



ESPEN endorsed recommendation

## Management of acute intestinal failure: A position paper from the European Society for Clinical Nutrition and Metabolism (ESPEN) Special Interest Group



Stanislaw Klek <sup>a,\*</sup>, Alastair Forbes <sup>b</sup>, Simon Gabe <sup>c</sup>, Mette Holst <sup>d</sup>, Geert Wanten <sup>e</sup>, Øivind Irtun <sup>f,g</sup>, Steven Olde Damink <sup>h</sup>, Marina Panisic-Sekeljic <sup>i</sup>, Rosa Burgos Pelaez <sup>j</sup>, Loris Pironi <sup>k</sup>, Annika Reintam Blaser <sup>l,d</sup>, Henrik Højgaard Rasmussen <sup>d</sup>, Stéphane M. Schneider <sup>m</sup>, Ronan Thibault <sup>n</sup>, Ruben G.J. Visschers <sup>h</sup>, Jonathan Shaffer <sup>o</sup>

<sup>a</sup> General and Oncology Surgery Unit, Stanley Dudrick's Memorial Hospital, Skawina, Poland

<sup>b</sup> Norwich Medical School, University of East Anglia, Norwich, UK

<sup>c</sup> The Lennard-Jones Intestinal Failure Unit, St Mark's Hospital and Academic Institute, Harrow, UK

<sup>d</sup> Department of Gastroenterology, Centre for Nutrition and Bowel Disease, Aalborg University Hospital, Aalborg, Denmark

<sup>e</sup> Radboud University Medical Center, Nijmegen, Netherlands

<sup>f</sup> Gastrosurgery Research Group, UiT The Arctic University of Norway, University Hospital North-Norway, Tromsø, Norway

<sup>g</sup> Dept. of Gastroenterologic Surgery, University Hospital North-Norway, Tromsø, Norway

<sup>h</sup> Department of Surgery, Maastricht University Medical Centre, Maastricht, Netherlands

<sup>i</sup> Department for Perioperative Nutrition, Clinic for General Surgery, Military Medica Academy, Belgrade, Serbia

<sup>j</sup> Nutritional Support Unit, University Hospital Vall d'Hebron, Barcelona, Spain

<sup>k</sup> Center for Chronic Intestinal Failure, St. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

<sup>l</sup> Clinic of Anaesthesiology and Intensive Care, University of Tartu, Puusepa 8, 51014 Tartu, Estonia

<sup>m</sup> Gastroenterology and Clinical Nutrition, CHU of Nice, University of Nice Sophia Antipolis, Nice, France

<sup>n</sup> Nutrition Unit, Department of Endocrinology-Diabetology-Nutrition, CHU Rennes, Université Rennes 1, INSERM U991, Rennes, France

<sup>o</sup> Intestinal failure Unit, Salford Royal Hospital, Salford, UK

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### SUMMARY

Intestinal failure (IF) is the consequence of a reduction of gut function below the minimum necessary for the absorption of nutrients from the gastrointestinal tract. Types I and II comprise acute intestinal failure (AIF). Although its prevalence is relatively low, type II AIF is serious and requires specialist multidisciplinary care, often for prolonged periods before its resolution. The key aspects are: sepsis control, fluid and electrolyte resuscitation, optimization of nutritional status, wound care, appropriate surgery and active rehabilitation. The ESPEN Acute Intestinal Failure Special Interest Group (AIF SIG) has devised this position paper to provide a state-of-the-art overview of the management of type II AIF and to point out areas for future research.

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### 1. Introduction

Intestinal failure (IF) has been defined from reduction in gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or

growth [1]. A reduction of absorptive function that does not require intravenous supplementation to maintain health and/or growth, can be considered as “intestinal insufficiency or deficiency” [2]. IF may be acquired or congenital, and of gastrointestinal or systemic, benign or malignant origin [2–4]. It may have an abrupt onset, or be the slow, progressive evolution of a chronic illness, and it may be a self-limiting short-term or a long-lasting condition (chronic intestinal failure, CIF).

On the basis of onset, and metabolic and expected outcome criteria, IF has been classified as [1,3]:

\* Corresponding author. Stanley Dudrick's Memorial Hospital, General Surgery Unit, 32-050 Skawina, 15 Tyniecka Street, Poland. Tel./fax: +48 12 424 80 07.

E-mail address: [klek@poczta.onet.pl](mailto:klek@poczta.onet.pl) (S. Klek).

- Type I – acute, short-term and usually self-limiting condition
- Type II – prolonged acute condition, often in metabolically unstable patients requiring complex multi-disciplinary care and intravenous supplementation over periods of weeks or months
- Type III – chronic condition (CIF), in metabolically stable patients, requiring intravenous supplementation over months or years. It may be reversible or irreversible (Table 1).

Type I and type II IF form the acute intestinal failure (AIF) group. Type I AIF is a common, short-lived, and in most cases self-limiting condition, diagnosed in approximately 15% patients in the perioperative setting after abdominal surgery, or in association with critical illness such as head injury, pneumonia, or acute pancreatitis, or after cardiac surgery [1]. Post-operative ileus usually spontaneously resolves within a few days and requires minimal therapeutic measures [1]. Such patients are usually managed in surgical wards, although some of those in critical care environments also fit into this category [1]. The term “acute gastrointestinal (GI) injury” has been proposed to address GI dysfunction as part of the multiple organ dysfunction syndrome in critically ill patients, whether or not they have primary abdominal pathology [6]. Acute GI injury grade I (self-limiting) and grade II (needs interventions) correspond roughly to AIF type I, with similar assessment and management needs [6].

Type II IF is an uncommon clinical condition accompanied by septic, metabolic and complex nutritional complications. It generally develops as a consequence of trauma; it may follow an acute event (such as intestinal volvulus, strangulated hernia, mesenteric thrombosis or abdominal trauma) necessitating massive enterectomy, or occur as a complication of intestinal surgery (anastomotic leak, unrecognized intestinal injury, fistula formation, abdominal wall dehiscence, laparostomy/open abdomen), often in a setting of considerable pre-existing co-morbidity [3]. The British study by Lal et al. showed that type II AIF patients comprised those with surgical complications (32%), Crohn's disease (21%), motility disorders (14%), vascular ischaemia (13%), malignancy (8%), radiation injury (2%), coeliac disease (2%) and others (8%) [3].

Type II AIF patients often need dedicated medical facilities, such as specialized IF units, and intensive care, with the capacity for multi-disciplinary IF team care [1,3]. The annual incidence of type II IF has been estimated to be 9 patients per million population [1,5]. The most frequent outcomes are full intestinal rehabilitation (about 40%), long-term enteral tube nutrition (including distal feeding by enteroclysis or chyme reinfusion), or transition to type III IF status requiring prolonged HPN (together about 50%). In-hospital mortality of Type II IF has been reported to be as high as 9.6–13% [1,7–15].

On the occasion of launching its new disease-specific guidelines, the European Society for Clinical Nutrition and Metabolism (ESPEN)

mandated its Special Interest Groups (SIG) in Acute Intestinal Failure (AIF) and Chronic Intestinal Failure (CIF) to provide a definition paper and management guidelines [16]. However, data on AIF are scarce, only a few relevant reviews have been published, and no recommendations have previously been proposed [1,3,10]. The AIF SIG accordingly decided to work on a position paper rather than guidelines. The main aims of this position paper are to provide a state-of-the-art overview of the management of type II AIF and to point out areas for future research.

## 2. Management

### 2.1. General considerations

A typical type II AIF patient presents with a high output fistula or enterostomy, associated sepsis and problems associated with a short bowel syndrome (up to 30% of new AIF admissions) [3]. There is no consensual clinical approach to AIF, although this phenomenon, to some extent, must be seen in all gastrointestinal surgery settings. Some rough estimation of experience can be made thanks to the 2012 European survey on enterocutaneous fistula (ECF), performed by the AIF SIG and presented during the 2012 ESPEN Congress in Barcelona [14]. It showed that participants considered themselves experienced in ECF only to a limited extent: surgeons – 75%, physicians – 68%, nurses – 69%, dieticians – 61% and pharmacists – 44% [14]. Reimbursement was considered a major problem: only 18% of responders felt that the coding systems accounted for the full complexity of these patients, even if 27% felt that there was appropriate financial remuneration overall [14]. These data suggest a need for recommendations and guidelines as far as the diagnosis and treatment of AIF is concerned.

Although the key aspect of therapy is the treatment of the underlying condition that led to AIF, it is generally accepted that there are several therapeutic measures involving multiple disciplines (Fig. 1) that must be implemented to treat AIF successfully. For the particular context of the patient with AIF in whom there is an enterocutaneous fistula the Maastricht group has proposed a regimen summarised in Table 1 [9,11]. Very similar guidance (with the acronym SNAP: for Sepsis, Nutrition, Anatomy, Plan) has come from the Salford unit in the UK [3].

Table 1 – the SOWATS regimen for enterocutaneous fistula or temporary enterostomy.

S = sepsis control  
O = optimisation of nutritional status  
W = wound care  
A = anatomy of the bowel and the fistula

**Table 1**  
Types of intestinal failure.

		Description	Duration	Examples	Goals of management
Type I	Acute IF I	Acute condition. Other organ dysfunction often present. AIF often self-limiting when other organ dysfunction corrected.	Days	Paralytic ileus post-operatively or as a part of MODS	Survival of acute phase. Stabilisation of homeostasis. Resolution of IF.
Type II	Acute IF II	Prolonged acute condition. Continuing metabolic instability.	Weeks to months	Recurrent abdominal sepsis with or without fistulation. Acute phase of short bowel syndrome	Achievement of steady-state without sepsis and with no other organ dysfunction. Resolution of IF or moving to chronic IF.
Type III	Chronic IF	Chronic organ failure without concomitant acute organ dysfunction. Steady-state condition.	Months to years	Short bowel syndrome. Intestinal dysmotility	Maintenance of homeostasis. Optimisation of nutritional and wound status. Restoration of gut integrity where possible.

MODS – multiple organ dysfunction syndrome.  
Adapted from Ref. [1].



**Fig. 1.** Multidisciplinary management of type II AIF.

T = timing of surgery  
S = surgical planning

Sepsis control includes the detection of signs of sepsis, radiological/surgical drainage of fluid collections and abscesses, and individualized antibiotic treatment. Optimization of nutrition using parenteral and/or enteral nutrition will be preceded by optimization of acid–base balance, electrolyte and hydration status – including rehydration with fluids (intravenous, enteral, and/or oral) and the use of antisecretory and antimotility drugs (usually proton pump inhibitors and loperamide respectively). There will also be measures to prevent the refeeding syndrome after initiation of

nutritional support in severely malnourished patients. Wound care requires specialist nursing care, which may include wound managers, stoma appliances, sump suction, vacuum-linked dressing systems, etc. There should be active rehabilitation and use of any remaining/excluded intestine, which will usually include enteral feeding – sometimes with fistuloclysis, or reinfusion of proximal effluent. Later, precise assessment of gastrointestinal tract state and function by radiological assessment will permit subsequent surgical planning, but with the recognition that surgery is rarely wise until at least 3 months have elapsed since the initial injury, and then only when there is good evidence that the acute inflammatory response has largely resolved (improvement of weight and serum

albumin; normal inflammatory markers, and perhaps lower fistula output) [11,17].

Careful adherence to the above-mentioned items is predictive of the chances of successful treatment of an ECF. The similar ‘SNAP’ approach, also focuses on detection and treatment of sepsis [3] with performance of cultures and swabs, abdominal imaging, and identification of other possible sources of infection (e.g. respiratory and urinary tract infection, endocarditis). Nutritional and dietetic assessment is required, with supplementary feeding where necessary using the most appropriate route: enteral (nasogastric tube, enteroclysis, chyme reinfusion) or parenteral (peripheral or central).

Both therapeutic approaches thus concentrate on a common set of key elements which can be applied to the general clinical care of AIF with or without enterocutaneous fistula.

### 3. Main aspects of the management of AIF

#### 3.1. Controlling sepsis

Sepsis is the leading cause of death in AIF. If it originates from the abdominal cavity, immediate removal of the source and/or adequate drainage is mandatory. However, in some cases, no obvious removable source is found, and then sepsis may have been caused by bacterial translocation (e.g. in colitis, severe bowel distension, subacute bowel ischaemia without perforation, etc) [18,19]. It is imperative to look for and recognise early signs of sepsis. According to Visschers et al., these signs are often blunted due to poor nutritional status, or accompanying disease [9,11,13]. Therefore, patients may not demonstrate typical signs of infection, such as fever or an increase in serum C-reactive protein (CRP) levels. Clinical signs of uncontrolled sepsis may however include tachycardia, fatigue, encephalopathy, fluid retention and oedema, jaundice, and – eventually – features of new or worsening organ failure. Laboratory tests may reveal leucopenia or leucocytosis, isolated lymphopenia, low haemoglobin, reduced plasma albumin and transferrin levels as well as abnormal liver function tests.

Although individualized, targeted antimicrobial therapy, based on culture results, is required, as sole therapy it is sufficient in only a minority of AIF patients. It is imperative therefore to identify and treat causes of sepsis, such as by (percutaneous or surgical) drainage of an abdominal abscess. Additional non-abdominal sources of sepsis need to be considered, pneumonia being the most common of them [20]. The central venous catheter should always be considered as a possible source of infection [10]. One should be aware of the risk of secondary fungal sepsis in critically ill patients with prolonged sepsis and exposure to antibiotics. This is particularly likely in those with poor dental hygiene [10].

#### 3.2. Optimizing hydration and nutritional status

The clinical and metabolic status of a patient with AIF depends on the extent and site of GI dysfunction as well as the underlying disease and the function of other organs. In the case of short bowel syndrome (SBS) it also depends on the extent of resection and the presence or absence of the ileo-caecal valve and/or colon. During the initial phase, the management of AIF regarding fluids and nutrition is directed towards achieving haemodynamic stabilization with fluid and electrolyte replacement. Thereafter, controlling fluid losses and covering energy needs are the main tasks.

##### 3.2.1. Fluid and electrolyte replacement

Fluid resuscitation is fundamental in all AIF patients, and needs to be started before any nutritional intervention. The fluid flux

though the small bowel is approximately 6–8 l of fluid daily, mainly from GI secretions but also from drinking. Around 80% of this volume is absorbed in the jejunum and ileum, and only 1–1.5 l of fluid normally enter the colon, where all except about 150 ml is absorbed. The spare capacity of the colon is substantial and the colon may increase its reuptake of water to 5 l in 24 h [15]. In patients who have undergone extensive intestinal resection, intestinal loss of fluids is inversely associated to the length of the remnant small bowel, and is worsened by a concomitant partial or total resection of the colon. Patients with an end-jejunosomy or proximal ileostomy often develop dehydration, and electrolyte deficiencies (especially magnesium, potassium and sodium). Normal values of electrolytes should be achieved in all patients with AIF, not least because electrolyte disturbances may aggravate gastrointestinal dysmotility [21]. Resection of the ileum results in proportionately greater malabsorption and diarrhoea (bile salt diarrhoea and steatorrhea) than loss of the jejunum, due in part to the excess of bile salts and unabsorbed fats reaching the colon and also because the jejunum is less able to adapt. The magnitude of the intestinal losses in AIF is greatest in the early period after resection and may be further aggravated by concomitant factors like intestinal inflammation or dysmotility. The presence of intra-abdominal sepsis or other underlying disease (e.g. Crohn's, coeliac disease, radiation enteritis or Addison's disease) can markedly increase an output however much small bowel is present (i.e. absence of short bowel syndrome *per se*).

Fluids should be infused to cover all losses and to maintain a urine output of at least 1 ml/kg/h (or 25 ml/kg/day). Patients should always receive adequate amounts of water, usually exceeding the standard volume of 30–40 ml/kg/day [14]. Large volumes of fluids and electrolytes lost through diarrhoea, excessive stoma effluent and nasogastric tube drainage must be carefully monitored and replaced. Measurement of urine sodium concentration is a sensitive gauge of hydration status, with a urine sodium < 20 mmol/l (or <50 mmol/24 h), together with Na/K ratio < 1, indicating fluid and/or sodium depletion. This will precede any changes in blood urea or creatinine. This should be monitored several times a week until a steady-state fluid balance is achieved.

Our European survey showed that appropriate hydration was a challenging issue – for example only 75% and 51% of centres had policies on when or whether to eat and drink with a new or chronic EC fistula, respectively [11].

Fluid therapy in sepsis is most challenging, and a positive fluid balance is difficult to avoid at this stage, as optimization of fluid status is subverted by needs to maintain adequate organ perfusion to avoid further organ damage. At the same time, prompt and appropriate control of the source of sepsis is needed to limit the duration of the unstable phase and allow early “de-resuscitation” (late goal-directed fluid removal) to be able to achieve temporary negative fluid balance without compromising blood flow [22].

##### 3.2.2. Nutritional support

Nutritional intervention is a key aspect in all patients with AIF, and requires assessment, planning, therapy and monitoring.

**3.2.2.1. Assessment of nutritional status.** Several malnutrition screening tools can be used to evaluate nutritional status or nutritional risk. All of them combine comparable variables, typically weight loss, body mass index (BMI), food intake, and a grading of on-going disease severity (NRS-2002), and these are described in more detail in the recent ESPEN Consensus Statement [23]. According to this, there are two options for the diagnosis of malnutrition [23]. Option one requires body mass index (BMI), <18.5 kg/m<sup>2</sup> to define malnutrition [23]. Option two requires the combined finding of unintentional weight loss (mandatory) and at least one of

either reduced BMI or a low fat free mass index (FFMI). Weight loss could be either >10% of habitual weight indefinite of time, or >5% over 3 months. Reduced BMI is <20 or <22 kg/m<sup>2</sup> in subjects younger and older than 70 years, respectively. Low FFMI is <15 and <17 kg/m<sup>2</sup> in females and males, respectively [23].

In all AIF patients, however, the initial screening must be extended to a full assessment of nutritional status. Anthropometry represents a credible diagnostic modality for the latter. The most common anthropometric methods are body weight (actual, ideal, adjusted), body mass index (BMI), arm circumference, and skin fold thickness [15]. However the reliability of these anthropometric methods is compromised in AIF patients, who have day to day fluid variations, specifically in the early phases of critical illness, and in patients with unstable intestinal output who remain at high risk of dehydration. The same biases arise with respect to bioelectrical impedance analysis (BIA) [24]. BIA is a method of body composition assessment which could theoretically be used to assess tissue hydration and cell membrane integrity. However BIA results are only fully interpretable in patients with steady fluid balance [25]. BIA measurements yield impedance, resistance and reactance, phase angle (PhA), and bioelectrical impedance vector analysis (BIVA). The PhA in particular is currently considered a marker of tissue health, because it is determined by body cell mass, cell membrane integrity and function [26]. Many papers in several clinical situations, including HIV infection, cancer, surgery, and chronic liver disease have now demonstrated the prognostic value of PhA [26]. The prospective multicentre observational study of phase angle ([ClinicalTrials.gov](http://ClinicalTrials.gov) Identifier: NCT01907347), supported by ESPEN, is currently addressing its prognostic value in ICU patients. Other papers have shown that PA can be a sensitive marker in monitoring after nutritional interventions [27–29]. To date the validity of BIA, for body composition, PhA, or hydration status, has not been specifically assessed in AIF patients. Handgrip strength (or dynamometry) could be useful to assess muscle strength and function, but again its validity in the specific setting of AIF remains to be demonstrated.

Several blood tests have been used to assess nutritional state in AIF. These include: serum proteins (albumin, transferrin, transthyretin), creatinine, blood-urea nitrogen (BUN), and lymphocyte count [15]. However none of these are found to define the nutritional state clearly.

Serum albumin should be viewed as a marker of severity of illness and surgical risk. It should not be used as a determinant of nutritional state in the acute phase. Then, as with any inflammatory cytokine response, albumin will escape from the circulation into the extravascular space, decreasing the plasma concentration. This drop has no direct relationship with the patient's underlying nutritional condition.

**3.2.2.2. Defining nutritional needs and route of feeding.** After the assessment of body composition, nutritional requirements must be defined. The most accurate method to measure energy requirements is indirect calorimetry [15,30]. Its use, to capture the metabolic changes so as to permit appropriate adjustments in the nutritional plan, may improve outcome, as is proven for ICU patients [29]. If indirect calorimetry is not available, the patient should receive 25–35 kcal kg<sup>-1</sup> day<sup>-1</sup>, depending on the catabolic/anabolic state, or the disease phase [31–33]. The use of other predictive formulae is generally less accurate [31]. In AIF the protein intake should usually be increased up to 1.5 g/kg actual BW/day [15] or an equivalent quantity of amino acids in those on parenteral nutrition. All micronutrients (vitamins and trace elements) and electrolytes should be administered from the beginning of nutritional therapy. Appropriate precautions are required if the patient is at risk of refeeding syndrome [15].

Planning nutrition in sepsis is especially challenging as nutritional intervention in this highly catabolic state needs to address not only minimizing negative energy and protein balance and muscle loss by avoiding starvation, but also maintaining tissue function, particularly of the liver, the immune system and skeletal and respiratory muscles [15]. Although indirect calorimetry is the method of choice for assessing energy requirements, simple formulations can again be applied to plan the nutritional intervention. It can be concluded that the total energy needs of a septic patient rarely exceed 25–35 kcal/kg ideal body weight/day, and that the intake of protein should usually be increased to 1.5 g/kg/day. Excessive intake of energy, i.e. overfeeding or hyperalimentation, is detrimental and must be avoided, because it may impair liver function, and cause cholestatic jaundice, mental confusion and hypermetabolism, requiring more O<sub>2</sub> and producing more CO<sub>2</sub>, thus requiring increased pulmonary ventilation [15].

Sufficient oral intake is not possible in the majority of AIF patients. Therefore, an optimal alternative needs to be defined. Nutrients can be delivered either by the enteral route (via nasogastric or nasojejunal tube, or occasionally via gastrostomy or jejunostomy, or through entero/fistuloclysis into the distal small bowel) or parenterally (via a peripheral or more usually central vein). Even if enteral feeding is the preferred method of feeding, it must be borne in mind that it is often difficult to cover all the energy and protein needs of patients with abdominal sepsis exclusively via the enteral route. A negative cumulative energy balance is associated with an increasing number of complications [15]. Therefore supplemental if not total parenteral nutrition should be considered. However, even the most accurate nutrition intake will be ineffective in uncontrolled sepsis, as it will not result in the increase of muscle mass. Moreover, failure to thrive and a lack of weight gain during nutritional support may be key features indicating ongoing sepsis.

**3.2.2.3. Parenteral nutrition.** Although enteral nutrition has proven to be the most beneficial in almost all patient populations, it is relatively rare that it is sufficient in AIF/ECF individuals because of the compromised integrity of the gastrointestinal tract. Therefore, parenteral nutrition often represents the main option, alone or in association with EN (supplemental PN).

Intravenous lipid emulsions are an essential component of parenteral nutrition (PN) regimens, representing a major source of energy and the essential fatty acids (FAs) [15]. Soybean oil-based lipid emulsion was the first commercially available intravenous lipid, with a high content of essential and long-chain polyunsaturated fatty acids (PUFA). It has proved to be safe and well-tolerated in a wide range of clinical conditions. However, its high content of omega-6 PUFAs, which have pro-inflammatory effects, has prompted the development of alternative lipid emulsions with the partial replacement of soybean oil with other lipids such as medium-chain triglycerides (MCT), olive oil and fish oil [32]. MCT- and olive oil-rich emulsions are less prone to lipid peroxidation than PUFA, while fish oil contains eicosapentaenoic and docosahexaenoic acids, omega-3 PUFAs, which have favourable immunomodulatory and may be even anti-inflammatory properties. Supplementation with omega-3 PUFA from fish oil is now recommended in the European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines on PN for surgical and critically ill patients [33].

**3.2.2.4. Enteral nutrition.** Even if parenteral nutrition will be the nutritional support of choice, feeding via the enteral route should always be considered. This kind of support is impossible in gastrointestinal tract obstruction, perforation or ineffective external drainage, but will also be contraindicated when gastrointestinal blood flow is compromised during phases of

haemodynamic instability. Disease-specific formulae are probably not required; many different standard oral nutritional supplements or enteral feeds may be helpful in intestinal failure, selected according to their energy density and convenience [12]. The use of special immunonutrients, such as glutamine or omega-3-PUFAs, needs further research. The use of elemental feeding solutions is not recommended as a first choice because so many AIF patients have short bowel syndrome and are net secretors, but may be considered in the case of GI intolerance of polymeric formulas.

Enteral feeding has a trophic effect on the bowel and prevents mucosal atrophy. It also plays an important role in preservation of the immune system, not least in preventing bacterial translocation.

**3.2.2.5. Distal feeding.** In addition to the generally positive effects of enteral nutrition, distal delivery of feed exercises negative feedback on bilio-pancreatic secretions, the so-called ileal brake [9,34]. Specialized techniques, such as fistuloclysis and chyme reinfusion, should be considered to stimulate the distal intestine in patients where this would otherwise be inaccessible or “out-of-circuit” [9,11]. These methods allow the administration of proximal secretions and/or a nutrition formula into the intestine distal from a proximal stoma or ECF. This represents a physiological way to prepare the downstream (effluent) small bowel and colon for the reestablishment of digestive continuity, and will help to anticipate and avoid postoperative problems (diarrhoea, faecal incontinence, identification of colonic stenosis, etc).

The reinfusion technique consists of collection of the intestinal effluent and its reinfusion into the distal part of the intestine. In addition to reducing (sometimes eliminating) the need for parenteral support this has been convincingly shown to normalise alkaline phosphatase,  $\gamma$ -glutamyl transpeptidase and bilirubin in patients on PN with ECF-associated liver disease [34–40]. Chyme reinfusion appears to improve intestinal function and nutritional status [39,40].

The other technique is fistuloclysis, in which nutritional formulae are infused into the (normal) intestine distal to the proximal stoma or fistula. Fistuloclysis has (for example) been successfully applied in 11 of 12 patients in a study of patients being prepared for restorative surgery [36].

**3.2.2.6. Oral feeding.** Except in situations where fasting is believed to help promote fistula healing or control (e.g. acute phase, very proximal, high output fistula), patients will be advised to eat *ad libitum*. Regular meals as well as the use of oral nutritional supplements should be considered [15]. The supervision of an experienced dietician is essential for best results, not least because of the problems with the net secretory state of many of these patients and the consequent need to restrict salt-free fluids.

**3.2.2.7. Nutrition intake monitoring.** Registering nutrition intake as precisely as possible is important to allow timely modifications in nutrition and fluid supplementation. In intensive care patients, frequent investigations and procedures may cause interruptions in feeding (especially in the case of enteral nutrition) resulting in a clinically relevant divergence between prescribed and delivered nutrients [41–44]. The use of analogue visual scales could be helpful but is not specifically validated in this context [44].

### 3.2.3. Drugs to decrease gastrointestinal losses and/or to increase intestinal absorption

Several drugs may be used to reduce a fistula or stoma output. Hypergastrinaemia is a normal response to a small bowel resection and this will lead to increased gastric acid secretion by the stomach [15,43–45]. The use of proton pump inhibitors (initially intravenous, and subsequently oral or enteral) significantly reduces this

hypergastrinaemic response, decreasing the distal output [15,46–50].

Antimotility therapy, used to treat diarrhoea and improve nutrient absorption, includes loperamide, codeine phosphate and anticholinergic agents (such as Lomotil). Loperamide is not significantly absorbed, and has no cerebral effects; therefore high doses can be safely and effectively used to decrease output. To lengthen transit time, patients may be advised to open the capsules before ingestion (and to mix the powder with dairy products or fruit cordial) to improve drug efficiency. Codeine phosphate is well absorbed and readily crosses the blood-brain barrier and can cause drowsiness. However it has a longer duration of action than loperamide and works partly against different gut opiate receptor sites, and for this reason the two medications can be complementary. Anticholinergic agents are sometimes used for their antimotility effects, but the anticholinergic effects (especially the dry mouth which can cause confusion with dehydration) limit their use. Antimotility drugs should be avoided in the case of *Clostridium difficile*-associated diarrhoea, and used in critically ill patients only in the absence of digestive infection [51,52]. Cholestyramine or colestipol should be considered in patients with colon in continuity, as diarrhoea may be caused by the colonic toxicity of malabsorbed bile salts [15]. However, the timing of the bile acid sequestrants needs to be considered so as not to interact with the other medications that the patient is taking. Taking them two hours after or before any drug or food ingestion is advised. These drugs should be avoided or withdrawn in the case of extensive small bowel resection, as their use may increase fat malabsorption.

Somatostatin is a cyclic peptide hormone consisting of 14 amino acids. It inhibits the release of growth hormone and various gastrointestinal and pancreatic hormones. It can reduce secretion of digestive juices (pancreatic juice in particular), promote absorption of water and electrolytes, maintain water-electrolyte and acid–base balance, improve blood circulation in the intestinal wall, reduce absorption of bacteria and toxins, decrease the level of toxins in plasma, accelerate resolution of inflammation, stimulate T cell proliferation, and enhance physical immunity [34]. Synthetic forms of somatostatin, such as octreotide, are commonly used to decrease the enteral fluid load. Conflicting results were reported with regards to healing of postoperative pancreatic or GI fistulas [35]. However, a recent meta-analysis suggests that both somatostatin and octreotide increase the likelihood of and reduce the time to fistula closure [53]. On the other hand, review of the literature suggests that, while spontaneous closure occurs in about 30% of patients with enterocutaneous fistulas, 90–95% of fistulas that spontaneously resolve do so within the first 4–5 weeks [9,45]. Moreover, gall bladder sludge or gallstones occur in 20–50% of patients treated with synthetic analogues of somatostatin. Therefore, although this hormone may reduce fistula output, simplifying care of some of these patients, its routine use remains controversial.

No data are available about the role of intestinal growth factors for the treatment of AIF.

With regard to pharmacological options in general, the aforementioned European survey showed that IF centres uniformly use acid suppression, but the other approaches differ significantly: 82% of them use opioids (mainly loperamide), 78% octreotide and 65% an oral rehydration solution [14].

### 3.3. Avoiding complications and promoting rehabilitation through nursing care

#### 3.3.1. Wound care

Good wound care, stoma care, and collection of intestinal output and wound discharge with a focus on meticulous skin protection, are crucial for the successful treatment of AIF [10]. A large array of

products, which can be used for routine wound care, is available, but the key aspect of successful intervention is a dedicated team of wound care and stoma care nurses. Fistulae residing in an abdominal wall defect constitute the greatest challenge and will often be best treated with a wound manager, with or without sump suction. Placement of a suction drain causes negative pressure (a “slight vacuum”) in the bag resulting in a constant diversion of fluid from the wound, helping the wound to heal. This system also creates a moist environment stimulating the production of healthy granulation tissue. The application of a specific vacuum-assisted closure technique has also been suggested to be of benefit. However, when applied to bowel exposed in an abdominal wall defect, a vacuum-assisted closure technique is probably more likely to cause damage to the bowel than to promote fistula and wound closure: it is not routinely recommended [9]. Planned cleansing of the wound two or three times a day with saline plus antiseptic or digestive contaminant must be associated with nutritional care to improve the chance of fistula closure.

### 3.3.2. Oral care

In the patient who needs to fast or to be “Nil By Mouth” for more than just a few hours, specific patient guidance and nursing care are necessary to reduce discomfort and to encourage continued compliance with this status. Being nil by mouth often leads to discomfort, including that from: xerostomia (dryness of mouth and tongue); difficulties in speaking; thick and stringy saliva; teeth that feel coated and unclean; and dry, cracked lips [54]. A stringent approach to evidence-based oral care has moreover been proven to reduce the risk of aspiration pneumonia in other fasting populations [55]. This should therefore be taken into consideration in sicker type II AIF patients.

### 3.3.3. Catheter care

It is important that only suitably trained personnel are responsible for the insertion of intravenous catheters. Equally, all nurses involved in their care should be trained to a strict asepsis protocol. Methods shown to reduce central venous catheter (CVC) infections include education in hand washing, use of full sterile barrier techniques, chlorhexidine skin preparations, reminders to remove unnecessary catheters, and avoidance of femoral venous siting [56]. Antimicrobial-coated catheters may reduce catheter colonisation and catheter-related infections, but no benefit with regards to clinically diagnosed sepsis or mortality has been shown [57]. Adherence to a clear catheter-care protocol should lead to the virtual absence of catheter sepsis in a specialist IF unit [58].

The choice of catheter used is less important than its care; peripherally inserted central catheters (PICC), cuffed tubes or ports all have their advocates. A common compromise is the use of PICCs initially and a transfer to a cuffed line if the patient requires home parenteral nutrition. All catheters should be placed with full aseptic conditions, ideally in a dedicated area [3].

### 3.3.4. Mobilization

Despite a lack of specific evidence for early rehabilitation of patients with type II AIF, the generally deleterious effects of bed rest require nursing staff to engage in early mobilization of these patients [59]. Mobilization, under the supervision of physiotherapists and with a strict nurse-driven protocol for assessment of the patient's abilities, is needed to achieve early ambulation in general ICU and intermediate care populations [60]; it is logical to extrapolate these data to the AIF patient.

### 3.3.5. Avoiding respiratory and other complications

Patients with AIF are at high risk of respiratory complications. Weakness of the respiratory muscles with decreased chest wall

expansion and increased incidence of pulmonary complications has been shown in malnourished patients undergoing elective upper abdominal surgery [61]. Factors increasing the risk of pulmonary complications after emergency abdominal surgery include age >50 years, BMI <21 or ≥30 kg/m<sup>2</sup>, upper or upper/lower abdominal incision [18]. Risk factors for aspiration of gastric contents include endotracheal intubation, vomiting, flat supine position, presence of a gastric tube, increasing age, abdominal surgery, and decreased alertness [62]. Clearly all of these adverse factors are common in AIF patients with prolonged sepsis, who additionally have profound fatigue, and increased risk of encephalopathy and critical illness polyneuromyopathy. Their multiple interventions and associated high needs for analgesia further increase the risks.

It is crucial to avoid sedative agents in these patients when they are breathing spontaneously. Radiological procedures such as abdominal CT scans performed in the flat supine position with enterally given contrast media in spontaneously breathing AIF patients also pose extra risks and should be clearly justified and carefully conducted. During daily care, nurses play a crucial role in managing patients, including elements such as keeping the head of the bed elevated whenever possible, performing respiratory exercises, and assuring adequate swallowing before any oral intake, which should then take place in a strictly optimized (preferably sitting) position.

Adequate pain control is required to achieve the comfort and allow mobilisation of the patient as well as to minimize the risk of respiratory complications due to hypoventilation with atelectasis-formation. Epidural analgesia after abdominal surgery may be associated with superior pain control and avoidance of opiates, but is often not applicable to AIF II patients due to their prolonged course and the high risk of septic complications [63–65].

### 3.3.6. Psychology

Patients with type II AIF often need to be hospitalized considerable distances away from their family for many weeks. The development of post-traumatic stress disorder, particularly when there have been post-operative complications, is a frequent occurrence. The input of a psychologist experienced in managing these conditions is helpful both to treat the patients and to guide the ward staff.

## 3.4. Surgical approaches

The effective management of abdominal sepsis is the most important factor in determining outcome in patients with AIF, and any delay worsens the outcome [65,66]. The treatment of abdominal sepsis requires source control, either by laparotomy/laparoscopy or by radiologically-guided minimally invasive drainage, sometimes even by the combination of both methods. Antimicrobial therapy targeting organisms found in any frank abscess should accompany surgery.

From the surgical perspective if the small bowel has been opened it is important not to attempt an anastomosis when there is peritonitis. Instead the two bowel ends should be exteriorised, if it is not possible to drain any collections without resection. One must bear in mind that the abdominal cavity may be hostile for several weeks or even months after the initial laparotomy, hence any reconstructive surgery would be dangerous under those circumstances. Therefore, early surgery should be limited to sepsis control. In the case of severe abdominal contamination, possible continuing ischaemia/development of necrosis and/or persisting intra-abdominal hypertension the abdomen can be left open (‘open-abdomen’ or laparostomy) for a few days.

In accordance with the recommendations of the Association of Surgeons of Great Britain and Ireland, reconstructive surgery in

type 2 AIF should not be attempted until the patient has recovered and entered the chronic phase of their IF. That time should be used to correct nutritional deficiencies and to heal wounds [65–67].

### 3.5. Intestinal failure associated liver disease

AIF patients are at risk of developing hepatic complications [67–69]. These abnormalities should be named ‘intestinal failure-associated liver disease (IFALD)’, as that term adequately depicts liver aberrations, rather than the now obsolete term parenteral nutrition-associated liver disease (PNALD) [69–72].

The prevalence of abnormal liver function tests during PN varies from 15 to 85%, according to the authors’ definitions [66–70]. Generally speaking, those elevations are mild, often normalise at the time of reinstating enteral or oral diet, even if PN is continued, and usually resolve fully once it is discontinued [68,70]. The severity of IFALD depends also on underlying disease, especially ongoing sepsis and pre-existing liver disease. It is particularly common in neonates and infants. Aetiological factors for IFALD can be divided into three main groups, with most patients having more than one cause [69,72]:

- PN-related (excess or deficiency of nutrients, i.e. over- or under-feeding, nutrient toxicity),
- IF-related (SBS, oral fasting, bacterial overgrowth, disruption of the enterohepatic cycle, drugs especially antibiotics, etc),
- systemic and/or abdominal inflammation related (e.g. sepsis, intra-abdominal infections)

Undoubtedly, the principal reason for liver complications in AIF patients is sepsis. Therefore, the efficient management of sepsis is the key point of all interventions. Prophylaxis against other types of IFALD includes the elimination as much as is possible of the other above-mentioned risk factors. The management concentrates on [69]:

- treatment of non-nutritional causes (surgery for gall bladder stones, treatment of sepsis, etc.)
- optimisation of parenteral nutrition (adjustment of lipid and glucose delivery, avoiding energy overload, use of 2nd and 3rd generation of lipid emulsions, etc.)
- reinstatement of enteral or oral intake when not contraindicated; chyme reinfusion

is associated with improvement probably thanks directly to the reinfusion of bile salts together with digestive secretions, restoring the enterohepatic cycle of bile salts and bile salt signalling, and indirectly through PN weaning [37].

When these are not sufficient consideration will be given to:

- pharmacological treatment (potentially including ursodeoxycholic acid, choline and taurine administration)
- transplantation of liver and small intestine (IFALD is one of the commonest reasons for performing intestinal transplantation)

Despite best efforts IFALD remains a major adverse prognostic marker and in patients presenting to a specialist intestinal failure unit, the mere presence of a raised bilirubin on admission was associated with poorer short- and long-term prognosis [69].

### 3.6. Intestinal failure centres

To improve the outcome of AIF, it is recommended that the treatment is provided by dedicated, experienced and multidisciplinary teams, in units with adequate diagnostic, therapeutic and

financial resources, as summarized in Fig. 1. Specialist IF centres exist only in some countries – the same units also managing home parenteral nutrition.

As experience appears to be one of the key aspects determining the quality of IF centres, the AIF SIG proposes that centres aiming to specialise in the management of Type II intestinal failure should be seeing at least 20 patients/year. Intensivists, interventional radiologists, urologists, gynaecologists, plastic surgeons, psychologists, occupational therapists and social workers are all valued members of the wider multidisciplinary team necessary to manage these complex patients. Patients require complex management of open abdominal wounds, high intestinal outputs and need a multidisciplinary nutrition team, especially during the minimum three months period before surgical reestablishment of intestinal continuity. To achieve this goal, rehabilitation centres which are more adapted than acute care hospitals to manage these patients are needed. Only a few units have the necessary resources but these complete rehabilitation centres should be developed worldwide to improve the management of IF patients.

The AIF SIG proposes the following quality measures for an intestinal failure centre treating patients with Type II intestinal failure:

#### Structure

1. Specialist unit or dedicated area within a ward
2. Critical mass of staff with experience in intestinal failure management
  - Multidisciplinary intestinal failure team
  - Specialist gastroenterologists & surgeons with dedicated time allocated to intestinal failure care
  - Specialist nurses (nutrition, stoma care, wound care), pharmacists and dietitians allocated to the intestinal failure team
3. Essential facilities available
  - Appropriate ward nursing ratio for intestinal failure patients
  - On site intensive care facilities
  - Interventional radiology support
  - Venous access expertise
  - Multi-professional intestinal failure outpatient clinics
  - Arrangements for 24h access to specialist advice available

#### Processes

- Assessment and management protocols (eg nutritional assessment, catheter care, wound care, fluid balance, parenteral and enteral nutrition)
- Structured data collection for patient management, follow up and quality control
- Regular audit of clinical practice

#### Outcome measures

- Mortality
- Re-fistulation rate
- CVC infection rate\*
- Unplanned re-hospitalisation rate
- Unplanned surgery/invasive treatment
- Quality of life (QoL) measurements

\*Catheter-related bloodstream infection rates in experienced referral centres can be expected to range from 0.14 to 1.09 episodes per catheter year in patients with chronic IF [73,74].

### 3.7. Areas of future research

Future studies should address epidemiology, risk factors and outcome of types I and II AIF. The role of bile salt signalling on the onset of liver test abnormalities should be better explored. Research

on surgical and medical treatment modalities should aim to provide evidence on selection and timing of the methods for initial treatment, but also in the later stages when there may have been multiple reoperations/interventions. Special attention should be paid to strategies which avoid fistula formation or encourage healing. Patient numbers are known to be small, and therefore multicentre studies are encouraged. The future multicentre prospective randomized controlled trial FRY granted by the French Public Clinical Research Programme, the French Speaking Society for Clinical Nutrition and Metabolism (SFNEP) and ESPEN will assess the impact of chyme reinfusion compared to parenteral nutrition on the incidence of complications until one month after surgical reestablishment of intestinal continuity in patients with a temporary high-output double enterostomy. Additional areas of research will include those of surgical and radiological techniques (including plugs and implants) as well as medical treatments including growth factors to foster intestinal adaptation and promote fistula closure.

The place of new nutritional and surgical interventions, and of pharmacological innovations in general, will all need formal evaluation prior to their confident inclusion in treatment algorithms for patients with type II AIF. Despite the challenges of investigation of a relatively rare condition in a non-homogeneous population where adequately powered studies are difficult to construct, several important developments are beginning to emerge.

### Conflict of interest

There are no conflicts of interest.

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