About 2%-5% of patients may present with epistaxis following ENET placement<sup>[35,36]</sup>, a complication shown to be equally common in patients undergoing transnasal *vs*

**Table 1 Tube-related complications of enteral tube feeding<sup>[203]</sup>**

Mechanical complications	Tube obstruction
	Primary malposition
	Perforation of the intestinal tract
	Secondary displacement of the feeding tube
	Knottting of the tube
	Accidental tube removal
	Breakage and leakage of the tube and bleeding from insertion site
	Erosion, ulceration and necrosis of skin and mucosa
	Intestinal obstruction (ileus)
	Hemorrhage
Infectious complications	Inadvertent IV infusion of enteral diet
	Infection at the tube insertion site
	Aspiration pneumonia
	Nasopharyngeal and ear infections
Metabolic complications	Peritonitis
	Infective diarrhea
	Electrolyte disturbances
	Hyper- and hypoglycemia
	Vitamin and trace element deficiency
Tube feeding syndrome ("Refeeding syndrome")	

transoral endoscopy for ENET placement<sup>[37]</sup>. Tube-related complications (Table 1) depend not only on the route of enteral access, but also on the material and diameter of the feeding tube.

A critical review of pulmonary complications associated with the blind placement of narrow-bore nasogastric tubes (NETs) was recently performed by Sparks and colleagues<sup>[38]</sup>. Of the 9931 NET placements reviewed, a total of 187 were improper tube placements in the tracheobronchial tree, translating to a 1.9% mean overall malposition rate. These 187 misplacements included 35 (18.7%) reported pneumothoraces, at least 5 of which resulted in patient death. NET malpositioning was reported in 13%-32% of subsequent repositioning attempts<sup>[38]</sup>.

Occlusion of the NET is an underestimated and underreported complication of ETF. It has been reported to occur in 9%-35% of patients<sup>[36,39,40]</sup>, but actual incidence is much higher. The most important underlying cause is ignorance of tube feeding care among nursing staff. The following technical factors predispose to tube occlusion: inadequate irrigation with water, especially after feed or medicine administration; instillation of medications, particularly crushed tablets; narrow lumen; long tubes (for further details, see occlusion of the PEG tube, below).

## TECHNICAL ASPECTS OF PERCUTANEOUS FEEDING TUBE PLACEMENT

### *Percutaneous endoscopic gastrostomy*

Percutaneous endoscopic gastrostomy (PEG) is indicated for patients requiring long-term nutritional support (> 30 d) who have a functional gastrointestinal

(GI) tract but insufficient oral intake of nutrients. The most common indications include inadequate swallowing as a result of a neurological event, oropharyngeal or esophageal cancer, and severe facial trauma<sup>[41,42]</sup>. Based on data from 1327 patients, Kurien *et al*<sup>[43]</sup> demonstrated in a recently-published trial that patients who underwent gastrostomy had significantly lower mortality compared to those who deferred the procedure.

### *PEG techniques*

In principle, there are three techniques for PEG tube placement; the peroral pull technique, the peroral push technique and the direct percutaneous procedure. The most widely-used technique for PEG placement is the "pull" method introduced by Gauderer *et al*<sup>[44]</sup> in 1980, which has replaced surgical gastrostomy as the medium- and long-term solution to enteral nutrition delivery<sup>[45]</sup>, being safer and more cost-effective, with lower procedure-related mortality (0.5%-2%) and lower complication rates<sup>[46-48]</sup>. Furthermore, tube displacement occurs less frequently than with nasogastric tubes (NGT). The Sack-Vine "push" variant (placing a catheter over a Seldinger wire) yields comparable results<sup>[49]</sup>.

Alternative procedures such as sonographically-controlled PEG are not yet sufficiently technically developed to be adopted on a wide scale<sup>[50]</sup>. The introducer PEG, using a balloon catheter placed transabdominally into the stomach, was described by Russell *et al*<sup>[51]</sup>. The main problem initially associated with this technique was deflection of the stomach wall due to the puncture, combined with the risk of catheter misplacement. However, its safety has since been improved by the use of an intragastrically-positioned T-fastener under fluoroscopic or endoscopic control to fix the stomach to the abdominal wall<sup>[52,53]</sup>. A new, safe introducer method (Freka Pexact<sup>®</sup>) has recently become available for patients in whom the standard "pull" PEG cannot be used or would involve an increased risk during passage of the internal bumper. Its main advantage is the combination of a double gastropexy with a peel-away sheath introducer to effect secure fixation of the stomach wall, analogous to surgical gastropexy<sup>[54,55]</sup>.

The success rate of PEG tube placement is as high as 99.5% (range 76%-100%). Reasons for failure include inadequate transillumination, complete oropharyngeal or esophageal obstruction, and gastric resections<sup>[21]</sup>. The average life span of PEG tubes has been described to be one to two years, with tube degradation being the most common reason for tube replacement<sup>[21]</sup>.

### *Jejunal tubes through the PEG and direct percutaneous endoscopic jejunostomy*

Long-term jejunal feeding can be achieved endoscopically with jejunal tubes through the PEG (JET-PEG) and direct percutaneous endoscopic jejunostomy (DPEJ). Jejunal feeding is appropriate in patients with recurrent vomiting and/or tube feeding-related aspiration, severe gastroesophageal reflux, gastroparesis, gastric outlet ob-

struction, or total or partial gastrectomy<sup>[56]</sup>. Though not definitively proven to reduce tube feeding-related aspiration (see below), the combination of gastric decompression *via* PEG and simultaneous jejunal nutrition shows clinical benefit in many patients.

JET-PEG placement can be carried out by pushing a jejunal feeding tube through the previously-placed PEG using a “beneath the scope” (BTS) or “over the wire” tube technique. Initial positioning of the tube beyond the ligament of Treitz is essential to reduce the retrograde migration rate. Although feeding tube placement beyond the ligament of Treitz may be considered a technical success, its functional success is largely disappointing because of frequent retrograde tube migration into the stomach and tube dysfunction caused by kinking or obstruction (as the diameter of the jejunal tube is restricted to 12 F). Furthermore, JET-PEG has not been demonstrated to effectively decrease enterorespiratory aspiration compared with PEG tube feeding alone<sup>[57,58]</sup>. In combined gastric decompression/feeding jejunostomy tubes, the small diameter of the tube often provides inadequate gastric venting and may cause jejunal lumen clogging.

JET-PEG tubes have a high success rate of up to 93%. The mean functional duration of the tubes was found to be 55 d in adults and 39 d in children<sup>[21]</sup>. Retrograde dislodgment of the jejunal extension tube, tube obstruction and mechanical failure have been described as the most common device-related complications<sup>[21]</sup>. Endoscopically-placed clips may secure the tube and prevent retrograde migration<sup>[59]</sup>, but this does not overcome the problem of occlusion common to small-caliber tubes.

DPEJ, a modification of the pull PEG technique, appears to be the ideal procedure for long-term jejunal feeding<sup>[60]</sup>. A colonoscope or an enteroscope is introduced orally into the small bowel, and transillumination is observed on the anterior abdominal wall as an indicator of the scope’s position in the jejunum. A trocar is passed through the anterior abdominal wall directly into the jejunum. As a sounding device for needle puncture, a 21-gauge 1.5 inch needle used for infiltration of local anesthetic may be used. The puncture should be performed with a purposeful, swift stabbing motion of the wrist. Grasping the tip of the sounding needle with a forceps helps to stabilize the jejunal segment and allows proper orientation for insertion of the larger trocar/needle assembly alongside the indwelling sounding needle. A 120-inch insertion wire is advanced through the cannula and grasped by the awaiting forceps or snare, and the procedure is completed as described for a pull-type PEG placement. Though similar to PEG placement, DPEJ is a considerably more difficult technique<sup>[60,61]</sup>. There are three retrospective studies on DPEJ outcome involving a total of 230 patients from a cancer center, a surgical unit, and a gastroenterological referral center. Successful placement was achieved in 72%-88%<sup>[62]</sup>.

### **Skin-level gastrostomy**

Skin-level gastrostomy was introduced to reduce skin irritation, minimize granulation tissue and improve the patients’ quality of life. It provides easy and convenient access for enteral nutrition and is well established in pediatric patients<sup>[63]</sup>.

The most popular system is the button skin-level nonrefluxing device, first described by Foutch *et al*<sup>[64]</sup>. Currently, three button types with two different retaining elements (retention dome and balloon type) are available<sup>[65]</sup>.

Indications for this device are usually peristomal problems and/or the patient’s wish to be independent from the PEG tube. Contraindications are active peristomal infection, a stoma existing less than four weeks after primary PEG insertion, a fistulous stoma channel, and a stomal tract longer than 4.5 cm. Initial application of the button should be carried out under endoscopic control or under fluoroscopic guidance *via* a guide wire to prevent misplacement and to allow removal of the previously-placed gastrostomy catheter<sup>[56]</sup>. Despite the potential advantages of a skin-level device, the largest prospective multicenter evaluation of a single-step button (86 patients) reported serious placement problems and a high complication rate<sup>[66]</sup>.

### **Initiation of feeding**

There are various techniques for administering feeds in ETF patients, the most common of which are summarized below (Table 2). The recommendation to delay feeding initiation until 12-24 h after PEG or transabdominal gastrostomy placement was based on a presumption that the GI system would return to normal function during this period of time, allowing a better seal of the enteral opening<sup>[46,67]</sup>. More recently, however, several prospective randomized studies have clearly demonstrated that, at least in the case of PEG placement, much earlier initiation of feeding after as little as 1-3 h is equally safe<sup>[68-71]</sup>. This was confirmed in a meta-analysis by Bechtold *et al*<sup>[72]</sup>.

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## **COMPLICATIONS ASSOCIATED WITH PEG PLACEMENT: INCIDENCE AND MANAGEMENT**

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About 13%-40% of patients with PEG placement experience minor complications such as maceration due to leakage of gastric contents around the tube, and peristomal pain<sup>[46,47,73,74]</sup>. Serious complications requiring further intervention have been reported in 0.4%-4.4% of procedures and include peristomal leakage with peritonitis, necrotizing fasciitis of the anterior abdominal wall, gastric bleeding, injury to internal organs, tumor seeding at the PEG site, and death. The 30-d incidence of mortality after PEG has been reported to be in the range of 6.7%-26%<sup>[46,47,73]</sup>. This high value is due rather to the underlying comorbid factors of these patients than to the

**Table 2** Techniques for delivery of feeds in enteral tube feeding

Method of feeding	Indication	Comments
Bolus intermittent (by syringe or bulb)	Ambulatory patients	100-400 mL over 5-10 min multiple times, high risk of aspiration and diarrhea, cheap and convenient for NGT
Cyclic intermittent (by gravity or pump)	Partially recumbent	Higher infusion rate for a shorter period (8-16 h); while changing from tube feeds to oral
Intermittent drip (by gravity or pump)	Home enteral feeding	1.5-2 L over 8-12 h overnight, no daytime feeds
Constant infusion (by gravity or pump)	Bedridden patients ICU patients	Initiate with 20-50 mL/h, altered periodically depending on gastric residual volume, increased chances of aspiration and metabolic abnormalities; incline head end of bed to 45° to reduce aspiration and regurgitation

NGT: Nasogastric tube; ICU: Intensive care unit.

procedure itself<sup>[21,75,76]</sup>.

### Peristomal wound infections

**Incidence and causes:** Peristomal wound infections are the most common complication associated with the PEG procedure, with an incidence ranging from 4%-30%<sup>[77]</sup>. About three quarters of these are minor and resolve when treated with antibiotics. While regular skin and stoma care are crucial for the prevention of local infection, bandaging techniques also play an important role: In a comparative study, Chung *et al.*<sup>[78]</sup> showed that excessive traction on the gastrostomy tube significantly increases the rate of local infection. Factors predisposing to infection can be (1) technique-related, such as a narrow incision or lack of antibiotic prophylaxis; (2) host factors, *e.g.*, malnutrition, obesity, diabetes, malignancy, drug therapy (immunosuppressive medication, chronic corticosteroid therapy); and (3) nursing care-related, such as improper wound dressing or excessive traction between the internal bumper and the stomach wall.

**Prevention and treatment:** Two recently-published meta-analyses involving 1100 patients from 10 randomized controlled trials assessing the efficacy of antibiotic prophylaxis in PEG insertion have demonstrated antibiotic prophylaxis to effect a relative risk reduction of 64% and an absolute risk reduction of 15%. Either a first-generation cephalosporin or a penicillin-based prophylaxis should be selected<sup>[79,80]</sup>.

During the last decade, methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as an important cause of PEG-related wound infection. Horiuchi *et al.*<sup>[81]</sup> suggested that, in addition to standard prophylactic antibiotics, MRSA decolonization using oral and nasally-delivered preparations might reduce the risk of MRSA-related peristomal infections in these patients. A recently-published randomized controlled study demonstrated that the use of glycerin hydrogel (GHG) dressings significantly decreases the number of peristomal infections, and that the frequency of dressing changes can be safely extended to 7 d during the first week, making it a less labor-intensive and more cost-effective option for post-PEG wound management.

In the case of transabdominal gastrostomy, where

direct transabdominal access of the gastrostomy tube avoids its exposure to oropharyngeal flora, another recent randomized controlled trial demonstrated no statistically significant difference in the rate of peristomal infection with or without preprocedural administration of antibiotics<sup>[55]</sup>.

### Clogged feeding tubes

**Incidence and causes:** The incidence of clogged feeding tubes in PEG is reported to be as high as 23%-35%. Clogging is especially common when thick enteral feeds, bulking agents and medications are delivered through relatively small PEG tubes (*i.e.*, 9 F). Tube occlusion is classified as either obstruction of the internal lumen or mechanical tube failure<sup>[39,82]</sup>.

**Prevention and treatment:** Since pH values below 4 have been described to promote protein coagulation, repeated gastric residual aspiration should be avoided or minimized<sup>[83]</sup>. Tubes should also be flushed with 40-50 mL water before and after delivering medications or bulking agents (*i.e.*, psyllium, resins). If possible, all medications should be completely dissolved in water prior to flushing or applied as liquid formulations<sup>[84]</sup>. Saline should be avoided, since it can crystallize within the tube and promote gradual clogging<sup>[85]</sup>. Pancreatic enzymes mixed with bicarbonate have been reported to prevent tube clogging effectively<sup>[39,82]</sup>. Furthermore, they were found superior to carbonated beverages in dissolving clogs<sup>[86]</sup>. In a recent systematic review, water flushes have been shown to be the most effective method of preventing enteral feeding tube clogging<sup>[87]</sup>. Finally, clogged tubes can be cleared mechanically using various endoscopic catheters, braided quid wires, or special "de-clogging" plastic brush devices<sup>[25,88]</sup>.

### Peristomal leakage

**Incidence and causes:** Although its reported incidence appears low (1%-2%), peristomal leakage is in fact a much more common complication<sup>[85,88,89]</sup>. Several factors contributing to the risk of peristomal leakage have been identified, including excessive cleansing with hydrogen peroxide, infections, gastric hypersecretion and excessive side torsion along the PEG tube, as well as patient-

specific factors that inhibit wound healing (malnutrition, immunodeficiency, diabetes). Furthermore, the risk of peristomal leakage is increased if the tube is not stabilized by means of an external bolster<sup>[25,85]</sup>.

**Prevention and treatment:** Prevention of peristomal leakage must focus on the reduction of risk factors (*e.g.*, antisecretory therapy with PPIs), while barrier creams containing zinc and skin protectants are also recommended<sup>[85]</sup>. If these fail, the PEG tube can be removed. After waiting 4–6 d to allow the tract to partially close, a new PEG can then be placed through the same tract<sup>[85,90]</sup>. However, this procedure should only be attempted if sufficient time has passed to ensure scarring of the stomach to the abdominal wall<sup>[85,90]</sup>. If this is not the case, the PEG tube must be removed and a new PEG tube placed at a different site. On no account should the original PEG tube be replaced by a larger diameter tube, as this may cause enlargement of the tract, resulting in exacerbation of the leakage<sup>[85,90]</sup>. Conversion of the PEG to a PEG/double-lumen system has been reported to be a successful alternative<sup>[25,88]</sup>, while conversion to a gastrojejunal (GJ) tube can also be considered for feeding distal to the stomach.

### Bleeding

**Incidence and causes:** Acute bleeding is not uncommon after PEG tube placement, with a reported incidence of up to 2.5%<sup>[46,91,92]</sup>. The most common causes of acute bleeding immediately following PEG tube placement are local vessel injury at skin level, and mucosal tear in the upper GI tract. Risk factors include previous anatomic alteration, anticoagulation, and antiplatelet therapy<sup>[41]</sup>. In a recent single-center study of 990 patients, Richter *et al.*<sup>[93]</sup> recently demonstrated the use of serotonin reuptake inhibitors (SRIs) during the 24 h before PEG placement to be a risk factor for increased bleeding. In this cohort, however, no association with aspirin or clopidogrel intake (at any dose) either before or after the procedure was found. The influence of SRI intake on bleeding risk is of particular significance in geriatric patients, since these drugs are administered to a large proportion of this patient population.

Delayed bleeding can be caused by esophagitis, gastritis, gastric erosion, gastric or duodenal ulceration, and the buried bumper syndrome<sup>[94]</sup>. One study has demonstrated that esophagitis was the cause of delayed GI bleeding in 39% of PEG patients undergoing endoscopy<sup>[95]</sup>.

**Prevention and treatment:** Current American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommend the continuation of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), especially in high-risk patients, and the discontinuation of Clopidogrel therapy in low-risk patients, and where appropriate also in individuals with a higher risk of bleeding<sup>[92]</sup>. Discontinuation of warfarin therapy should also be considered, with the application of unfractionated heparin as bridging thera-

py<sup>[92]</sup>. Furthermore, in the light of their aforementioned study, Richter *et al.*<sup>[93]</sup> recommend the interruption of SRI intake 24 h before the procedure.

### Colonic fistulae

**Incidence, types and causes:** Colonic misplacement of the PEG tube may lead to serious complications, in particular the development of gastrocolic, colocutaneous or gastrocolocutaneous fistulae<sup>[96,97]</sup>. While these fistulae are rare and cited mostly only as isolated case-reports, Friedmann *et al.*<sup>[97]</sup> describe 28 cases of colocutaneous fistula resulting from colonic malpositioning of PEG, including 12 cases of gastrocolocutaneous fistula and one of jejunocolocutaneous fistula. In contrast to the gastrocolic fistula, a fistulous passage connecting the stomach with the colon, the gastrocolocutaneous fistula is defined as an epithelial connection between the mucosa of the stomach, the colon, and the skin. Its probable etiology is the penetration of a bowel loop (mostly transverse colon) interposed between the stomach and the abdominal wall, either by inadvertent puncture during tube placement or, more commonly, due to gradual erosion of the tube into the adjacent bowel<sup>[98]</sup>. Factors predisposing to its occurrence in acute settings are insufficient gastric insufflation, past history of laparotomy causing adhesions and consecutive trapping of bowel loops, and improper transillumination. Up to 45% of colocutaneous fistulae are seen in patients with prior abdominal surgery<sup>[99]</sup>. These patients should undergo contrast study to rule out an overlap of stomach and colon.

**Prevention and treatment:** To prevent colonic misplacement, the transillumination of the gastroscope through the abdominal wall, and the endoscopically visible imprint of a finger (or needle) on the skin is still a “*conditio sine qua non*” before introduction of the needle into the stomach<sup>[100]</sup>. In the absence of appropriate transillumination, the use of ultrasound and/or computed tomography is recommended to exclude abnormal abdominal anatomy<sup>[101]</sup>, with slow advancement of a small-gauge anesthetic needle (*e.g.*, the needle used to infiltrate local anesthetic into the PEG site) through the abdominal wall into the stomach, aspirating on the attached syringe. A “safe tract” is established by endoscopic visualization of the needle in the gastric lumen and simultaneous return of air into the syringe. Return of fluid or gas into the syringe before the needle is endoscopically visualized within the gastric lumen suggests entry into bowel interposed between the abdominal wall and the stomach<sup>[85,97,102]</sup>.

The most common clinical symptoms associated with fistulae are watery diarrhea containing feed, or the presence of stool around the PEG tube. Rarely, fistulae present acutely with peritonitis, infection, fasciitis, or failure of the formula infusion<sup>[97]</sup>.

Fistulae are diagnosed using contrast agent given *via* the PEG tube. Several approaches have been suggested for fistula management, ranging from conservative re-

removal of the PEG tubes without laparotomy, hereby allowing the fistula tract to close spontaneously within a few days, to invasive exploration of the colon. Colonic clipping has been reported by Kim *et al.*<sup>[103]</sup>. While challenging the necessity for such a sophisticated endoscopic intervention in this case (after only 10 d of conservative treatment), Gyökeres *et al.*<sup>[104]</sup> suggest that the method may be considered an option for the closure of persistent gastrocolic fistulae associated with PEG placement.

### **Buried bumper syndrome**

**Incidence and causes:** Buried bumper syndrome (BBS) is a rare, mainly long-term complication of PEG, in which the internal bolster migrates from the gastric lumen and lodges in the gastric wall (incomplete BBS) or anywhere along the GI tract outside the gastric lumen (complete BBS)<sup>[105-107]</sup>. It has a reported prevalence of 1.5%-8.8%<sup>[74,88,108-111]</sup>. Though normally a late complication (usually presenting not until at least four months post-PEG), BBS has also been reported to occur as early as 21 d after PEG placement<sup>[89,94,112]</sup>. Common symptoms include immobilization of the PEG tube, feeding difficulties or the need for more pressure when giving feeds, peritubular leakage, complete occlusion of the tube, and the occurrence of abdominal pain.

The main causative factor of BBS is excessive traction between internal and external bumper. Other possible contributing factors include malnutrition, poor wound healing, weight gain due to PEG feeding, and a stiff internal bumper (polyurethane). Diagnosis is mainly clinical but requires endoscopy for confirmation, and may reveal anything from simple ulceration and mucosal overgrowth around the internal bumper to complete outward erosion of the tube with non-visualization of the internal bumper.

**Prevention and treatment:** To prevent BBS, it is advisable to allow an additional 1.5 cm of space between the external bumper of the PEG tube and the skin in order to minimize the risk of pressure-induced necrosis. Mucosal overgrowth of the inner bumper can be prevented by mobilizing and loosening the PEG from the outside at least every other day. The incidence of BBS is lower in patients with PEG tubes made from Foleys urinary catheter-type silicone tube and in patients with balloon-assisted PEG-introducer devices than in routine PEG patients and those with balloon-tipped replacement tubes (probably because fluid inside the balloon can regulate the pressure more effectively<sup>[113]</sup>).

Even if it is asymptomatic, buried bumper must be removed once diagnosed, as continued bumper migration may lead to bleeding, perforation, peritonitis and death. Various techniques can be employed to remove the buried device and either reaccess the luminal tract with a new tube or secure an entirely new access site: The “needle-knife” technique can be used in cases of partial or superficial burial<sup>[110,114]</sup>. Alternatively, the buried tube can be pulled out and simultaneously replaced

with a new pull-type feeding tube following insertion of a guide wire through the old tube<sup>[109]</sup>. Müller-Gerbes *et al.*<sup>[115]</sup> describe a minimally-invasive technique (push method) where the inner bumper is cut by means of a papillotome brought into the stomach from the outside through the shortened PEG while under constant endoscopic control. Last but not least, it has been reported that the buried tube may be safely removed simply by external traction<sup>[111,113,116]</sup>. In cases of deep impaction or migration into the abdominal wall, surgical intervention in the form of laparotomy or a laparoscopic approach is required<sup>[111,117]</sup>.

### **Pneumoperitoneum**

Pneumoperitoneum (PNP) following PEG or JET-PEG placement is a known finding occurring after 8%-18%<sup>[118-122]</sup> of procedures. PNP usually has a benign and self-resolving course which does not warrant any further intervention. However, the recent reported higher incidence of complications requiring intervention in ICU patients with post-PEG PNP suggests the need for more intensive investigation of patients with this finding<sup>[119]</sup>.

### **Liver injury**

Hepatic injury during PEG placement (*e.g.*, transhepatic PEG placement) occurs infrequently, but is a potentially life-threatening and probably underdiagnosed complication<sup>[123-125]</sup>. Unexplained pain after PEG placement in the absence of wound infection should always raise the suspicion of liver injury. If hepatomegaly is suspected or improper transillumination is present at the puncture site, transabdominal ultrasound must be performed. In addition, the tube insertion site should generally be chosen left of the upper abdominal midline and combined with the “safe tract” technique (see above).

### **Abdominal wall metastasis at the PEG site**

Abdominal wall metastasis as a late complication at the PEG site has been reported with an incidence of < 1%<sup>[126,127]</sup>. Although it is a rare complication, the malignant seeding of tumor cells is associated with an extremely poor prognosis<sup>[126]</sup>. Risk factors for abdominal wall metastasis include primary pharyngoesophageal cancer, squamous cell histology, less differentiated and large-sized cancers, and an advanced cancer stage<sup>[128]</sup>. Since direct mechanical tumor implantation is the most likely mechanism, the pull-string or direct-introducer technique for PEG placement is preferable<sup>[55]</sup>. If these techniques are not available, an overtube should be used<sup>[129]</sup> or the PEG placement should be performed after surgical removal of the primary cancer<sup>[126-128]</sup>.

## **GASTROINTESTINAL COMPLICATIONS**

The most common complications observed with ETF involve GI function<sup>[51,130-132]</sup>. These complications and their possible causes and solutions are listed in Table 3.

**Table 3** Gastrointestinal complications of enteral nutrition; causes, prevention and treatment

Complication	Cause	Prevention/treatment
Diarrhea	Too rapid increase in amount of feed per day	Observe adaptation phase
	Too rapid infusion rate	Reduce/control infusion rate
	Feed temperature too cold	Increase to room temperature
	Hyperosmolar feedings (> 300 mOsm)	Use isotonic feeding solution, initially dilute hyperosmolar feeding solutions
	Lactose intolerance	Use low-lactose or lactose-free diet
	Fat malabsorption	Use low-fat or MCT-containing diet
Nausea/vomiting	Hypoalbuminemia	Use chemically defined diet and/or feed
	Antibiotic therapy or medications	Review medications
	Chemotherapy/radiotherapy	Prescribe anti-diarrheal medications
Cramps/bloating	Too rapid infusion rate	Reduce/control infusion rate
	Bacterial contamination of formula feed/delivery equipment contamination	Handle administration systems hygienically, change delivery equipment every 24 h, keep opened bottles of formula no more than 24 h in refrigerator
Regurgitation/aspiration	Lactose intolerance	Use low-lactose or lactose-free diet
	Fat malabsorption	Use low-fat or MCT-containing diet
Constipation	Gastric retention	Reduce/control infusion rate, use duodenal tubes, incline patient during food administration
	Inadequate fluid intake	Increase fluid intake, check fluid balance
	Fiber intake too low	Use fiber-containing formulas
	Fecal impaction	Enemas
	Electrolyte and hormonal derangement	Osmotic laxatives (lactulose 15-60 mL), peristaltic agents (e.g., prochlorperazine 0.25-0.5 mg <i>iv</i> )

MCT: Medium-chain triglyceride.

Nausea occurs in 10%-20% of patients, while abdominal bloating and cramps from delayed gastric emptying are also common. Additional complications include aspiration and nonocclusive bowel necrosis, which are associated with high mortality<sup>[130,133]</sup>. In a multicenter observational study of 400 patients, Montejo *et al.*<sup>[130]</sup> found that 251 patients (63%) experienced one or more GI complications during their feeding course. In a subsequent study, the same group evaluated the incidence of GI complications in gastric- and jejunally-fed patients, and found it to be 57% and 24%, respectively<sup>[130,134]</sup>.

### Diarrhea

**Incidence and causes:** Diarrhea is the most commonly reported GI side effect in patients receiving ETF. Depending on definition<sup>[135]</sup>, diarrhea occurs in up to 30% of patients in medical and surgical wards and more than 80% of patients in the intensive care unit (ICU)<sup>[136-139]</sup>.

The pathogenesis of diarrhea in enterally-fed patients is multi-factorial. Of those factors unrelated to the enteral formula or administration method, the use of antibiotics and/or specific medications is the most common reason for the development of diarrhea<sup>[136,139,140]</sup>. Diarrhea may be caused either by the medication itself (e.g., oral magnesium or phosphate supplements, antacids, prokinetic agents), or by the formulation in which it is delivered. Medications containing sorbitol can cause diarrhea due to osmotic effects, while antibiotics alter the intestinal flora, favoring the growth of *Clostridium difficile* (*C. difficile*), *E. coli* and *Klebsiellae*. Thus, courses of antibiotic treatment should be kept as short as possible and the use of prophylactic antibiotics limited. Pseudomembranous colitis is a complication observed with increas-

ing frequency, especially during antibiotic exposure (for reviews see<sup>[136,141]</sup>). Patients receiving ETF are nine times more likely to develop *C. difficile*-associated diarrhea than matched non tube-fed patients<sup>[142]</sup>. Antibiotics can also reduce colonic bacterial production of short chain fatty acids from insoluble carbohydrates and fiber<sup>[143]</sup>.

Hypoalbuminemia (serum albumin level < 2.5 g/dL) has long been implicated as a cause of diarrhea as a result of intestinal edema. However, studies aiming to confirm this have yielded conflicting results<sup>[144]</sup>.

**Prevention and treatment:** The early identification of diarrhea risk factors and the development of a diarrhea risk management algorithm are recommended. Over the last two decades, several RCTs investigating the use of fibers in the treatment and prevention of ETF-associated diarrhea have been carried out<sup>[136]</sup>. Results from a meta-analysis suggest fiber to be highly effective in reducing the incidence of diarrhea in patients at increased risk (e.g., postsurgical, critically ill patients)<sup>[145]</sup>. However, mixed results have been reported regarding the use of different types of fiber (insoluble or soluble) to prevent ETF-induced diarrhea. Schultz *et al.*<sup>[146]</sup> demonstrated the relative effectiveness of pectin combined with an insoluble fiber formula compared to an insoluble fiber formula alone. The usefulness of soluble fibers for the treatment of diarrhea during enteral nutrition has been demonstrated only in two small studies<sup>[147,148]</sup>. Partially hydrolyzed guar gum (PHGG) has been shown to reduce the incidence of ETF-induced diarrhea compared with standard, fiber-free formula in both general ward and ICU settings<sup>[147,149]</sup>. In contrast, supplementation with inulins or fructooligosaccharide (FOS) has been shown to increase



**Table 4** Randomized controlled trials measuring the impact of probiotics on enteral nutrition-related diarrhea

Ref.	Study population	Treatment groups	Sample size (placebo)	Daily dose	Outcome	
					Probiotics	Controls
Heimburger <i>et al</i> <sup>[204]</sup>	Adults starting EN	<i>Lactobacillus acidophilus</i> and <i>L. bulgaricus</i>	41 (23)	3000 CFU/d	31% developed diarrhea	11% developed diarrhea
Alberda <i>et al</i> <sup>[205]</sup>	Adults starting EN on ICU	VSL#3 - live cells	10/9 (9)	$9 \times 10^{11}$ mg/d	14%/12% <sup>1</sup> of days with diarrhea	23% of days with diarrhea
Frohman <i>et al</i> <sup>[206]</sup>	Adults starting EN on ICU	VSL#3	45 (25)	$9 \times 10^{11}$ mg/d	0.5 liquid stools/d	1.1 liquid stools/d
Ferrie <i>et al</i> <sup>[207]</sup>	Adults with diarrhea during EN on ICU	<i>L. rhamnosus</i> GG	36 (18)	( $2 \times 10^{10}$ cells/d) and inulin (560 mg/d)	3.8 d duration of diarrhea	2.6 d duration of diarrhea
Barraud <i>et al</i> <sup>[208]</sup>	Adults starting EN on ICU	<i>Ergyphilus</i>	167 (80)	( $2 \times 10^{10}$ CFU/d)	55% developed diarrhea	53% developed diarrhea
Bleichner <i>et al</i> <sup>[209]</sup>	Adults starting EN on ICU	<i>Saccharomyces boulardii</i>	128 (64)	$4 \times 10^{10}$ CFU/d	7.7% of days with diarrhea	9.1% of days with diarrhea
Schlotterer <i>et al</i> <sup>[210]</sup>	Burnt adults	<i>Saccharomyces boulardii</i>	18 (9)	$4 \times 10^{10}$ CFU/d	1.5% of days with diarrhea	14% of days with diarrhea
Tempe <i>et al</i> <sup>[211]</sup>	Adults in ICU	<i>Saccharomyces boulardii</i>	40 (20)	$1 \times 10^{10}$ CFU/d	8.7% of days with diarrhea	16.9% of days with diarrhea

<sup>1</sup>Viable probiotics/probiotic sonicates. VSL#3 consists of *Lactobacillus casei*, *Lactobacillus plantarum*, *Lactobacillus acidophilus*, *Lactobacillus delbrueckii*, *Bifidobacterium longum*, *Bifidobacterium breve*, *Bifidobacterium infantis*, and *Streptococcus salivarius*. Ergyphilus consists of mainly *Lactobacillus rhamnosus* GG, *Lactobacillus casei*, *Lactobacillus acidophilus*, and *Bifidobacterium bifidum*.

flatulence and bowel movement frequency in enterally fed patients<sup>[150,151]</sup>.

The fiber consensus panel of the European Society for Parenteral and Enteral Nutrition (ESPEN) recommends supplementing ETF with PHGG to prevent EN-induced diarrhea in both ICU and postsurgical patients (grade A recommendation)<sup>[152]</sup>. Guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN) recommend the use of PHGG in ICU patients (grade D recommendation). However, insoluble fibers should be avoided in all ICU patients (grade C recommendation), as their use may increase the risk of bowel obstruction in the critically ill<sup>[9]</sup>. A recent systematic review suggests that the use of different fiber mixtures may be the most promising strategy for the prevention of ETF-induced diarrhea<sup>[145]</sup>.

Despite the potential for manipulation of the intestinal microflora in ETF, few studies have investigated the effects of prebiotics or fermentable carbohydrates on the incidence of ETF-associated diarrhea<sup>[136,153,154]</sup>. To date, eight RCTs have assessed the impact of probiotics in the prevention of ETF-associated diarrhea (Table 4). Of these, five were shown to be beneficial (for review, see<sup>[136,155]</sup>). The safety of probiotics in critically ill and/or immunocompromised patients has, however, been called into question following an RCT which reported increased mortality in a group of patients with severe acute pancreatitis who took probiotics<sup>[156]</sup>. Whelan and Myers performed a systematic review focused on adverse events related to probiotics in patients receiving enteral nutrition<sup>[157]</sup>. Only 3 of 53 trials showed increased complications, which were largely non-infectious in nature and occurred in specific patient groups (*e.g.*, transplant and pancreatitis). The total of 50 trials (> 4000 patients) showed either no effect or a positive effect on outcomes

related to safety (*e.g.*, mortality and infections). Thus, in spite of contrasting evidence, it may be concluded that the use of probiotics in enteral formula is a useful tool in preventing ETF-associated diarrhea, but should not be used in transplant patients or the critically ill. A systematic approach to the management of diarrhea in ETF patients is depicted in Figure 1.

### Constipation

Constipation is less common than diarrhea during ETF, and more prevalent in patients requiring long-term ETF. The primary goal of constipation management in these patients is prevention. Despite the theoretical rationale for fiber supplementation of enteral formulae, there are still no convincing data demonstrating the benefits of fiber supplementation in terms of improved bowel function or prevention of constipation. A meta-analysis from seven RCTs in the acute setting (two ICUs, three surgical and two medical wards) showed that fiber supplementation effected at least a downwards trend in the percentage of patients reporting constipation. Furthermore, a significant reduction in laxative use in patients receiving fiber formula was observed in four studies<sup>[145]</sup>. In spite of the lack of sufficient data, fiber formulae should therefore be used at least in patients requiring long-term ETF.

## PULMONARY COMPLICATIONS

Pneumonia is a potentially life-threatening complication which is usually a consequence of pulmonary aspiration of oral secretions or, less commonly, of gastric and small-bowel contents. It may occur with no obvious evidence of vomiting. Pulmonary aspiration is more common when patients are fed with NGT in a supine

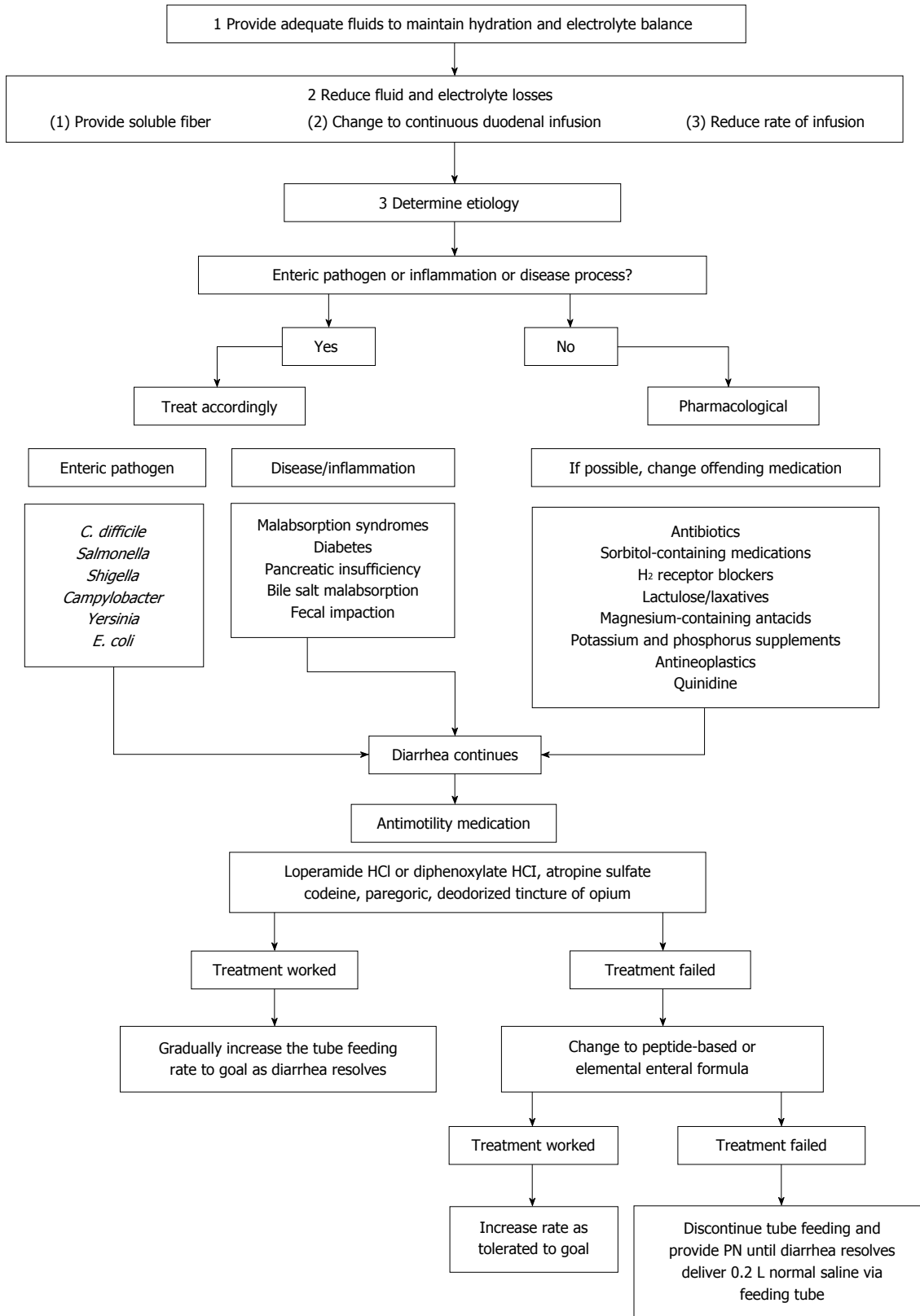


Figure 1 Management of diarrhea in enteral tube-fed patients. Adapted from reference<sup>[212]</sup>.

position<sup>[25,158-160]</sup> and is caused by a combination of gravitational back-flow, impairment of the lower esophageal sphincter (LES), lack of swallow-induced LES relaxation, infrequent esophageal body contractions, and the

presence of the tube across the gastric cardia<sup>[161]</sup>. It is very common in patients with impaired consciousness or poor gag reflexes, occurring in up to 30% of those with tracheotomies<sup>[162]</sup> and 12.5% of neurology patients<sup>[163]</sup>.

**Table 5 Patients at high risk of refeeding syndrome**

Patients with anorexia
Patients with chronic alcoholism
Oncology patients
Postoperative patients
Elderly patients (comorbidities, decreased physiological reserves)
Patients with uncontrolled diabetes mellitus (electrolyte depletion, diuresis)
Patients with chronic malnutrition:
Marasmus
Prolonged fasting or low energy diet
Morbid obesity with profound weight loss
High stress unfed for > 7 d
Malabsorptive syndromes (inflammatory bowel disease, cystic fibrosis, short bowel syndrome)

Adapted from reference<sup>[188]</sup>.

However, while feeding *via* PEG may reduce the risk of aspiration, it will not eliminate it altogether<sup>[164]</sup>, especially in patients in whom GI motility disturbances inhibit this route of feeding<sup>[158,165]</sup>.

Since the incidence of reflux depends on the position of the tip of the feeding tube (6% with the tube tip in the duodenum, 4% near the ligament of Treitz, and 0.4% distal to the ligament of Treitz), several published guidelines favor small bowel over gastric feeding in patients who are at risk for aspiration. This applies in particular to critically ill patients, in whom gastroduodenal atony, caused by increased intracranial pressure, hyperglycemia and stress, can lead to delayed or impaired gastric emptying and decreased transpyloric transport of nutrients (for extended review see Waseem *et al.*<sup>[161,166]</sup>). However, the results of more than 10 controlled clinical trials<sup>[134,167-175]</sup> are contrary and inconclusive, particularly with regard to nasoenteral tube feeding<sup>[164,168]</sup>. Meta-analyses of these studies have also presented conflicting views<sup>[164,176,177]</sup>.

Since it has been shown that even in patients with normal intestinal motility both naso- and gastrojejunal tubes, once correctly positioned, will be moved in a proximal direction by the phase II migrating motor complex, placement of enteral nutrition tubes  $\geq 40$  cm distal to the ligament of Treitz is considered the optimal method<sup>[165,168]</sup>.

## METABOLIC COMPLICATIONS

Artificial feeding may cause a variety of metabolic problems including deficiency or excess of fluids, electrolytes, vitamins and trace elements. Overhydration occurs frequently, particularly when ETF patients are also receiving supplementary intravenous nutrition or fluids. Furthermore, underlying metabolic diseases including diabetes mellitus and renal or hepatic insufficiency must be taken into account while administering ETF.

### Refeeding syndrome

Refeeding syndrome (RFS) was first described in malnourished Far East prisoners of war after the Second World War who developed cardiac and neurological

symptoms soon after starting eating<sup>[178,179]</sup>, and remains an often forgotten condition. RFS is characterized by electrolyte depletion, fluid shifts and glucose derangements that occur upon oral, enteral or parenteral reinstitution of nutrition in malnourished patients<sup>[180]</sup>.

**Incidence:** The true incidence of RFS is still not known. The majority of reported cases are prospective and retrospective cohort studies or case series. Patients with anorexia represent the prototypical population of RFS<sup>[181]</sup>, and a recently-published multicenter study from France reported an incidence of 10% in these patients<sup>[182]</sup>. Other common conditions associated with RFS include hyperemesis, alcoholism, cancer, and malabsorptive syndromes such as short bowel syndrome, inflammatory bowel disease, cystic fibrosis, and various forms of bariatric surgery<sup>[181]</sup>.

**Pathophysiology:** The pathophysiology of RFS remains poorly understood. It occurs because the body adapts to undernutrition by down-regulating membrane pumping in order to conserve energy. This, in turn, causes leakage of intracellular potassium, magnesium, calcium and phosphate, with subsequent whole-body depletion. Simultaneously, sodium and water also leak into the cells.

Sudden refeeding reverses these processes and, along with insulin, drives electrolytes into the cells, potentially leading to a precipitous fall in circulating levels of the aforementioned electrolytes. This may be accompanied by an acute increase in circulating and extracellular fluid (exogenous administration or endogenous movement of sodium and water out of the cells). To further aggravate the situation, undernourished kidneys have a limited capability to handle salt and water load.

Specific micronutrient deficiencies can compound these problems. Hypophosphatemia is the hallmark of RFS, and is responsible for significant morbidity and even mortality<sup>[180]</sup>. It can manifest as clinical features of RFS, *e.g.*, rhabdomyolysis, leukocyte dysfunction, respiratory failure, cardiac failure, hypotension, arrhythmia, seizure, coma and sudden death<sup>[183]</sup>.

In adult patients, refeeding hypophosphatemia is more common in enteral than parenteral feeding. This may be due to the incretin effect from absorption of glucose<sup>[184]</sup>. Cardiac arrest has been reported as a complication of RFS in patients presenting with less than 70% of prior body weight. Prolonged starvation results in a reduction of total cardiac volume, end diastolic volume, and left ventricular mass. During RFS, ventricular volume returns to normal while left ventricular mass remains reduced, leading to fluid retention and congestive cardiac failure. In addition, hypophosphatemia may lead to decreased sarcomere contractility and cause myocardial damage<sup>[185,186]</sup>.

**Prevention and treatment:** Awareness of RFS and identification of patients at risk are the first steps in pre-

**Table 6** Therapy and prevention of refeeding syndrome

Careful evaluation of cardiovascular system, check for any electrolyte abnormalities before initiating refeeding  
 In severe cases, an initial starting volume of 50%-75% of daily requirements should be used

< 7 yr old: 80-100 kcal/kg *bw*/d  
 7-10 yr: 75 kcal/kg *bw*/d  
 11-14 yr: 60 kcal/kg *bw*/d  
 15-18 yr: 50 kcal/kg *bw*/d  
 > 18 yr: 25 kcal/kg *bw*/d (or an average 1000 kcal/d initially)

If the initial food challenge is tolerated, caloric intake may be increased over the next 3-5 d. Each requirement should be tailored to the individual's needs, and the above values may need to be adjusted by as much as 30%. Frequent administration of small feeds is recommended. Feeds should provide a minimum of 1 kcal/mL to minimize volume overload

**Protein**  
 Initial regimen for malnourished patients: 0.8-1.0 g/kg *bw*/d  
 The feed should be rich in essential amino acids, and should gradually be increased, as an intake of 1.2-1.5 g/kg *bw*/d is needed for anabolism to occur

**Vitamins/trace elements**  
 Thiamine, folic acid, riboflavin, ascorbic acid and pyridoxine should be supplemented, as well as the fat-soluble vitamins A, D, E, and K  
 300 mg thiamine should be given *IV* at least 30 min. before refeeding is initiated, and should be continued with 100 mg *iv* for at least 7 d. Later on, oral thiamine can be supplemented as 100 mg tablets  
 Iron should be supplemented *iv* according to the Ganzoni formula {iron deficit (mg) = *bw* (kg) × [(target Hb - actual Hb (g/L)) × 2.4 + depot iron (500 mg)]

**Minerals**  
 Sodium should be restricted (about 1 mmol/kg *bw*/ or 1.5 g/d), but liberal amounts of phosphorus, potassium and magnesium should be given to patients with normal renal function  
 Magnesium (normal range: 0.8-1.6 mmol/L)  
 Mild to moderate hypomagnesemia (0.5-0.7 mmol/L)  
 →Initially 0.5 mmol/kg *bw*/d over 24 h *iv*, then 0.25 mmol/kg *bw*/d for 5 d *iv*  
 Maintenance requirement  
 →0.2 mmol/kg *bw* per day *iv* or 0.4 mmol/kg *bw* per day orally  
 Phosphate (normal range: 0.85-1.40 mmol/L)  
 Mild hypophosphatemia (0.6-0.85 mmol/L)  
 →0.3-0.6 mmol/kg *bw* per day orally  
 Moderate hypophosphatemia (0.3-0.6 mmol)  
 →0.3-0.6 mmol/kg *bw* per day orally  
 Severe hypophosphatemia (< 0.3 mmol/L)  
*iv* supplementation with either potassium phosphate or sodium phosphate (*e.g.*, 0.8 mmol/kg *bw* monobasic potassium phosphate in half-normal saline by continuous infusion over 8-12 h)  
 Plasma phosphate, calcium, magnesium and potassium should be monitored, and the infusion should be stopped once plasma phosphate concentration exceeds 0.30 mmol/L

Adapted from references<sup>[185,191]</sup>.

venting refeeding problems<sup>[187]</sup>. Any patient with no or negligible food intake for more than five days is at risk of developing refeeding problems. High-risk patients include the chronically undernourished and those who have diminished physiological reserves and/or are critically ill<sup>[188]</sup>. Table 5 summarizes criteria from the National Institute for Health and Clinical Excellence (NICE) for the identification of patients at high risk of RFS. Recommendations for therapy and prevention are shown in Table 6.

Despite the lack of high level (level A/B) recommendations, overall consensus favors the gradual introduction and advancement of feeding over several days while closely monitoring electrolytes and - to a lesser extent - vitamins and trace elements. Serum phosphate, magnesium, calcium, potassium, urea, and creatinine concentrations should be measured before feeding and repeated daily during the first week after feeding is started.

Caloric intake should generally start with approximately 1000 kcal or 10-15 kcal/kg (25%-50% of estimated requirements) daily, particularly during the first week of refeeding, and be increased by approximately 20%

daily until the determined goal is reached. The average weekly weight gain, particularly in extremely undernourished patients (*e.g.*, anorexia nervosa) should not exceed 0.5 kg/wk<sup>[189,190]</sup>. If hypophosphatemia occurs (< 0.50 mmol/L), it should be corrected with 50 mmol intravenous phosphate over 24 h<sup>[185,186,191,192]</sup>.

In the case of mild to moderate hypomagnesemia (0.5-0.7 mmol/L), 1 g magnesium should be given every 6 h intravenously. Should severe, clinically symptomatic hypomagnesemia occur, 8-12 g magnesium must be given daily in divided doses and serum magnesium monitored every 8-12 h<sup>[181,193]</sup>.

Few data are available regarding optimal vitamin and trace element supplementation. Some authors recommend 300 mg of thiamine (parenteral or enteral) before starting refeeding and 100 mg daily thereafter. In the presence of Wernicke's encephalopathy, even higher doses of thiamine (500-750 mg) may be warranted<sup>[193]</sup>.

In order to avoid fluid overload, fluid repletion should be carefully controlled. Some authors have recommended initial fluid and sodium restriction to prevent congestive heart failure<sup>[189]</sup>.

## ROLE OF NUTRITION SUPPORT TEAMS

Although still limited in number, studies of team *vs* non-team enteral management provide clear evidence for the positive effects of an organized multidisciplinary approach using protocols and recommendations based on published guidelines<sup>[194]</sup>. A study in a community hospital showed that management of ETF patients by a nutrition support team (NST) was associated with reductions in mortality rate, length of hospital stay and readmission rate<sup>[195]</sup>. In a prospective study comparing team *vs* non-team management of ETF patients at a Veterans Administration Medical Center, Powers and colleagues demonstrated that the former reduced complications and improved patients' nutrition status<sup>[196]</sup>. This finding was confirmed at a university teaching hospital<sup>[197]</sup>. In addition, cost-utility analyses of patients receiving ETF either as hospitalized patients or as outpatients have demonstrated a significant lowering of healthcare costs through the reduction of metabolic and mechanical complications<sup>[198-201]</sup>.

### Organization and tasks of nutrition support teams

A well-organized NST should include a physician, a nurse, a nutritionist and a pharmacist<sup>[202]</sup>. The goal of the NST is to provide high quality nutritional care. This is accomplished through (1) identification of patients who are at risk nutritionally; (2) performance of a comprehensive nutritional assessment to serve as a guide to nutritional therapy; and (3) provision of safe and effective nutritional support. To accomplish these goals, the NST should offer services including inpatient consultations, quality assurance protocols, research programs, home nutrition services, and last but not least, staff educational programs. Proper training of staff on the correct use of nutritional support is crucial, especially with regard to the reduction of complications.

## CONCLUSION

Endoscopic methods in particular have facilitated a variety of enteral feeding access options. These should be tried in all patients who are unable to ingest adequate amounts of food but have adequate absorptive capacity of the intestine. Well-trained endoscopists who are extremely proficient in these techniques are indispensable for the successful provision of hospital nutrition support and care. Optimal techniques for tube placement, together with the prompt recognition and immediate management of complications, can significantly reduce overall morbidity and mortality due to ETF-associated complications. To further promote positive patient outcomes and reduce the incidence of complications, ETF should always be managed by multidisciplinary nutrition support teams.

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