Proceedings of the Nutrition Society (2004), **63**, 105–113 DOI:10.1079/PNS2003317

Enteral feeding: the effect on faecal output, the faecal microflora and SCFA concentrations

Kevin Whelan[1]*, Patricia A. Judd[2], Victor R. Preedy[1] and Moira A. Taylor[3]
[1]*Department of Nutrition and Dietetics, King's College London, London SE1 9NN, UK*
[2]*Lancashire Postgraduate School of Medicine and Health, University of Central Lancashire, Preston PR1 2HE, UK*
[3]*School of Biomedical Sciences, University of Nottingham, Nottingham NG7 2UH, UK*

Enteral tube feeding is common in both the hospital and community environment; however, patients can suffer alterations in faecal output that can have serious clinical sequelae. Problems associated with accurate characterisation of faecal output and definition of diarrhoea impede the comparison of research studies and prevent standardised assessment of therapeutic interventions in clinical practice. The colonic microflora may protect the patient against diarrhoea by preventing enteropathogenic infection and by producing SCFA that stimulate colonic water absorption. However, studies in healthy volunteers suggest that the composition of the enteral formula may have a negative impact on the microflora and SCFA concentrations. The addition of fructo-oligosaccharides to the enteral formula may partially prevent negative alterations to the microflora, although conclusive data from studies in patients are not yet available. Modification of the microflora with probiotics and prebiotics may hold potential in prophylaxis against diarrhoea during enteral tube feeding.

Enteral nutrition: Microflora: Short-chain fatty acids: Diarrhoea: Fibre: Prebiotics

Enteral tube feeding

Enteral tube feeding (ETF) is a common method of nutritional support for patients who are unable to achieve their nutritional requirements through oral diet alone. Approximately 5% of the patients on general wards (Bowling, 1995), 46% of the patients on the intensive therapy unit (ITU; Hill *et al*. 1995) and ≤25 000 patients in the community (Elia, 2003) receive ETF at any one time.

Despite the wide use of ETF, alterations in faecal output occur and diarrhoea is a common complication with a variety of negative clinical sequelae. Diarrhoea in patients on the ITU results in a reduction in the efficacy of ETF, patients receive less enteral formula, ETF may be stopped or the patient transferred to parenteral nutrition, and patients have an increased length of stay on the ITU (Montejo, 1999). The increased risk of faecal incontinence associated with diarrhoea (Bliss *et al*. 2000) is not only distressing for the patient and carer, but also increases the risk of infection of surgical or pressure wounds. Fluid and electrolyte abnormalities are common and the prescription of anti-diarrhoeal medication may be required (Bowling, 1995). These factors are likely to cause further distress to the patient and result in greater financial cost to the healthcare provider (Dobb, 1986). The aim of the present review is to discuss the validity and reliability of characterising faecal output and diarrhoea during ETF, the role of the colonic microflora and SCFA in its pathogenesis and the effect of the composition of the enteral formula on these characteristics.

Reporting diarrhoea during enteral tube feeding

The reported incidence of diarrhoea in patients receiving ETF ranges from 2% (Cataldi-Betcher *et al*. 1983) to 95% (DeMeo *et al*. 1998). This wide range of reported incidences is due to two main factors. First, since the pathogenesis of diarrhoea includes a number of clinical variables, the reported incidence is greatly influenced by the disease state of the patient population under investigation. For example, for patients receiving ETF those on the ITU are at greater risk of diarrhoea than those not on the ITU (Pesola *et al*. 1989). Second, there is no

Abbreviations: ETF, enteral tube feeding; FOS, fructo-oligosaccharides; ITU, intensive therapy unit.
***Corresponding author:** Mr Kevin Whelan, fax +44 20 7848 4185, email kevin.whelan@kcl.ac.uk

standard definition of diarrhoea in patients receiving ETF. Thirty-three different definitions appear in the literature, with some studies using more than one definition (Lebak *et al.* 2003). Diarrhoea is usually defined using descriptors of faecal frequency, faecal consistency, faecal quantity and time. The effect of using different definitions of diarrhoea on its reported incidence was investigated in a prospective study of twenty-nine male patients starting ETF (Bliss *et al.* 1992). The most liberal definition of diarrhoea (one or more liquid faeces per d) resulted in a reported incidence of 72% of patients, whereas the strictest definition (five or more faeces per d) resulted in an incidence of 21%. The incidence was also positively associated with the number of days on which the patients were monitored (Bliss *et al.* 1992).

Most prospective investigations of ETF use predetermined definitions of diarrhoea, whereas in clinical practice standard definitions are rarely used. Instead, the healthcare professional, usually the nurse, relies on their own subjective opinion of whether or not patients have diarrhoea. The nurse then reports the presence of diarrhoea to the relevant clinician, usually the doctor or dietitian. A survey of thirty-five nurses, doctors and dietitians identified the importance of different characteristics used when defining diarrhoea during ETF (Whelan *et al.* 2003*b*). Whilst, in general, faecal frequency was considered to be more important than consistency and quantity ($P = 0{\cdot}048$), there was no absolute agreement either between or within professional groups on the order of importance of these characteristics (Whelan *et al.* 2003*b*).

The lack of intra-profession agreement on the importance of different faecal characteristics in defining diarrhoea during ETF is likely to reduce the reliability of subjective nurse opinion. The reliability of nurses in reporting diarrhoea has been investigated in thirty-six paediatric in-patients (Allen *et al.* 1994). Following independent inspection of thirty faecal samples, two different nurses agreed on the presence or absence of diarrhoea on 90% of occasions (percentage agreement corrected for chance agreement, κ 0·78), demonstrating substantial agreement. However, the patients were not receiving ETF and nurses were advised to consider only faecal consistency, thus removing the variability caused by intra-profession differences in the faecal characteristics used to define diarrhoea. The reliability of subjective nurse opinion in reporting diarrhoea has recently been investigated in thirty-six adult patients receiving ETF (Whelan *et al.* 2003*b*). Following independent inspection of fifty-nine faecal samples, two different nurses agreed on the presence or absence of diarrhoea on 75% of occasions (κ 0·48), demonstrating only fair reliability. In clinical practice, where agreement is not assessed under experimental conditions, the inter-rater reliability may be even lower (Topf, 1988). Thus, in the absence of substantial agreement, health professionals should be discouraged from using their subjective opinion to define and report diarrhoea during ETF. Rather, health professionals should be encouraged to give a more detailed report of the characteristics of faecal output. This approach will facilitate improved communication between those who observe actual faecal output and those who make treatment decisions.

Characterising faecal output during enteral tube feeding

A variety of methods are available for the characterisation of faecal output during ETF. Whilst faecal frequency is easy to record, the accurate characterisation of faecal consistency and quantity requires experimental methods.

The experimental methods available to characterise faecal consistency include penetrometry, viscometry and lyophilisation. Penetrometry measures the penetration of a standard cone into a faecal sample (Exton-Smith *et al.* 1974) and data have been shown to correlate with faecal water content (Nakaji *et al.* 2002). Viscometry measures the force required to rotate a standard spindle in a faecal sample and data have been shown to correlate with subjective descriptors of faecal consistency (Wenzl *et al.* 1995). Lyophilisation of a faecal sample allows calculation of the percentage water content, a major predictor of faecal consistency (Wenzl *et al.* 1995).

However, each of these experimental methods has several disadvantages. Penetrometry cannot be conducted on small or liquid samples (Davies *et al.* 1986), viscometry cannot be conducted on formed faeces (Wenzl *et al.* 1995) and complete lyophilisation of a faecal sample can take up to 3 d (Bliss *et al.* 1999). Meanwhile, experimental characterisation of faecal weight requires the collection of the entire sample without contamination by urine and often requires the use of a bedpan or commode, or the weighing of incontinence pads (Benya *et al.* 1991). Most importantly, the intensive nature of these experimental methods precludes their routine use in the research or clinical setting.

In view of the impractical nature of experimental methods, nurses routinely characterise faecal output visually. The reliability of visual characterisation of faecal consistency has been measured in a number of studies. The reported agreement beyond chance between nurses visually characterising faecal consistency ranges from fair (κ 0·25; Allen *et al.* 1994) to substantial (κ 0·68; Bliss *et al.* 2001), although none of these patients was receiving ETF (Landis & Koch, 1977). The validity of visual characterisation of faecal weight has been measured in a simulated study in which thirty-four nurses estimated the weight of common patient inputs and outputs (Daffurn *et al.* 1994). The mean estimated weight of 100 g faeces in a bedpan was 135 (SD 59) g, indicating a systematic overestimation of actual faecal weight.

Experimental methods of characterising faecal output are accurate but impractical, whereas visual characterisation is practical but inaccurate. This situation presents problems for monitoring faecal output in both the research and clinical setting. A variety of charts have been developed to improve visual characterisation of faecal output. The Bristol Stool Chart (Lewis & Heaton, 1997) incorporates verbal and pictorial descriptors of faecal consistency; however, it does not include other important faecal characteristics and has not been validated in patients receiving ETF. A chart has been developed recently that incorporates verbal and pictorial descriptors of faecal frequency, consistency and quantity to assist in the accurate visual characterisation of faecal output in patients

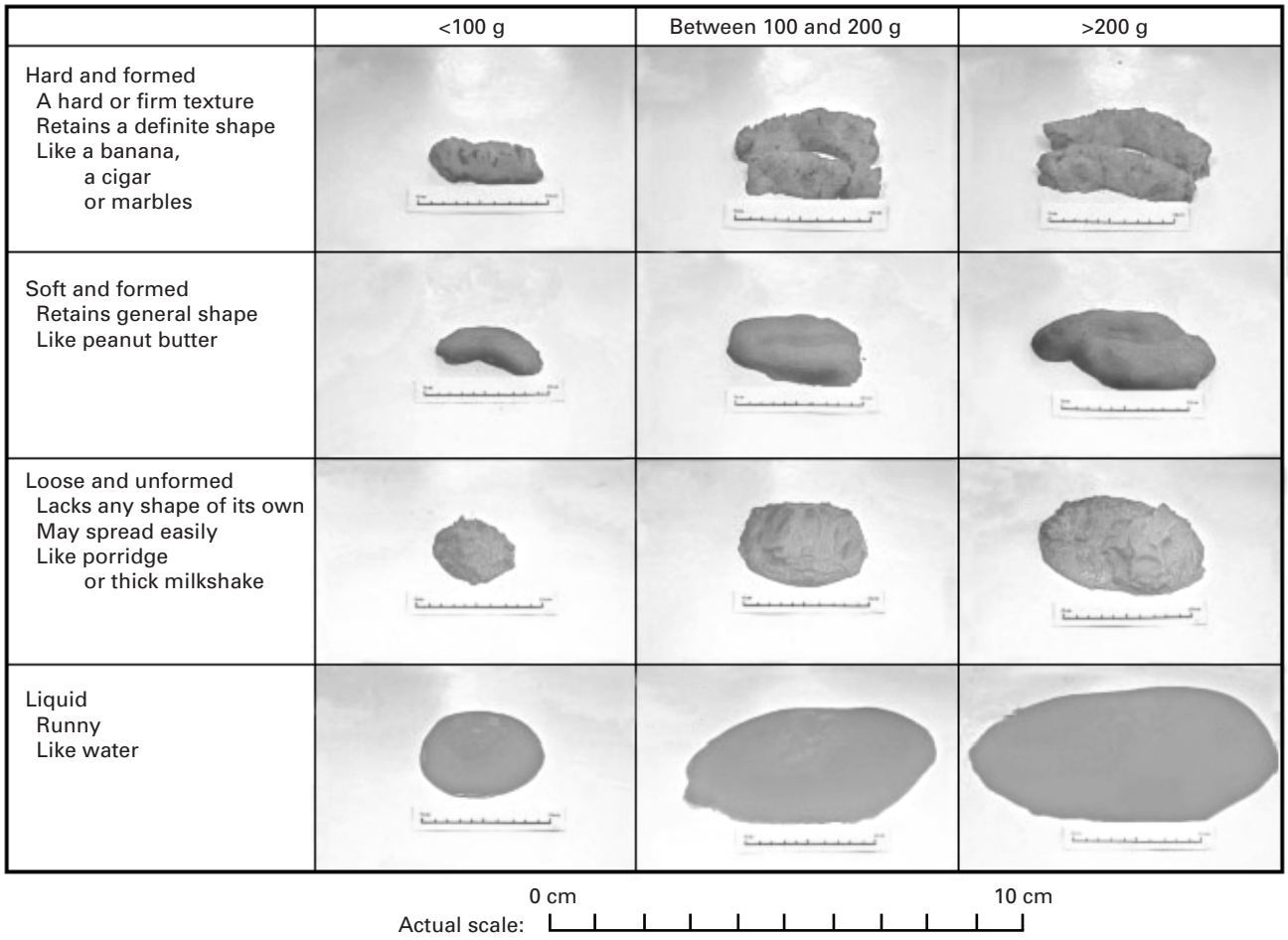

Fig. 1. A novel chart containing verbal and pictorial descriptors to assist in the characterisation of faecal output in patients receiving enteral tube feeding. (Reproduced with permission from King's College London; the chart can be downloaded from www.kcl.ac.uk/stoolchart)

receiving ETF (Fig. 1; Whelan *et al*. 2001*b*). The chart includes four categories for faecal consistency: hard and formed; soft and formed; loose and unformed; liquid; and three categories for faecal weight: <100 g; between 100 and 200 g; >200 g. Faecal frequency is incorporated by recording each time that faeces are voided. The chart has been validated in a questionnaire survey of health professionals and a clinical study of thirty-six patients starting ETF (Whelan *et al*. 2001*b*). When two different nurses used the chart to independently characterise fifty-nine faecal samples, the agreement beyond chance was almost perfect for faecal consistency (95%; κ 0·91) and substantial for faecal weight (83%; κ 0·75). In addition, 83% of faecal samples were assigned to the correct faecal-weight category (κ 0·75). The chart can assist in the accurate visual characterisation of faecal output in the research and clinical setting.

Pathogenesis of diarrhoea during enteral tube feeding

The pathogenesis of diarrhoea in patients receiving ETF has been extensively investigated and a number of mechanisms have been identified. First, microbial contamination of the enteral formula with $>10^4$ colony-forming units/ml is associated with diarrhoea (Okuma *et al*. 2000) and can occur due to non-sterile handling of the feeding system (Beattie & Anderton, 1999). Second, the risk of infection with *Clostridium difficile*, a Gram-positive enteropathogen, which can cause diarrhoea, pseudomembranous colitis and fulminant colitis (Mylonakis *et al*. 2001), is threefold greater in patients receiving ETF than matched patients not receiving ETF (Bliss *et al*. 1998). Third, intragastric infusion of enteral formula stimulates an abnormal secretion of fluid into the lumen of the ascending colon (Bowling *et al*. 1994). Fourth, the prescription of antibiotics increases the risk of diarrhoea (Keohane *et al*. 1984; Guenter *et al*. 1991) as a result of their deleterious effect on the colonic microflora (Levy, 2000). Several other mechanisms for diarrhoea during ETF have been established, including drug therapy and hypoalbuminaemia, and have been thoroughly reviewed elsewhere (Bowling, 1995). However, the role of the colonic microflora remains an area of increasing interest.

https://doi.org/10.1079/PNS2003317 Published online by Cambridge University Press

Colonic microflora

The gastrointestinal tract contains a complex microbial ecosystem of >500 different species of bacteria. The numbers and type of bacteria vary between the sections, with 10^3 colony-forming units/g stomach contents, rising to 10^{12} colony-forming units/g in the colon (Steer *et al*. 2000). The indigenous microflora can inhibit the growth of enteropathogens in the colonic lumen by competing for nutrients and space and by producing antimicrobials (Gibson & Wang, 1994; Lievin *et al*. 2000) and acids (Wang & Gibson, 1993), a process termed colonisation inhibition. The microflora can also inhibit adhesion of enteropathogens to the colonocytes via steric and chemical hindrance of receptor sites (Bernet-Camard *et al*. 1997), a process termed competitive exclusion.

The colonic microflora may be able to prevent enteropathogenic infection through their potential to exert colonisation inhibition and competitive exclusion. In patients receiving ETF the increased risk of enteropathogenic infection may therefore result from negative alterations to the microflora, predisposing the patient to diarrhoea. In view of the involvement of enteropathogens in the pathogenesis of diarrhoea during ETF, the effect of consumption of enteral formulas on the faecal microflora has been investigated in a series of studies in healthy subjects (Table 1).

The results of these studies are conflicting, with some demonstrating large reductions (Winitz *et al*. 1970) and some demonstrating no significant changes (Attebery *et al*. 1972; Crowther *et al*. 1973; Bounous & Devroede, 1974; Bornside & Cohn, 1975) to the major genera of the faecal microflora when healthy subjects change from normal diet to a fibre-free 'low-residue' enteral formula. These earlier studies have major methodological weaknesses, including sample sizes that were so small they precluded statistical analysis (Winitz *et al*. 1970; Attebery *et al*. 1972; Crowther *et al*. 1973). Furthermore, the aim of these studies was often to investigate the efficacy of low-residue enteral formulas for preoperative bowel preparation. Consequently, subjects often received an enema (Winitz *et al*. 1970) or laxatives (Bornside & Cohn, 1975), or both (Attebery *et al*. 1972) before starting consumption of the enteral formula, a procedure that does not accurately model ETF.

Despite their major limitations, these early experiments indicated that the carbohydrate source in the enteral formula might affect the extent to which alterations occur to the microflora. Winitz *et al*. (1970) showed that replacing glucose in enteral formulas with sucrose prevented a decrease in the concentrations of coliforms and bacteroides. Indeed, some carbohydrates may even be able to stimulate the growth of beneficial bacterial groups, a phenomenon termed the 'prebiotic concept'. A prebiotic is defined as a 'non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improving host health' (Gibson & Roberfroid, 1995). The most extensively studied prebiotics are fructo-oligosaccharides (FOS), which are polymers of glucose and fructose monomers in varying ratios. FOS are found naturally in artichokes, chicory, leeks, asparagus, onions

Table 1. Published studies investigating the effect of changing from a normal diet to enteral formula as the only source of nutrition on the major genera of the faecal microflora in healthy human subjects

Reference	ETF formula	Sample size	Consumption period (d)	Effect on major genera of faecal microflora
Winitz *et al*. (1970)	Elemental (glucose)	4	13	Decrease: Total bacteria, bacteroides, clostridia, coliforms, enterococci, lactobacilli
	Elemental (glucose)	8	4	Decrease: Total bacteria, bacteroides, clostridia, coliforms, enterococci, lactobacilli
	Elemental (sucrose)	8	4	Decrease: Total bacteria, clostridia, enterococci, lactobacilli No change: Bacteroides, coliforms
Attebery *et al*. (1972)	Elemental (glucose)	3	8–10	No change: Anaerobes, aerobes
Crowther *et al*. (1973)	Elemental	3	10	Decrease: Enterococci No change: Total bacteria, bacteroides, clostridia, bifidobacteria, lactobacilli
Bounous & Devroede (1974)	Elemental	14	12	Decrease: Enterococci No change: Anaerobes, aerobes, coliforms
Bornside & Cohn (1975)	Elemental (dextrin)	10	7	No change: Total bacteria, anaerobes, aerobes, bacteroides, clostridia, bifidobacteria
Garleb *et al*. (1996)	Low residue	9	14	Decrease: Bifidobacteria
	Low residue + FOS (5 g/l)	9	14	No change: Bifidobacteria
	Low residue + FOS (10 g/l)	9	14	Increase: Bifidobacteria
Whelan *et al*. (2003*a*)	Low residue	10	14	Decrease: Total bacteria No change: Clostridia, bacteroides, bifidobacteria
	Fibre (15 g/l) + FOS (5 g/l)	10	14	Decrease: Total bacteria, clostridia No change: Bacteroides Increase: Bifidobacteria

ETF, enteral tube feeding; FOS, fructo-oligosaccharides.

https://doi.org/10.1079/PNS2003317 Published online by Cambridge University Press

and garlic (Van Loo *et al*. 1995). When given as a supplement to the normal diet of human subjects they have been shown to increase the concentration of faecal bifidobacteria and reduce clostridia (Gibson *et al*. 1995).

FOS have been added to enteral formulas for some time because of their bifidogenic capabilities and their inhibition of potentially-pathogenic bacteria (Wolf *et al*. 2003). Two studies have investigated the effect of fortification of enteral formulas with FOS on the faecal microflora of healthy subjects. In a prospective randomised double-blind trial consumption of a low-residue enteral formula caused a reduction in faecal bifidobacteria, whereas fortification with 5 g FOS/l prevented this reduction and fortification with 10 g FOS/l caused an increase in bifidobacteria (Garleb *et al*. 1996). In a prospective randomised double-blind cross-over trial fluorescent *in situ* hybridisation, a highly-specific nucleotide probe method (Blaut *et al*. 2002), was used to quantify the effect of enteral formulas on the faecal microflora of healthy subjects (Whelan *et al*. 2003*a*). Consumption of a low-residue enteral formula resulted in a 52% reduction in the concentration of total faecal bacteria, but without marked changes to the concentrations of bifidobacteria, clostridia and bacteroides. However, fortification of the formula with 15 g mixed fibre and 5 g FOS/l resulted in an increase in the concentration of bifidobacteria and a reduction in clostridia (Whelan *et al*. 2003*a*).

The results of these recent studies clearly suggest that low-residue enteral formulas cause negative alterations to the faecal microflora in healthy subjects, which can be partially prevented by fortification with FOS. However, alterations to the microflora may also affect colonic fermentation and SCFA production.

Colonic fermentation and SCFA production

The colonic microflora ferment polysaccharides, oligosaccharides, proteins, peptides and glycoproteins to produce SCFA (Macfarlane & Macfarlane, 2003). The carbohydrates account for the majority of SCFA production and reach the colon in the form of dietary NSP and oligosaccharides that are resistant to digestion in the upper gastrointestinal tract, or as disaccharides in conditions such as lactose malabsorption (Cook & Sellin, 1998). Acetate, propionate and butyrate constitute approximately 90% of the SCFA produced by the microflora, with valerate, hexanoate, isobutyrate and isovalerate being produced in smaller amounts (Cook & Sellin, 1998). *In vitro* studies suggest that the extent of fermentation of the carbohydrate affects not only the amount but also the pattern of SCFA production. SCFA production rates for fibres commonly used in enteral formulas were compared *in vitro* using faecal inoculum from healthy subjects (Kapadia *et al*. 1995). Poorly-fermentable oat husk did not result in a change in the production of total SCFA, acetate, propionate or butyrate, whereas highly-fermentable soyabean oligosaccharide increased their production (Kapadia *et al*. 1995). Approximately 95% of the SCFA produced in the colon are then absorbed and metabolised in the colonocytes, liver, muscle and brain tissue (Topping & Clifton, 2001). SCFA absorption occurs by diffusion, anion-exchange or carrier-mediated exchange, resulting in the concomitant absorption of water and Na (Tyagi *et al*. 2002). Interestingly, the abnormal secretion of fluid into the colon of subjects receiving ETF is reversed during an infusion of SCFA into the caecum (Bowling *et al*. 1993).

In view of the ability of SCFA to stimulate colonic water absorption during ETF, the effect on SCFA production of changing from a normal diet to consuming enteral formula as the only source of nutrition has been investigated in three experiments in healthy subjects (Table 2). Low-residue enteral formula caused a reduction in the concentration of total faecal SCFA in two studies (Zimmaro *et al*. 1989; Whelan *et al*. 2003*a*), a reduction in acetate and propionate in one study (Whelan *et al*. 2003*a*) and a reduction in butyrate in all three studies (Zimmaro *et al*. 1989; Lampe *et al*. 1992; Whelan *et al*. 2003*a*). Fortification of the formula with a fibre source still caused a reduction in butyrate (Lampe *et al*. 1992;

Table 2. Published studies investigating the effect of changing from a normal diet to enteral formula as the only source of nutrition on SCFA concentrations in healthy human subjects

Reference	ETF formula	Sample size	Consumption period (d)	Effect on SCFA concentrations
Zimmaro *et al*. (1989)	Low residue	13	8	Decrease: Total SCFA, butyrate No change: Acetate, propionate
Lampe *et al*. (1992)	Low residue	11	18	Decrease: Butyrate No change: Total SCFA, acetate, propionate
	Fibre (15 g/d modified guar)	11	18	Decrease: Butyrate No change: Total SCFA, acetate, propionate
	Fibre (15 g/d soya polysaccharide)	11	18	Decrease: Butyrate No change: Total SCFA, acetate, propionate
Whelan *et al*. (2003*a*)	Low residue	10	14	Decrease: Total SCFA, acetate, propionate, butyrate No change: Isobutyrate, valerate, isovalerate
	Fibre (15 g/l mixed) + FOS (5 g/l)	10	14	Decrease: Butyrate No change: Total SCFA, acetate, propionate, isobutyrate, valerate, isovalerate

ETF, enteral tube feeding; FOS, fructo-oligosaccharides.

https://doi.org/10.1079/PNS2003317 Published online by Cambridge University Press

Whelan *et al.* 2003*a*), but in one study it also prevented the reduction in total SCFA, acetate and propionate (Whelan *et al.* 2003*a*). The differences in the results of these studies may reflect the fibre source in the enteral formula and also the sample collection method used. Zimmaro *et al.* (1989) and Lampe *et al.* (1992) both measured the concentration of SCFA in samples of colonic fluid collected from orally-ingested dialysis bags; however, the effect of colonic transit time on the absorption of SCFA into the dialysis bags is unknown. Whelan *et al.* (2003*a*) measured the faecal concentration of SCFA; however, this measurement reflects only the amount remaining in the faeces following colonic absorption. Furthermore, colonic absorption of SCFA is higher when transit time is longer and, since low-residue enteral formula increases the transit time through the gastrointestinal tract (Silk *et al.* 2001), it is possible that the reduction in faecal SCFA reflects an increase in absorption rather than a reduced production *per se*. In the future, novel stable-isotope methods using [1-^{13}C]acetate to measure endogenous peripheral turnover may assist in accurately measuring exogenous SCFA production in the colon (Pouteau *et al.* 2003).

Healthy subjects are frequently used in studies investigating the effect of diet on the faecal microflora and SCFA concentrations, because they otherwise have a stable microflora (Bornside, 1978). However, whilst they can accurately model the effect of the composition of the enteral formula on the faecal microflora they are not a true reflection of patients receiving ETF. Patients receiving ETF frequently receive a variety of medications, such as antibiotics, which have gross effects on the faecal microflora (Levy, 2000) and SCFA concentrations (Clausen *et al.* 1991). Furthermore, patients frequently have comorbidities that are known to have altered faecal microflora (such as Crohn's disease; Seksik *et al.* 2003) and SCFA concentrations (such as patients following surgery on the gastrointestinal tract; Scheppach *et al.* 1989). Age is also known to influence the faecal microflora (Hopkins *et al.* 2001), yet healthy subjects recruited to trials of enteral formula consumption are often much younger than patients receiving ETF. Despite the need for parallel studies in patients, there have been only three studies that have investigated the faecal microflora and SCFA concentrations in those receiving ETF (Table 3).

Faecal microflora and SCFA concentrations in patients receiving enteral tube feeding

Faecal SCFA concentrations were measured in a prospective non-randomised cross-over trial in nine patients at baseline, after 7 d of ETF with a low-residue formula and after a further 7 d of ETF with an enteral formula fortified with 15 g FOS/l (Sobotka *et al.* 1997). There were no significant changes to the concentrations of total SCFA, acetate, propionate or butyrate following either low-residue ETF or FOS-fortified ETF. However, analysis of the individual data shows that some patients had large increases, some had large reductions and some had stable concentrations of SCFA.

In a cross-sectional study Schneider *et al.* (2000) demonstrated lower concentrations of faecal anaerobes and higher concentrations of aerobes in eight patients receiving long-term low-residue ETF compared with healthy controls, despite no differences in faecal bacteroides, clostridia and bifidobacteria. However, the difference in anaerobes : aerobes may be explained by the patients being older than the healthy controls (57 years *v.* 30 years), a factor known to have similar effects on the microflora (Hopkins *et al.* 2001). Despite the different microbial profile, there were no differences between patients and healthy controls in the concentrations of total SCFA, acetate, propionate or butyrate. However, there were large inter-individual variations in concentrations and only small sample sizes.

The faecal microflora and SCFA concentrations of twenty patients with diarrhoea during ETF who were treated with ≤28 g galactomannan were measured in a prospective observational study (Nakao *et al.* 2002). Following 4 weeks of treatment, diarrhoea had resolved in all patients and there was a reduction in the concentration of faecal aerobes. However, whether the change in microflora was a result of treatment with galactomannan, the resolution of diarrhoea or the extended period of ETF is unclear. Following treatment there were also increases in the concentrations of faecal SCFA, acetate and propionate. However, faecal water content decreased with the resolution of diarrhoea and, since the data for SCFA were expressed per g wet faeces, the reported increase in SCFA concentration was likely to be due to less-dilute faeces rather

Table 3. Published studies investigating the effect of enteral tube feeding (ETF) on the faecal microflora and SCFA concentrations of patients

Reference	Design	Sample size	ETF formula	Effect on faecal microflora	Effect on SCFA concentrations
Sobotka *et al.* (1997)	Prospective, cross-over trial	Nine patients starting ETF	Low residue *v.* 15 g FOS/l	Not measured	No change: Total SCFA, acetate, propionate, butyrate
Schneider *et al.* (2000)	Cross-sectional with control	Eight patients on long-term ETF *v.* ten controls	Low residue	Decreased: Anaerobes No difference: Total bacteria, bacteroides Increased: Aerobes	No difference: Total SCFA, acetate, propionate, butyrate
Nakao *et al.* (2002)	Prospective, observational	Twenty patients with diarrhoea on ETF	28 g soluble fibre/d	Decrease: Aerobes No change: Total bacteria, anaerobes	No change: Butyrate Increase: Total SCFA, acetate, propionate

FOS, fructo-oligosaccharides.

https://doi.org/10.1079/PNS2003317 Published online by Cambridge University Press

than an increase in production *per se* (Whelan *et al*. 2002).

The studies of patients receiving ETF indicate a potential imbalance between faecal anaerobes and aerobes. This imbalance is likely to be associated with a variety of factors, including antibiotic prescription and alterations in faecal output. However, studies in healthy subjects indicate that the composition of the enteral formula may also be a factor. There is a need for larger longitudinal studies investigating the faecal microflora in patients receiving ETF.

Profiling the microflora of patients may elucidate factors associated with the incidence of diarrhoea. This procedure has already been undertaken in patients with *C. difficile*-associated diarrhoea that are known to have reduced microbial diversity, lower concentrations of bacteroides and bifidobacteria and higher concentrations of enterobacteria and lactobacilli (Hopkins *et al*. 2001). If the faecal microflora of patients receiving ETF are altered, their ability to exert colonisation inhibition and competitive exclusion may be reduced. This outcome would not only indicate a mechanism for the increased risk of *C. difficile* infection in patients receiving ETF (Bliss *et al*. 2000), but would also assist the prediction of patients at greatest risk of developing diarrhoea and *C. difficile*-associated diarrhoea. However, the most appropriate management strategy for patients with an altered microflora is unclear. No prospective randomised controlled trials of the use of prebiotics to prevent or treat diarrhoea in patients receiving ETF have been published (Whelan *et al*. 2001*a*). An alternative strategy is to provide patients with exogenous bacteria, or 'probiotics'. The revised definition of a probiotic is 'a preparation of or a product containing viable, defined micro-organisms in sufficient numbers, which alter the microflora (by implantation or colonisation) in a compartment of the host and by that exert beneficial effects in this host' (Schrezenmeir & de Vrese, 2001). Two prospective randomised controlled trials have investigated the effect of probiotic prophylaxis against diarrhoea during ETF (Whelan *et al*. 2001*a*). The use of lactobacilli did not affect the incidence of diarrhoea in forty-one patients starting ETF (Heimburger *et al*. 1994), whereas the use of *Saccharomyces boulardii* in 128 patients on the ITU starting ETF reduced the number of patient days with diarrhoea by 25% (Bleichner *et al*. 1997). Investigation of other probiotic strains and their use in different patient populations is required in order to elicit the efficacy of probiotics in preventing diarrhoea during ETF.

Conclusion

Diarrhoea is a common and serious complication of ETF. Problems associated with the definition of diarrhoea and the accurate characterisation of faeces have impeded the comparison of research studies and prevented the standardised assessment of therapeutic interventions in clinical practice. Microflora and SCFA in the colon may protect the patient against diarrhoea. However, studies in healthy volunteers suggest that the composition of the enteral formula may have a negative impact on the microflora and SCFA concentrations, which may be modulated by the use of prebiotic carbohydrates. Conclusive data in patients receiving ETF are not yet available.

Acknowledgements

The authors would like to thank the Department of Nutrition and Dietetics, St George's Hospital, London and the Digestive Health Group, Nestlé Research Centre, Lausanne, Switzerland for their invaluable assistance. K.W. was supported by a grant from King's College London and Nestlé UK.

References

Allen UD, Deadman L & Wang EEL (1994) Standardising the assessment of diarrhoea in clinical trials: results of an interobserver agreement study. *Acta Paediatrica* **83**, 179–182.

Attebery HR, Sutter VL & Finegold SM (1972) Effect of a partially chemically defined diet on normal human fecal flora. *American Journal of Clinical Nutrition* **25**, 1391–1398.

Beattie TK & Anderton A (1999) Microbiological evaluation of four enteral feeding systems which have been deliberately subjected to faulty handling procedures. *Journal of Hospital Infection* **42**, 11–20.

Benya R, Layden TJ & Mobarhan S (1991) Diarrhoea associated with tube feeding: the importance of using objective criteria. *Journal of Clinical Gastroenterology* **13**, 167–172.

Bernet-Camard MF, Lievin V, Brassart D, Neeser JR, Servin A & Hudault S (1997) The human lactobacillus strain La1 secretes a nonbacteriocin antibacterial substance(s) active in vitro and in vivo. *Applied and Environmental Microbiology* **63**, 2747–2753.

Blaut M, Collins MD, Welling GW, Dore J, Van Loo J & de Vos W (2002) Molecular biological methods for studying the gut microbiota: the EU human gut flora project. *British Journal of Nutrition* **87**, S203–S211.

Bleichner G, Blehaut H, Mentec H & Moyse D (1997) *Sacchromyces boulardii* prevents diarrhoea in critically ill tube fed patients. *Intensive Care Medicine* **23**, 517–523.

Bliss D, Larson SJ, Burr JK & Savik K (2001) Reliability of a stool consistency classification system. *Journal of Wound, Ostomy and Continence Nursing* **28**, 305–313.

Bliss DZ, Guenter PA & Settle RG (1992) Defining and reporting diarrhoea in tube-fed patients – what a mess! *American Journal of Clinical Nutrition* **55**, 753–759.

Bliss DZ, Johnson S, Savik K, Clabots CR & Gerding DN (2000) Fecal incontinence in hospitalised patients who are acutely ill. *Nursing Research* **49**, 101–108.

Bliss DZ, Johnson S, Savik K, Clabots CR, Willard K & Gerding DN (1998) Acquisition of *Clostridium difficile* and *Clostridium difficile*-associated diarrhoea in hospitalised patients receiving tube feeding. *Annals of Internal Medicine* **129**, 1012–1019.

Bliss DZ, Savik K, Jung H, Jensen L, LeMoine M & Lowry A (1999) Comparison of subjective classification of stool consistency and stool water content. *Journal of Wound, Ostomy and Continence Nursing* **26**, 137–141.

Bornside GH (1978) Stability of human fecal flora. *American Journal of Clinical Nutrition* **31**, S141–S144.

Bornside GH & Cohn I Jr (1975) Stability of normal human fecal flora during a chemically defined, low residue liquid diet. *Annals of Surgery* **181**, 58–60.

Bounous G & Devroede GJ (1974) Effects of an elemental diet on human fecal flora. *Gastroenterology* **66**, 210–214.

Bowling TE (1995) Enteral-feeding-related diarrhoea: proposed causes and possible solutions. *Proceedings of the Nutrition Society* **54**, 579–590.
Bowling TE, Raimundo AH, Grimble GK & Silk DBA (1993) Reversal by short chain fatty acids of colonic fluid secretion induced by enteral feeding. *Lancet* **342**, 1266–1268.
Bowling TE, Raimundo AH, Grimble GK & Silk DB (1994) Colonic secretory effect in response to enteral feeding in humans. *Gut* **35**, 1734–1741.
Cataldi-Betcher EL, Seltzer MH, Slocum BA & Jones KW (1983) Complications occurring during enteral nutrition support: a prospective study. *Journal of Parenteral and Enteral Nutrition* **7**, 546–552.
Clausen MR, Bonnen H, Tvede M & Mortensen PB (1991) Colonic fermentation to short chain fatty acids is decreased in antibiotic-associated diarrhoea. *Gastroenterology* **101**, 1497–1504.
Cook SI & Sellin JH (1998) Short chain fatty acids in health and disease. *Alimentary Pharmacology and Therapeutics* **12**, 499–507.
Crowther JS, Drasar BS, Goddard P, Hill MJ & Johnson K (1973) The effect of a chemically defined diet on the faecal flora and faecal steroid concentration. *Gut* **14**, 790–793.
Daffurn K, Hillman KM, Bauman A, Lum M, Crispin C & Ince L (1994) Fluid balance charts: do they measure up? *British Journal of Nursing* **3**, 816–820.
Davies GJ, Crowder M, Reid B & Dickerson JWT (1986) Bowel function measurements of individuals with different eating patterns. *Gut* **27**, 164–169.
DeMeo M, Kolli S, Keshavarzian A, Borton M, Al-Hosni M, Dyavanapalli M, Shiau A, Tu N, Frommel T, Zarling E, Goris G, Shawaryn G & Mobarhan S (1998) Beneficial effect of a bile acid resin binder on enteral feeding induced diarrhea. *American Journal of Gastroenterology* **93**, 967–971.
Dobb GJ (1986) Diarrhea in the critically ill. *Intensive Care Medicine* **11**, 7–9.
Elia M (2003) *Annual Report of the British Artificial Nutrition Survey 2002*. Redditch, Worcs.: Sovereign/BAPEN.
Exton-Smith AN, Bendall MJ & Kent F (1974) A new technique for measuring the consistency of faeces: a report on its application to the assessment of Senokot therapy in the elderly. *Age and Ageing* **3**, 1–3.
Garleb KA, Snook JT, Marcon MJ, Wolf BW & Johnson WA (1996) Effect of fructooligosaccharide containing enteral formulas on subjective tolerance factors, serum chemistry profiles, and faecal bifidobacteria in healthy adult male subjects. *Microbial Ecology in Health and Disease* **9**, 279–285.
Gibson GR, Beatty ER, Wang X & Cummings JH (1995) Selective stimulation of bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* **108**, 975–982.
Gibson GR & Roberfroid MB (1995) Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *Journal of Nutrition* **125**, 1401–1412.
Gibson GR & Wang X (1994) Regulatory effects of bifidobacteria on the growth of other colonic bacteria. *Journal of Applied Bacteriology* **77**, 412–420.
Guenter PA, Settle RG, Perlmutter S, Marino PL, DeSimone GA & Rolandelli RH (1991) Tube feeding related diarrhoea in acutely ill patients. *Journal of Parenteral and Enteral Nutrition* **15**, 277–280.
Heimburger DC, Sockwell DG & Geels WJ (1994) Diarrhoea with enteral feeding: Prospective reappraisal of putative causes. *Nutrition* **10**, 392–396.
Hill SA, Nielsen MS & Lennard-Jones JE (1995) Nutritional support in intensive care units in England and Wales: a survey. *European Journal of Clinical Nutrition* **49**, 371–378.
Hopkins MJ, Sharp R & Macfarlane GT (2001) Age and disease related changes in intestinal bacterial populations assessed by cell culture, 16S rRNA abundance, and community cellular fatty acid profiles. *Gut* **48**, 198–205.
Kapadia SA, Raimundo AH, Grimble GK, Aimer P & Silk DBA (1995) Influence of three different fiber-supplemented enteral diets on bowel function and short-chain fatty acid production. *Journal of Parenteral and Enteral Nutrition* **19**, 63–68.
Keohane PP, Atrill H, Love M, Frost P & Silk DBA (1984) Relation between osmolality and gastrointestinal side effects in enteral nutrition. *British Medical Journal* **288**, 678–680.
Lampe JW, Effertz ME, Larson JL & Slavin JL (1992) Gastrointestinal effects of modified guar gum and soy polysaccharide as part of an enteral formula diet. *Journal of Parenteral and Enteral Nutrition* **16**, 538–544.
Landis JR & Koch GG (1977) The measurement of observer agreement for categorical data. *Biometrics* **33**, 159–174.
Lebak KJ, Bliss DZ, Savik K & Patten-Marsh KM (2003) What's new on defining diarrhea in tube-feeding studies? *Clinical Nursing Research* **12**, 174–204.
Levy J (2000) The effects of antibiotic use on gastrointestinal function. *American Journal of Gastroenterology* **95**, S8–S10.
Lewis SJ & Heaton KW (1997) Stool form scale as a useful guide to intestinal transit time. *Scandinavian Journal of Gastroenterology* **32**, 920–924.
Lievin V, Peiffer I, Hudault S, Rochat F, Brassart D, Neeser JR & Servin AL (2000) Bifidobacterium strains from resident infant human gastrointestinal microflora exert antimicrobial activity. *Gut* **47**, 646–652.
Macfarlane S & Macfarlane GT (2003) Regulation of short-chain fatty acid production. *Proceedings of the Nutrition Society* **62**, 67–72.
Montejo JC (1999) Enteral nutrition-related gastrointestinal complications in critically ill patients: a multicentre study. The Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units. *Critical Care Medicine* **27**, 1447–1453.
Mylonakis E, Ryan ET & Calderwood SB (2001) *Clostridium difficile*-associated diarrhea: a review. *Archives of Internal Medicine* **161**, 525–533.
Nakaji S, Fukuda S, Iwane S, Murakami H, Tamura K, Munakata A & Sugawara K (2002) New method for the determination of fecal consistency and its optimal value in the general population. *Journal of Gastroenterology and Hepatology* **17**, 1278–1282.
Nakao M, Ogura Y, Satake S, Ito I, Iguchi A, Takagi K & Nabeshima T (2002) Usefulness of soluble dietary fiber for the treatment of diarrhea during enteral nutrition in elderly patients. *Nutrition* **18**, 35–39.
Okuma T, Nakamura M, Totake H & Fukunaga Y (2000) Microbial contamination of enteral feeding formulas and diarrhea. *Nutrition* **16**, 719–722.
Pesola GE, Hogg JE, Yonnios T, McConnell RE & Carlon GC (1989) Isotonic nasogastric tube feedings: do they cause diarrhea? *Critical Care Medicine* **17**, 1151–1155.
Pouteau E, Nguyen P, Ballevre O & Krempf M (2003) Production rates and metabolism of short-chain fatty acids in the colon and whole body using stable isotopes. *Proceedings of the Nutrition Society* **62**, 87–93.
Scheppach W, Sachs M, Bartram P & Kasper H (1989) Faecal short-chain fatty acids after colonic surgery. *European Journal of Clinical Nutrition* **43**, 21–25.
Schneider SM, Le Gall P, Girard-Pipau F, Piche T, Pompei A, Nano JL, Hebuterne X & Rampal P (2000) Total artificial nutrition is associated with major changes in the fecal flora. *European Journal of Nutrition* **39**, 248–255.

Schrezenmeir J & de Vrese M (2001) Probiotics, prebiotics, and synbiotics: approaching a definition. *American Journal of Clinical Nutrition* **73**, S361–S364.

Seksik P, Rigottier-Gois L, Gramet G, Sutren M, Pochart P, Marteau P, Jian R & Dore J (2003) Alterations of the dominant faecal bacterial groups in patients with Crohn's disease of the colon. *Gut* **52**, 237–242.

Silk DBA, Walters ER, Duncan HD & Green CJ (2001) The effect of a polymeric enteral formula supplemented with a mixture of six fibres on normal human bowel function and colonic motility. *Clinical Nutrition* **20**, 49–58.

Sobotka L, Bratova M, Slemrova M, Manak J, Vizda J & Zadak Z (1997) Inulin as the soluble fibre in liquid enteral nutrition. *Nutrition* **13**, 21–25.

Steer T, Carpenter H, Tuohy K & Gibson GR (2000) Perspectives on the role of the human gut microbiota and its modulation by pro- and prebiotics. *Nutrition Research Reviews* **13**, 229–254.

Topf M (1988) Interrater reliability decline under covert assessment. *Nursing Research* **37**, 47–49.

Topping DL & Clifton PM (2001) Short-chain fatty acids and human colonic function: roles of resistant starch and nonstarch polysaccharides. *Physiology Reviews* **81**, 1031–1064.

Tyagi S, Venugopalakrishnan J, Ramaswamy K & Dudeja PK (2002) Mechanism of n-butyrate uptake in the human proximal colonic basolateral membranes. *American Journal of Physiology* **282**, G676–G682.

Van Loo J, Coussement P, de Leenheer L, Hoebregs H & Smits G (1995) On the presence of inulin and oligofructose as natural ingredients in the western diet. *Critical Reviews in Food Science and Nutrition* **35**, 525–552.

Wang X & Gibson GR (1993) Effects of the *in vitro* fermentation of oligofructose and inulin by bacteria growing in the human large intestine. *Journal of Applied Bacteriology* **75**, 373–380.

Wenzl HH, Fine KD, Schiller LR & Fordtran JS (1995) Determinants of decreased fecal consistency in patients with diarrhoea. *Gastroenterology* **108**, 1729–1738.

Whelan K, Gibson GR, Judd PA & Taylor MA (2001*a*) The role of probiotics and prebiotics in the management of diarrhoea associated with enteral tube feeding. *Journal of Human Nutrition and Dietetics* **14**, 423–433.

Whelan K, Judd PA, Preedy VR & Taylor MA (2003*a*) Alterations in faecal microflora and short-chain fatty acid concentrations following consumption of enteral formula by healthy subjects. *Proceedings of the Nutrition Society* **62**, 10A.

Whelan K, Judd PA & Taylor MA (2001*b*) Development and validation of a chart for measuring stool output in patients receiving enteral tube feeds. *Proceedings of the Nutrition Society* **60**, 192A.

Whelan K, Judd PA & Taylor MA (2002) Diarrhea during enteral nutrition – appropriate outcome measurement. *Nutrition* **18**, 790.

Whelan K, Judd PA & Taylor MA (2003*b*) Defining and reporting diarrhoea during enteral tube feeding: do health professionals agree? *Journal of Human Nutrition and Dietetics* **16**, 21–26.

Winitz M, Adams RF, Seedman DA, Davis PN, Jayko LG & Hamilton JA (1970) Studies in metabolic nutrition employing chemically defined diets: effects on gut microflora populations. *American Journal of Clinical Nutrition* **23**, 546–559.

Wolf BW, Chow J, Snowden MK & Garleb KA (2003) Medical foods and fructooligosaccharides: a novel fermentable dietary fibre. In *Oligosaccharides in Food and Agriculture*, pp. 118–134. Washington, DC: American Chemical Society.

Zimmaro DM, Rolandelli RH, Koruda MJ, Settle RG, Stein TP & Rombeau JL (1989) Isotonic tube feeding formula induces liquid stool in normal subjects: reversal by pectin. *Journal of Parenteral and Enteral Nutrition* **13**, 117–123.

https://doi.org/10.1079/PNS2003317 Published online by Cambridge University Press