

# Nutritional Considerations in Pediatric Pancreatitis: A Position Paper from the NASPGHAN Pancreas Committee and ESPGHAN Cystic Fibrosis/Pancreas Working Group

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## ABSTRACT

**Objectives:** Wide variations exist in how physicians manage the nutritional aspects of children affected by acute pancreatitis (AP), acute recurrent pancreatitis (ARP), and chronic (CP) pancreatitis. Better consensus for optimal management is needed.

**Methods:** This consensus statement on nutrition in pediatric pancreatic diseases was developed through a joint ESPGHAN-NASPGHAN working group that performed an evidence-based search of the literature on nutrition in AP, ARP, and CP with a focus on pediatrics. The literature was summarized, quality of evidence reviewed, and expert recommendations developed. The authorship met to discuss the evidence and statements. Voting on recommendations occurred over 2 rounds based on feedback. A consensus of at least 75% was required to approve a recommendation. Areas requiring further research were identified.

**Results and Discussion:** The literature on nutrition in pediatric pancreatitis is limited. Children with mild AP benefit from starting an early nutritional regimen in the course of the attack. Early nutrition should be attempted in severe AP when possible; enteral nutrition is preferred over parenteral nutrition. Children with ARP are likely to tolerate and benefit from a regular diet. Children with CP need ongoing assessment for growth and nutritional deficiencies, exocrine and endocrine insufficiencies.

**Conclusions:** This document presents the first authoritative recommendations on nutritional considerations in pediatric pancreatitis. Future research should address the gaps in knowledge particularly relating to optimal nutrition for AP in children, role of diet or dietary supplements on recurrent attacks of pancreatitis and pain episodes, monitoring practices to detect early growth and nutritional deficiencies in CP and identifying risk factors that predispose children to these deficiencies.

**Key Words:** acute pancreatitis, chronic pancreatitis, endocrine insufficiency, enteral nutrition, exocrine insufficiency, parenteral nutrition

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## What Is Known

- Nutritional care of children with pancreatic disorders varies widely.
- No guidelines exist on optimal nutrition for children with acute pancreatitis, acute recurrent pancreatitis, or chronic pancreatitis.

## What Is New

- An expert working group ESPGHAN/ NASPGHAN reviewed literature, and made recommendations based on available literature and expert opinion for nutritional management of children with acute pancreatitis, acute recurrent pancreatitis, and chronic pancreatitis.
- Areas of research necessary to advance the field are discussed.

## INTRODUCTION

Acute, acute recurrent, and chronic pancreatitis are increasingly recognized and diagnosed in children (1). Few studies are published to answer fundamental questions regarding pancreatitis and nutrition management in pediatric patients. Although adult studies have investigated the role of nutrition in pancreatitis, caution should be exercised when extrapolating these data to pediatric patients, as pancreatitis in children has different etiologies,

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presentations, and outcomes compared with adults (2). Management of nutritional needs in children affected by pancreatic diseases varies widely. Historically, most therapy has been based on institutional preferences rather than scientific evidence.

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Cystic Fibrosis/Pancreas Working Group and the NASPGHAN (North American Society for Pediatric Gastroenterology, Hepatology and Nutrition) Pancreas Committee combined efforts with the goal to review the available scientific evidence for various nutritional interventions (nil per os [NPO], total parenteral nutrition [TPN], polymeric versus elemental formulas, use of nasogastric and nasojejunal tubes, low vs normal vs high-fat diet, supplementation of vitamins or pancreatic enzymes, etc) in pancreatic disease (acute pancreatitis [AP], acute recurrent pancreatitis [ARP], chronic pancreatitis [CP]). The literature reviews were utilized to make management recommendations based on scientific evidence. Consensus/expert opinion was provided when evidence was insufficient. Suggestions were provided for further research based on identified gaps.

This clinical document summarizes various aspects of nutritional care in pediatric pancreatic diseases during: AP; between episodes of AP; and chronic pancreatitis, with or without exocrine pancreatic insufficiency (EPI), and provides recommendations for management and suggestions for further research. Definitions as per Morinville et al are summarized as follows: AP is defined as requiring at least 2 out of 3 criteria: abdominal pain suggestive of, or compatible with AP (ie, abdominal pain of acute onset, especially in the epigastric region); serum amylase and/or lipase activity at least 3 times greater than the upper limit of normal (international units/liter); and imaging findings characteristic of or compatible with AP (eg, using ultrasound, contrast-enhanced computed tomography, endoscopic ultrasonography, and/or magnetic resonance imaging and magnetic resonance cholangiopancreatography) (3). Severity of AP has been defined following various classification schemes in the past, but has recently been more uniformly defined as mild AP: AP without organ failure, local or systemic complications, and usually resolving within the first week; moderately severe AP including the presence of transient organ failure that resolves in no longer than 48 hours, or local complications or exacerbation of co-morbid disease; and severe AP having organ failure that persists for longer than 48 hours (3). ARP diagnosis requires at least 2 distinct episodes of AP (each as defined above), along with either complete resolution of pain ( $\geq 1$ -month pain-free interval between the diagnoses of AP), or complete normalization of serum pancreatic enzyme levels (amylase and lipase), before the subsequent episode of AP is diagnosed, along with complete resolution of pain symptoms, irrespective of a specific time interval between AP episodes (3). CP is diagnosed in the presence of abdominal pain consistent with pancreatic origin and imaging findings suggestive of chronic pancreatic damage; evidence of EPI and suggestive pancreatic imaging findings; evidence of endocrine pancreatic insufficiency and suggestive pancreatic imaging findings; or surgical or

pancreatic biopsy specimen demonstrating histopathologic features compatible with CP (4).

## METHODS

The working group involved in the development of these NASPGHAN-ESPGHAN clinical recommendations included members of the NASPGHAN Pancreas Committee, under the leadership of Committee Chair (V.M.), and members of the ESPGHAN Cystic Fibrosis/Pancreas Working Group under the leadership of Committee Chair (M.W.) and experts in the field of pancreatitis nutrition.

Three subgroups were created, headed by the 3 co-first authors (M.A.-E.-J. for AP section, S.W. for ARP section, A.U. for CP section), under whose guidance main topics of interest were subdivided for thorough review of the medical literature through MEDLINE and PubMed up to August 2016. E-mail correspondence between the subgroup leaders and 2 senior authors, and teleconferences between the 2 senior authors led to the preparation of a draft by each subgroup leader with input of other authors. The manuscript was then shared with the remainder of the authorship for review before a group discussion was held at the October 2016 World Congress of Pediatric Gastroenterology, Hepatology and Nutrition in Montreal, Quebec, Canada. At this face-to-face meeting, each subgroup presented pertinent literature review, estimated strength of evidence, and proposed the statement recommendations to vote for each element under consideration. The summary statements/recommendations were discussed, and approved, rejected, or modified based on the feedback of attendees.

Subsequent to group discussion, each recommendation was voted upon for the first time, using a 5-point scale (5—strongly agree; 4—agree; 3—neutral: neither agree nor disagree; 2—disagree; 1—strongly disagree). It had been previously agreed that consensus could only be reached if at least 75% of the group voted “4” (agree) or “5” (strongly agree) on a particular recommendation. A modified version of the GRADE recommendations system was carried out, classifying recommendations based on 3 levels (A = high-quality evidence; B = moderate-quality evidence; and C = low-quality evidence), in addition to designating recommendations as 1 = strong recommendation or 2 = weak recommendation (5). Authors had reviewed the modified GRADE methodology (as described in [www.uptodate.com](http://www.uptodate.com)) (6) ahead of evaluating the various recommendations. Of note, this modified methodology (6) differed from the official GRADE mechanism in that evaluators were not independent from the group developing the recommendations, no independent opinion on level of evidence was provided, and no formal GRADE report of the literature was created for the statements derived. Additionally, the strength of a recommendation was based on the authors' expert opinion regarding the recommendation, and not directly related to the GRADE criteria. A second round of voting occurred via e-mail in April–May 2017 utilizing the modified recommendations, and request to return voting results within a 14-day timeframe, with responses printed and tabulated. The final manuscript draft was approved by all authors.

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## Nutrition During Acute Pancreatitis

One of the main principles in treating patients with AP of any age has been to follow an NPO (7) approach, with or without the use of TPN, with the aim to suppress pancreatic enzyme secretion and obtain bowel rest. Recent experimental and clinical studies have, however, demonstrated that this approach can actually lead to an increased risk of infectious complications due to bacterial overgrowth and translocation from the gut, resulting in higher morbidity and mortality in patients with severe acute pancreatitis (SAP) (8). In general, nutrition support will begin after any necessary fluid resuscitation and ensuring hemodynamic stability in the AP patient.

Determining the optimal nutritional support is considered an essential part of AP management, but this is not well studied in pediatrics (9,10). Consequently, few recommendations exist. For the purpose of this document, enteral nutrition will relate to any form of food taken into the gastrointestinal tract—by mouth, gastric, duodenal, or jejunal route. This section will review the evidence for various forms of nutritional support and attempt to derive recommendations based on the literature with respect to the management of children with AP.

### Enteral Nutrition (Oral, Gastric, Jejunal) During an Episode of Acute Pancreatitis

Most studies regarding AP and nutrition have been conducted in the adult population, with limited evidence in children.

#### Nutrition in Mild Acute Pancreatitis

Compelling evidence in the adult literature supports early introduction of enteral feeds in mild AP. Enteral support including a full solid diet in mild AP appears to be safe and well-tolerated and is associated with positive outcomes including reduced length of hospital stay (11–13). Eckerwall et al found that length of stay was shorter in patients with predicted mild AP when patients received enteral support compared with “conventional fasting or NPO” (14). In fact, the group that received enteral nutrition had similar pain severity to the group that was NPO (14).

In the pediatric literature, Abu-El-Haija et al, reported that enteral nutrition was well tolerated and not associated with adverse pain outcomes in a small cohort of 38 children admitted with AP (15). Another study by the same group found that early enteral nutrition in mild AP was associated with shorter length of stay, lower rate of intensive care admissions and lower rates of progression to severe AP. A general diet, without restrictions of type of food or fat content, was tolerated in patients who were allowed to eat by mouth (16).

**Summary 1.1:** Initiation of enteral nutrition in mild AP has proven to be of benefit in both adults and children. Early initiation of a normal diet (<48 hours) is feasible in most cases. Oral food intake in children with mild AP is likely to be safe.

**Recommendation 1.1a:** Children with mild AP should be started on a general (regular) diet and advanced as tolerated\*

13/13 = 100% agreement with recommendation.

Voting results: 10 strongly agree; 3 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1B: Strong recommendation; moderate quality evidence

\*As soon as feasible (preferably within 48 hours of admission)

**Recommendation 1.1aa:** Children with mild acute pancreatitis should be nourished preferably via mouth in contrast to nasogastric route.

13/13 = 100% agreement with recommendation.

Voting results: 12 strongly agree; 1 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

#### Enteral Nutrition in Severe Acute Pancreatitis

Most studies involving nutrition in SAP have utilized predicted SAP as criterion. The evidence suggests that enteral nutrition (EN) is superior to lack of EN in SAP outcomes, and EN was associated with reduced complications and lower mortality according to previous studies (14,17–20). SAP carries a high mortality in adult pancreatitis, and carries an increased morbidity in pediatric patients with pancreatitis. Clear evidence from adult data supports EN as beneficial in patients with SAP and as superior to parenteral nutrition (PN) (18,21–28). In a prospective clinical trial, the feasibility and safety of oral food were studied in adult AP and were shown to decrease the length of hospitalization without a difference in adverse outcomes from oral food (29). Retrospective studies, controlled clinical trials, and a meta-analysis have suggested that EN started within 24 and 48 hours after admission is superior to PN and is associated with reduced complications and lower mortality (30–33).

A recent clinical trial did not show superiority of early nasogastric tube feeding compared with an oral diet begun after 72 hours, in terms of reducing the rate of infection or death in patients with predicted SAP (34). It is important to highlight that this study looked at predicted SAP patients, not whether the patients had a complicated course or not. Additionally, both groups eventually received EN (whether eating by mouth in the “on demand” group vs the enteral tube group) and hence the study focused on the timing and type of nutrition in SAP and did not directly study the impact of using nutrition or not in SAP.

**Summary 1.1b:** Initiation of EN in predicted SAP and SAP seems safe. Early initiation (<72 hours from presentation) may be beneficial.

**Recommendation 1.1b:** Enteral nutrition (oral, nasogastric, or nasojejunal as tolerated) should be attempted in children with SAP within 72 hours from presentation to medical care, once deemed hemodynamically stable.

13/13 = 100% agreement with recommendation.

Voting results: 10 strongly agree; 3 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### Enteral Versus Parenteral Nutrition in Acute Pancreatitis

Studies advocate for EN given its safety profile, lower cost, and lower risk of infection compared with PN (17,26). Enteral nutrition is an integral part of AP management as it is associated with lower incidence of infection, less multi-organ failure, lower surgical rates, reduced mortality rates, and shorter hospital stay compared with PN in adult patients according to randomized controlled trials (RCTs) and meta-analyses (33,35,36). No studies have, however, been performed in children to compare EN and PN in AP.

Questions have been raised for patients who do not fully tolerate EN, for example, whether there could be a role for combined therapy with EN and PN. In a randomized study of 100 SAP patients who received PN alone versus PN in addition to EN versus EN only, the groups with EN included as part of the management had fewer complications compared with the group that had no EN included (62 vs 94 patients). Complications included superinfections (8% vs 30%), hepatic functional insufficiency (4% vs 24%), and intraperitoneal infections (4% vs 12%). Groups with EN had earlier restoration of oral nutrition (18.5 vs 24.8 days,

$P < 0.05$ ), a shorter hospital stay (24.5 vs 30.2 days) and a lower hospital cost (4.1 vs 5.8 10,000 yuan,  $P < 0.05$ ) (37). A consideration particularly in younger children is the frequent need for sedation for placement of even peripherally placed central access intravenous lines.

**Summary 1.2:** For patients not meeting caloric goals with EN alone, a combination of EN and PN appears preferable to PN alone.

### Timing of Initiation of Enteral Feedings in Acute Pancreatitis

Studies in adults have shown that EN should be initiated as soon as possible, ideally within 48 hours from admission, especially in the presence of preexisting malnutrition (15,17–19,38). Such comparative studies are not available in pediatrics; therefore, management in children is variable due to this lack of guidelines (39).

In adult patients with AP who are critically ill and hospitalized in an intensive care unit, EN initiated within 48 hours of admission is associated with a reduction of infectious complications and mortality compared to delayed nutrition (38). In 1 systematic review of 11 randomized controlled studies, Petrov et al (40) noted significant benefits of EN over TPN in patients with AP only if nutrition was started within the first 48 hours of admission, whereas no significant benefits were noted if nutritional support was started afterwards. According to published guidelines for adults with AP, early EN initiated within 48 hours of admission improves clinical outcomes by reducing the risk of infections, organ failure, hyperglycemia and death, and by shortening the length of hospitalization in both mild and severe forms of AP (40).

Early nutrition has not been standardized for the management of children with AP, due to lack of data (16,41). In 2010, Park et al (42) published the data of a retrospective chart review on 271 infants and older children with AP at Yale-New Haven Children's Hospital. They concluded that infants/toddlers were less likely than older children to directly transition from NPO to oral feedings. According to studies by Mekitarian Filho et al (43) and Kumar and Gariepy (44), early EN was better than late EN or TPN (the average fasting time for patients with mild disease was 58 hours). A retrospective review of 201 children with AP at Cincinnati Children's Hospital Medical Center reported that 49.7% of children received EN within 24 hours of admission, and 75% received EN within 48 hours. The conclusion of this latter study was that early EN along with early aggressive intravenous fluids management was safe and effective in the management of pediatric AP and was associated with improved outcomes mainly by decreasing the length of hospitalization and rate of SAP (16).

Abu-El-Haija et al (15) published the results of a small (39 patients) retrospective chart review of a prospectively collected nutrition database in mild AP admissions. They concluded that nutrition could be started orally (within 24–48 hours of admission) without increasing pain severity and the length of stay.

**Summary 1.3:** EN is preferred over PN in AP. No data are available on the timing of initiation of PN if EN fails.

**Recommendation 1.3a:** Enteral nutrition is favored over parenteral nutrition when possible in AP.

13/13 = 100% agreement with recommendation.

Voting results: 12 strongly agree; 1 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 1.3b:** Combination of enteral nutrition and parenteral nutrition, rather than parenteral nutrition alone, should be used in children who do not meet caloric goals with enteral nutrition alone and have not received full calories for a week into hospitalization.\*

13/13 = 100% agreement with recommendation.

Voting results: 11 strongly agree; 2 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

\* In infants, there could be consideration for nutritional interventions even earlier than 1 week into the illness due to infants' increased fragility versus older children.

**Recommendation 1.3c:** Parenteral mode of nutrition should be used when oral/nasogastric/nasojejunal feeds are not tolerated.

13/13 = 100% agreement with recommendation.

Voting results: 8 strongly agree; 5 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### Gastric Versus Jejunal Feeding in Acute Pancreatitis

The studies that established the practice of early EN for SAP in adults all provided enteral nutrition via NJ tube (45). Jejunal feeding has the theoretical benefit to provide "rest" for the pancreas by diminishing exocrine secretion into the parenchyma in order to reduce the inflammatory reaction. Even if pancreatic secretions are preferentially reduced by using jejunal feedings rather than gastric feedings, whether this is clinically beneficial has, however, not been proven (46).

No study has compared the use of gastric versus jejunal feedings in adults or children with mild AP. In children, no controlled clinical trials or case control study has compared gastric to jejunal feedings in predicted or confirmed SAP. In adults with SAP, several small controlled clinical trials have been published (47–49). A meta-analysis of 3 RCTs, including 157 subjects with SAP, revealed no difference in mortality, exacerbation of pain, tracheal aspiration, diarrhea and achievement of the nutritional target when using NG versus NJ feeds (50). The relative risk of infection in gastric versus jejunal feedings calculated from 2 of the included studies ( $n = 109$ ) also demonstrated no difference (relative risk 0.78, 95% confidence interval 0.44–1.33) (48,49). These analyses suggested that gastric feeding is safe and well tolerated in AP. A more recent meta-analysis by Zhu et al reviewed 4 RCTs involving 237 patients with SAP and similarly found that NG nutrition was as safe and effective as NJ nutrition in SAP (51). No report has been published that investigate enteral feeding regimens in pediatric AP.

**Summary:** Adult studies suggest that NG feeding is as safe and as effective as NJ feeding in AP whenever clinically tolerated. NJ feedings are indicated when oral and NG feedings are not tolerated.

**Recommendation 1.4a:** Jejunal tube feeding should be reserved for those unable to tolerate oral or nasogastric tube feedings in mild AP.

13/13 = 100% agreement with recommendation.

Voting results: 12 strongly agree; 1 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 1.4b:** Based on the limited data from the adult literature, the use of oral or nasogastric tube feedings in children with SAP is likely to be safe and provide benefit. Clinical trials in children are, however, needed, since there are important differences in the etiology and pathogenesis of pancreatitis between adults and children.

12/13 = 92% agreement with recommendation.

Voting results: 7 strongly agree; 5 agree; 1 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 1.4c:** Even in SAP, jejunal tube feeding should be reserved for those unable to tolerate oral or nasogastric tube feeding.

11/13 = 85% agreement with recommendation.

Voting results: 5 strongly agree; 6 agree; 2 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Diet/Formula Composition in Acute Pancreatitis**

Despite studies in adults with AP demonstrating that nutrition should start as soon as possible, the optimal composition of the enteral feeding (elemental, semielemental, polymeric formulations) remains largely unknown with only few publications addressing this issue (19,40,52). Also uncertain is whether any supplementation of specific amino acids or fats or the addition of probiotics is beneficial. Olah et al (52) reviewed RCTs for enteral nutrition, including glutamine, arginine, nucleotides, and omega-3 fatty acids, and enteral nutrients supplemented with probiotics for patients with AP. These trials demonstrated that “immune-nutrition” could have beneficial effects including shortened hospital stay, reduced gut permeability and decreased plasma endotoxin levels, but clinical outcomes were not significantly different (53–56). A systematic review and meta-analysis (40) showed that the use of polymeric compared with (semi)elemental formulas did not lead to significantly different rates of feeding intolerance, infectious complications or death in patients with AP. A meta-analysis demonstrated that glutamine supplementation resulted in significantly reduced risk of mortality and infectious complications, but not decreased length of hospital stay (57).

Sathiaraj et al (58) and Moraes et al (12) reported a significantly decreased length of hospitalization in those receiving a soft diet compared with those receiving a clear liquid diet ( $P < 0.001$ ). Jacobson et al (59) reported no difference in the length of hospitalization, but that a solid diet provided more energy to patients compared with a liquid diet. The pediatric literature relates to different forms of nutrition. Kumar and Garipey (44) published pediatric experience reporting that rates of perceived intolerance to an initial oral diet were similar between clear liquid and solid diets, 26% and 31%, respectively. Abu-El-Haija et al published a pediatric series echoing the adult population findings of Moraes et al that a general oral diet was well tolerated in mild AP and was not associated with abdominal pain relapse (12,15,16).

The practice of separately providing probiotics in AP management was reviewed in a recent publication on the management of AP by Abu-El-Haija et al (60). There have been concerns about use of probiotics as not only of no benefit, but potentially of being harmful to patients with AP. No voting occurred relating to their use within this document.

**Summary 1.5:** No reports document any clinically important differences in outcomes between polymeric and elemental formulas in AP. No studies reveal any evidence that immune-enhanced nutrients or probiotics are beneficial in the management of AP.

**Recommendation 1.5a:**

The use of specialized formulas or immunonutrition is not necessary in the management of pediatric AP\*

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

\*Future studies could alter this recommendation

### **Areas of Potential Research Relating to Nutrition in Pediatric Acute Pancreatitis**

Based on the literature review and discussions regarding nutritional management in AP, several gaps of knowledge are

identified. Future research should focus on prospective randomized trials in pediatric AP that include management of pain and complications, disease duration, recurrence of attacks, and outcome. Particular areas identified for study in nutrition related to pediatric AP include the following:

- Determining the effect of low-fat versus diet on outcomes of mild AP
- Studying the use of early EN versus delayed nutrition in AP
- Defining benefits of early (within first 24, 48, or 72 hours) versus late EN and PN in the management of predicted SAP and confirmed SAP
- Prospective trials involving EN given via oral/NG versus NJ route in children with (predicted) SAP
- Confirming the effects of formula composition (complete protein, di-tri-peptides, elemental diet; and/or specifically added components such as glutamine, arginine, nucleotides, omega-3 fatty acids) on outcomes in SAP
- Studying the role of the microbiome and how it may relate to intestinal permeability changes and inflammation in AP

### **Nutrition Between Episodes of Acute Recurrent Pancreatitis**

Nutritional therapy following an AP episode or between episodes of ARP has been minimally studied in adults or children. Historically, patients were kept and maintained NPO during an episode of AP until pain and vomiting resolved and until serum levels of pancreatic enzymes returned to normal. This regimen frequently led to prolonged fasting. Since it was presumed that “resting the pancreas” was required to heal an inflamed gland, patients were subsequently treated with a low-fat diet, often for a prolonged period of several weeks or months.

In most reports, the term “low-fat diet” was not well-defined, nor was the length of time that low-fat diet was required. As a reference, a “normal-fat” pediatric diet is defined as a diet containing 30% to 40% fat for children 1 to 3 years old and 25% to 35% fat for 4 to 18 years old. Regular fat diets are typically utilized to provide appropriate caloric and nutrient intakes and food variety for growing children (61). “Low-fat diet” has been defined by adolescent obesity programs as <30% of total calories consisting of fat, with <10% of calories from saturated fats. “ultra/very low fat” has been defined as <20% of total calories from fat (62,63). Others consider “low fat” to be <10% of total calories from fat. Hence, there is disagreement even with respect to definitions of fat content and diet names, leading to a very heterogeneous clinical practice.

Recent evidence summarized above has clearly demonstrated that early, rather than delayed nutrition improves outcome and shortens the duration of disease in AP.

A variety of dietary interventions are recommended for adults following attacks of AP and between attacks of ARP. In spite of these recommendations, data supporting them are sparse. Most studies are small, uncontrolled or contradicted by other studies. Aside from case reports, no published evidence exists in children for any of the interventions discussed below.

### **Fat Content of Diet in Children With Acute Recurrent Pancreatitis**

A low-fat diet has frequently been prescribed following an episode of AP in order to “rest the pancreas.” This concept has led to delayed feeding of patients with AP, a practice that is now generally abandoned, since it is now known that these patients

tolerate enteral feedings (12). For the treatment of hypertriglyceridemia-induced ARP, a low-fat diet is required for the treatment of hypertriglyceridemia and prevention of recurrent attacks (64). For mild and moderate AP, the European Society for Parenteral and Enteral Nutrition recommends a diet with “moderate” (undefined) fat content for 3 to 7 days and a regular diet subsequently (65). A low-fat diet was helpful in the relief of dyspepsia in adults with mild non-alcoholic pancreatic disease. A recent small study in children with AP showed that those given  $>1$  g/kg per day fat had less pain compared to those given a low-fat diet during AP (15), negating the indication for low-fat diet in children with AP. None of these studies followed patients beyond the first AP episode. In general, a regular diet appears safe after the first week of illness in AP.

**Summary 2.1:** No studies have been reported on the use of low-fat versus regular-fat diets between episodes of AP. No evidence supports an indication for a diet differing from a regular diet between episodes of AP in children.

**Recommendation 2.1a:** When tolerated, children should receive a regular-fat diet in between episodes of acute recurrent pancreatitis.\*

12/13 = 92% agreement with recommendation.

Voting results: 10 strongly agree; 2 agree; 1 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

\*Of note: in selected patients who are intolerant of a regular diet, abdominal pain and vomiting may improve on a low-fat diet.

**Recommendation 2.1b:** A regular-fat diet can safely be started within 1 week after the onset of illness in AP as tolerated for cases other than caused by hypertriglyceridemia (triglycerides  $>10$  mmol/L or  $>1000$  mg/dL).\*

12/13 = 92% agreement with recommendation.

Voting results: 7 strongly agree; 5 agree; 1 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Use of Pancreatic Enzyme Replacement Therapy in Children With Acute Recurrent Pancreatitis**

Feedback regulation of pancreatic enzyme secretion is mediated by luminal cholecystokinin (CCK) – releasing factor (LCRF) that is inactivated by trypsin (66). Following a meal, LCRF interacts with CCK-secreting enterochromaffin cells in the proximal intestine, which stimulates CCK secretion. In theory, providing ingested pancreatic enzyme replacement therapy (PERT) will inactivate LCRF, with the consequence that the pancreas will not be stimulated and will be able to “rest.”

Because of this mechanistic rationale, pancreatic enzymes have been given to patients with CP to “rest the pancreas” and therefore to prevent and/or relieve pain. Although ample evidence shows that PERT is beneficial for the treatment of EPI in CP, whether it is beneficial in the treatment or prevention of pain in CP remains controversial. A Cochrane review and a recent meta-analysis cast doubt on the efficacy of PERT in CP (67,68). With respect to management between episodes of ARP, no studies report on the effectiveness of PERT following an episode of AP in adults or in children, or in between episodes in ARP. Patients with ARP by definition are pancreatic exocrine sufficient. Since some patients develop transient pancreatic insufficiency following an episode of severe AP, some authors, however, recommend the use of PERT during the recovery phase (69). The use of pancreatic supplements in patients without EPI is not indicated.

**Summary 2.2:** There is insufficient literature reporting on the benefit of pancreatic enzyme replacement therapy in ARP, whether in pediatrics or adults.

**Recommendation 2.2a:** Pancreatic enzyme replacement therapy should not be routinely used in children diagnosed with acute recurrent pancreatitis, who do not have EPI.

13/13 = 100% agreement with recommendation.

Voting results: 11 strongly agree; 2 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Use of Antioxidants in Acute Recurrent Pancreatitis**

Since oxidative stress is associated with pancreatitis and antioxidants are depleted during episodes of AP, it was hypothesized that antioxidant supplementation may be beneficial in the treatment and prevention of episodes (70). Despite data from animal models, published reports in humans has been contradictory (70). A recent meta-analysis demonstrated that in adults, antioxidants reduced the length of stay in AP by 2.59 days, but have no effect on CP pain (71). Another meta-analysis demonstrates no benefit in adult patients with CP (72). A recent Cochrane review also demonstrates no benefit for pain in CP (67).

In a case report, antioxidants were shown to be beneficial in reducing pain episodes in 3 children with hereditary pancreatitis (73). No other published data are available on the use of antioxidants for AP or ARP in children.

Certain vitamins have been used as part of anti-oxidant cocktails used in pancreatitis studies (vitamin C and vitamin E in particular) (73). No studies have specifically investigated whether the use of vitamins alone could be beneficial in AP or ARP.

**Summary 2.3:** No strong medical evidence supports the use of anti-oxidants in the ARP population—whether to reduce risk of recurrence, pain, or improve nutritional outcome. Studies have not demonstrated any negative effects of antioxidant use. Significant heterogeneity exists in types of antioxidants utilized and dosages across studies for AP and CP.

**Recommendation 2.3a:** There is insufficient evidence to support supplementing children with acute recurrent pancreatitis with antioxidants. We cannot recommend this therapy at this time.

13/13 = 100% agreement with recommendation.

Voting results: 11 strongly agree; 2 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Use of Probiotics in Acute Recurrent Pancreatitis**

Probiotics have been proposed for their potential immunomodulatory effects, restoration of gut integrity, to decrease bacterial translocation and for the prevention of the proliferation of harmful bacteria. No literature, however, exists on the application of probiotics between episodes of AP, whether for pediatric or adult populations. Due to lack of medical evidence supporting or refuting use of probiotics in ARP, no summary-voting occurred.

### **Areas of Potential Research in Nutritional Management of Acute Recurrent Pancreatitis**

Specific questions raised by the literature review and group discussion highlighted the following needs in pediatric ARP:

- Determining whether a normal-fat diet is harmful and whether or not a low-fat diet is beneficial in reducing pain and recurrent episodes of ARP.
- Studying whether PERT improves nutrition and/or reduces pain and recurrent episodes of AP in ARP patients—ideally via a randomized, double-blind, controlled study (based on adult CP literature with some studies showing benefit from PERT)

- Determining whether antioxidants and probiotics have beneficial effects such as decreased pain, fewer episodes of AP, and improved nutrition.

Due to the relative infrequency of ARP, all these proposed studies would need to be conducted as multicenter studies.

### **Nutrition in Children Diagnosed With Chronic Pancreatitis, With or Without Exocrine Pancreatic Insufficiency and/or Pancreatogenic Diabetes**

Data from the INSPPIRE cohort has shown that one-third of children with CP have EPI (74), and a Polish study has demonstrated that 25% of children with CP have malnutrition (75).

Nevertheless, data regarding nutrition in pediatric CP are scarce and mostly limited to small retrospective reviews that lack both power and consistency to offer real impact on clinical care. As such, clinicians have been required to extrapolate findings from the adult literature or rely on anecdotal experience. Given the differences in etiologies between adult and pediatric patients with CP, particularly the increased identification of *CFTR* mutations among patients with CP (76), many providers have begun to utilize the results from cystic fibrosis (CF) nutritional studies to guide long-term management.

CP and CF patients share many similar nutritional concerns that include, but are not limited to increased energy expenditure; possible EPI resulting in fat maldigestion/malabsorption and fat-soluble vitamin deficiencies; micronutrient deficiencies; development and impact of diabetes; and long-term effects on bone health. Therefore, the lessons learned through the broader body of research in CF nutrition provide a logical starting point in discussing nutrition in pediatric CP as many parallels are likely to exist, but do not replace the necessary studies that are required to optimize nutritional care for children with CP.

In this section, we review the limited work on pediatric CP nutrition as well as adult CP and pediatric CF nutritional studies as they may pertain to pediatric CP. Recommendations are made where appropriate, but more importantly we highlight the areas where research is required to optimize the nutritional care of pediatric patients with CP.

### **Calorie Requirements and Monitoring in Pediatric Patients with Chronic Pancreatitis**

The effect of CP on the resting energy expenditure (REE) in children is unknown. Adult literature suggests that REE may be 30% to 50% greater than normal or up to 1.5 to 1.8× the basal energy expenditure in patients with CP (77–79). This has led many to recommend a higher calorie diet in adult patients with CP. Given the lack of nutritional guidelines in children with CP, adequate growth and nutrition has been monitored via validated pediatric measures of nutrition including; weight, height, body mass index (BMI), mid arm circumference, triceps skin fold, handgrip strength, nutritional assessments, and bio-impedance in a few studies (80,81). Duggan et al reported that BMI is lower in patients with CP compared with controls, although 30% of patients with CP in their study were obese. They also reported lower handgrip strength, fat and muscle stores in patients with CP compared with controls (82). Recommendations exist for nutritional management of children and adults with CF and EPI (83). Rasmussen et al recommend screening patients with CP every 3 to 6 months; in comparison, children with CF are screened at least every 3 months (81).

**Summary 3.1:** Pediatric patients with CP may have higher resting energy requirements compared with healthy subjects.

Routine monitoring of growth parameters with weight, height and BMI is recommended. Limited data exist on other nutritional assessments including anthropometric measurements, handgrip strength, bioelectric impedance to monitor nutrition and adequate growth.

**Recommendation 3.1a:** Children with chronic pancreatitis should undergo routine surveillance to screen for signs of impaired growth and/or malnutrition utilizing validated measures of nutrition including weight, height, and BMI.

13/13 = 100% agreement with recommendation.

Voting results: 12 strongly agree; 1 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.1b:** The frequency of evaluation of children with chronic pancreatitis for signs of impaired growth/malnutrition should be every 3 to 6 months.

13/13 = 100% agreement with recommendation.

Voting results: 10 strongly agree; 3 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Macronutrient Requirements and Monitoring in Children With Chronic Pancreatitis**

The ideal dietary macronutrient (protein, fat, carbohydrate) composition for children with CP has not been studied. Adult recommendations vary from a regular diet with standard protein, fat and carbohydrate proportions to a carbohydrate-rich diet consisting of 1.0 to 1.5 g/kg body weight of protein per day, no more than 30% to 40% of total calories from fat and approximately 50% of total calories from carbohydrates (10,79,80,84). In some adult studies of patients with CP and persistent abdominal pain, decreasing fat content to less than 30% and/or increasing the proportion of medium chain triglycerides or transitioning to hydrolyzed formulas (10,85,86) result in decreased pain (85,87). In patients with CP and type 3c diabetes mellitus (T3cDM), carbohydrates and the proportion of medium chain triglycerides may need to be limited to prevent ketoacidosis (10,80,81). In pediatric patients with CF and EPI, a diet consisting of 35% to 40% fat, 20% protein, and 40% to 45% carbohydrates has been recommended (88–90).

**Summary 3.2:** No specific studies address the ideal macronutrient composition that is required in the diet of children with CP.

**Recommendation 3.2a:** Children with chronic pancreatitis, with or without EPI, should receive a regular diet.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.2b:** Children who have both chronic pancreatitis and type 3c diabetes mellitus require specialized diabetic nutritional evaluation.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Vitamin, Mineral and Trace Element Requirements and Monitoring for Deficiencies in Children With Chronic Pancreatitis**

Deficiencies in vitamins, minerals, and trace elements have only been studied in adults with CP, but not in children.

Deficiencies in the fat-soluble vitamins E, A, and D are common in patients with CP (82,91–99); vitamin A deficiency

specifically correlates with malnutrition (82). Likewise, in patients with CF, fat-soluble vitamin deficiencies are also common. Yearly screening for vitamin D status, preferably at the end of winter, using the serum 25-hydroxyvitamin D measurement is recommended. A minimal 25-hydroxyvitamin D concentration of 30 ng/mL (75 nmol/L) is considered indicative of vitamin D sufficiency in children with CF. If supplementation is required, the level is rechecked 3 months after initiating therapy or dosing change (100). Annual testing for vitamin A and E (alpha, beta, and gamma tocopherol) is also recommended in CF. Additionally, vitamin K (PIVKA-II or PT or vitamin concentrations) is monitored in CF if any patient has a history of liver disease and/or bleeding (101,102).

Data regarding water-soluble vitamin deficiencies and requirements is scarce and limited to small-size cohorts in pediatric CP. Serum ascorbate levels were low in a small cohort of adults with CP in South Africa (95). In another study, vitamin C levels were low in patients with alcoholic and tropical pancreatitis compared with controls (103). An additional study reported low levels of vitamin B12 in CP (104). Routine monitoring of ascorbate and other vitamins is not recommended for adults with CP (101).

Literature regarding deficiencies of trace elements and minerals is also limited. Selenium levels are low in patients with CP (95–98,105,106). One study including 7 children with CP revealed selenium levels significantly lower in CP compared with controls (107). Likewise, zinc levels have also been shown to be low in CP (98,108), while copper is reported as generally high (98,108,109). In 1 report, screening for trace elements in adults with CP was recommended 1 to 2 times per year (81). Although zinc deficiency may occur in patients with CF, routine zinc monitoring is not recommended. Additionally, zinc deficiency may occur despite normal serum levels (101). Selenium levels may be low in patients with CF; therefore, supplementing with selenium may be beneficial (ie, pain relief in CP from antioxidant preparations that contain selenium) (110), but routine monitoring is not currently recommended.

**Summary 3.3:** Children with CP are at risk for vitamin, mineral and trace element deficiencies.

**Recommendation 3.3a:** Children with chronic pancreatitis should have fat-soluble vitamin levels measured every 6 to 12 months.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.3b:** If supplemental vitamins are provided in chronic pancreatitis, levels should be repeated 3 months after dose adjustment.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.3c:** There is no evidence to recommend routine monitoring of other vitamins, minerals or trace elements in chronic pancreatitis unless their deficiencies are suspected clinically.

13/13 = 100% agreement with recommendation.

Voting results: 8 strongly agree; 5 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Bone Health and Monitoring for Osteoporosis in Children With Chronic Pancreatitis**

No data exist on bone health in children with CP. Adults with CP (alcohol-induced) have abnormal bone mineral density (BMD), which is accentuated in the presence of EPI even with use of

pancreatic enzymes (111). In 1 study, an abnormal dual-energy x-ray absorptiometry (DEXA) showing osteopenia/osteoporosis was associated with advanced CP, abnormal fecal elastase and vitamin D levels (112). In adults with CP, 65% have been shown to have low BMD compared to 10% of controls (113,114) with approximately 40% having osteopenia, and about 25% osteoporosis (115). Patients with CP are at a higher risk for bone fractures (hazard ratio: 1.7); risk is further increased with alcohol use, older age and longer duration of disease (116). Children with CP undergo baseline BMD if: >8 years of age, if <90% ideal weight, if forced expiratory volume in 1 second (FEV1) is <50% predicted, or if on steroids >5 mg/day for >90 days/year, delayed puberty or history of fractures. Follow-up DEXA depends on results of the baseline study (117). Decreased BMD in CF, similar to that seen in adults with CP, is more likely in adolescents and adults and is probably secondary to both systemic inflammation resulting in bone reabsorption and nutritional deficiencies secondary to EPI (118).

**Summary 3.4:** Abnormal BMD is reported in adults with CP and screening is recommended in patients with CF and selected predisposing factors. No data are available for pediatric CP.

**Recommendation 3.4a:** BMD should be measured in children with chronic pancreatitis and malnutrition, persistently low vitamin D or history of fractures, specifically in vertebrae, hip, or wrist.

13/13 = 100% agreement with recommendation.

Voting results: 10 strongly agree; 3 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

### **Complications of Chronic Pancreatitis (Exocrine Pancreatic Insufficiency and Type 3c Diabetes Mellitus) and Impact on Nutrition**

Patients with CP are at risk for developing both EPI and T3cDM, although the nutritional consequences of these complications in pediatric patients with CP have not been well explored.

Adult guidelines suggest that any patient with CP showing poor weight gain, nutritional deficiencies, chronic abdominal pain, or steatorrhea should be tested for EPI and treated with appropriate PERT (78,119,120). Fecal elastase-1 (FE-1) is widely used for the diagnosis of EPI (121). In general, a value <100 µg/g is diagnostic. Testing should be performed on formed (baseline) stool, as results may be falsely low with a watery stool. A 72-hour fecal fat test can be done to identify steatorrhea and coefficient of fat absorption [CFA: (grams of fat ingested-grams of fat excreted)/(grams of fat ingested) × 100] can be calculated. An absorption value of <85% of fat intake is considered abnormal in children younger than 6 months of age, and <93% is abnormal for children older than 6 months of age (122). Direct pancreatic secretion testing (collection of pancreatic/intestinal fluid) is considered invasive and not commonly used. A secretin-stimulated MRI/MRCP test to estimate exocrine pancreatic function in children is under investigation (123). Dosing of PERT is not known for children with CP, but well-studied in CF. Children with CF <4 years of age typically require 1000 to 2500 lipase units/kg per meal; 500 to 2500 lipase units/kg per meal are used for those >4 years of age and 25,000 to 40,000 units lipase/meal are used for adults. Lipase may also be dosed based on grams of fat ingested with 500 to 4000 units lipase per gram fat (average 1800 units lipase per gram fat ingested). For snacks, half the dose is recommended. Infants may be given 2000 to 4000 units per 120 mL of infant formula or per breast-feeding. Doses are adjusted based on effect (clinical, stool, growth). The daily dose for most patients is aimed at less than 10,000 units of lipase/kg per day or 6000 units of lipase/kg per meal to prevent fibrosing colonopathy (124).



The effect of diabetes on nutritional status in CP is less clear. It has been suggested that dietary restriction for blood sugar control should be less stringent in this population than in individuals with non-CP-related diabetes because of the combined risk of hypoglycemia and malnutrition associated with CP (80). Special concern must be paid to hyperglycemia as it may impair weight gain, possibly by increasing REE (125). Of special interest, a recent review has emphasized the importance of monitoring, and preventing hypo- and hyperglycemia, addressing malnutrition, treating EPI and diabetes-related complications in adults with CP and T3cDM (126). No published studies exist on children with CP and T3cDM.

Singh et al. reported no difference in vitamin A and E levels between patients with CP alone compared with CP and T3cDM (127), but Quilliot et al found lower levels in patients with CP and T3cDM (98). Both vitamin A and E levels can be lower in the presence of steatorrhea (93,94). In CF, recommendations for screening and treating with vitamins A, D, E and other vitamins apply to all patients with CF regardless of EPI or diabetes status.

Selenium and zinc are low in adults with CP regardless of the diabetes status, but significantly lower in patients with CP and T3cDM compared with controls (128). This finding, however, could not be replicated in a similar study done by the same team (98). Quilliot et al also showed low selenium and zinc levels and urine copper excretion correlate with diabetes status (129). In another study, serum zinc was higher in patients with CP and EPI, but not different if diabetes was present (130). Selenium has been described as low only in patients with CP and EPI (131), but a study of 7 children with only CP demonstrated low levels (107). In adults with CP and T3cDM, copper levels were not significantly different than in controls. Of note, in CF patients, recommendations for screening of trace elements and minerals are not different between CF, CF with EPI, or CF with T3cDM.

**Summary 3.5:** EPI and T3cDM are long-term risks associated with CP. Untreated EPI may result in maldigestion, malabsorption of fat and fat-soluble vitamins, nutritional deficiencies, and/or abdominal pain, which may all lead to poor growth. Uncontrolled diabetes in CP, likewise, may lead to poor growth and nutrition.

**Recommendation 3.5a:** Children with chronic pancreatitis should be screened for pancreatic exocrine insufficiency every 6 to 12 months utilizing fecal elastase or 72 hour fecal fat collection.  
12/13 = 92% agreement with recommendation.

Voting results: 7 strongly agree; 5 agree; 1 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.5b:** In children with chronic pancreatitis and EPI, pancreatic enzyme replacement therapy dosing should be similar to recommendations established for treating EPI in cystic fibrosis.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.5c:** Dosing of pancreatic enzyme replacement therapy should be followed clinically, and via repeating tests of fat maldigestion/ malabsorption as necessary.

13/13 = 100% agreement with recommendation.

Voting results: 10 strongly agree; 3 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.5d:** In patients with type 3c diabetes mellitus, strict adherence to glucose control should be maintained to prevent hypoglycemia, malnutrition and hyperglycemia-associated weight loss.

13/13 = 100% agreement with recommendation.

Voting results: 9 strongly agree; 4 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

**Recommendation 3.5e:** Children with chronic pancreatitis who develop EPI and/or type 3c diabetes mellitus require more frequent follow-up for malnutrition, growth delay and vitamin deficiencies than the general chronic pancreatitis population.

13/13 = 100% agreement with recommendation.

Voting results: 12 strongly agree; 1 agree; 0 neutral; 0 disagree; 0 strongly disagree

GRADE 1C: Strong recommendation; low-quality evidence

## Areas of Potential Research in Chronic Pancreatitis

The following areas are identified as key aspects requiring further study:

- Determining the changes in REE (or basal energy expenditure) in children with CP compared with those without CP
- Determining the changes in REE in children with CP and associated complications including EPI, chronic pain, T3cDM, and potentially pancreatic cancer
- Exploring whether other nutritional measures (mid arm circumference, triceps skin fold, handgrip strength, bioimpedance) are beneficial for nutritional monitoring in pediatric CP
- Determining the effect of dietary macronutrient composition on nutrition, growth and disease outcomes in children with CP
- Investigating the effect of dietary fat, protein and carbohydrate content on disease complications such as recurrent attacks (acute on chronic) and chronic abdominal pain
- Determining the prevalence of vitamin, mineral and trace element deficiencies in children with CP
- Defining adequate vitamin, mineral and trace element dosing requirements in pediatric CP
- Defining potential impact of these deficiencies on disease outcomes
- Determining whether children with CP are prone to low BMD
- Identifying risk factors that may predispose children to osteopenia and osteoporosis.
- Determining the effects of EPI and T3cDM on nutritional outcomes in children with CP
- Identifying adequate pancreatic enzyme and vitamin/mineral/trace element dosing for optimal nutrition in children with CP

## Summary Recommendations

Table 1 summarizes the recommendations made by the writing group. All 29 recommendations received at least 75% support (5 = strongly agree or 4 = agree). Most recommendations are supported by a Grade 1C evidence: strong recommendation but low-quality evidence, and several recommendations are based on expert opinion due to the lack of medical literature. Only 1 recommendation, recommendation 1.1a relating to advancement of nutrition in mild AP, is supported by moderate-quality evidence.

## Concluding Remarks

This document represents the first set of expert opinion recommendations on optimal nutritional management for children with AP, ARP, and CP, involving a combined international effort by NASPGHAN and ESPGHAN. Early enteral nutrition with a return to a normal-fat diet appears most optimal for children along the spectrum of AP, ARP, and CP. Little to no research is published

TABLE 1. Summary of recommendations

Category	Recommendation	
Acute pancreatitis	1.1a Children with mild AP should be started on a general (regular) diet and advanced as tolerated. *Grade 1B	
	1.1aa Children with mild AP should be nourished preferably via mouth as compared to nasogastric route.	
	1.1b Enteral nutrition (oral, NG or NJ as tolerated) should be attempted in children with SAP within 72 hours from presentation to medical care, once deemed hemodynamically stable.	
	1.3a EN is favored over PN when possible in AP.	
	1.3b Combination of EN and PN, rather than PN alone, should be used in children who do not meet caloric goals with EN alone and have not received full calories for a week into hospitalization.	
	1.3c Parenteral mode of nutrition should be used when oral/ NG/NJ feeds are not tolerated.	
	1.4a Jejunal tube feedings should be reserved for those unable to tolerate oral or nasogastric tube feedings in mild AP.	
	1.4b Based on the limited data from the adult literature the use of oral or NG tube feeding in children with SAP is likely to be safe and provide benefit. However, clinical trials in children are needed since there are important differences in the etiology and pathogenesis of pancreatitis between adults and children.	
	1.4c Even in severe AP, jejunal tube feeding should be reserved for those unable to tolerate oral or NG tube feeding.	
	1.5a The use of specialized formulas or immunonutrition is not necessary in the management of pediatric AP.	
	Acute recurrent pancreatitis	2.1a When tolerated, children should receive a regular-fat diet in between episodes of ARP
		2.1b A regular-fat diet can safely be started within 1 week after the onset of illness in AP as tolerated for cases other than caused by hypertriglyceridemia (triglycerides > 1000mg/dL or > 10mmol/L).
		2.2a PERT should not be routinely used in children diagnosed with ARP, who do not have EPI.
	Chronic pancreatitis	2.3a There is insufficient evidence to support supplementing children with ARP with antioxidants. We cannot recommend this therapy at this time.
		3.1a Children with CP should undergo routine surveillance to screen for signs of impaired growth and/or malnutrition utilizing validated measures of nutrition including weight, height and BMI.
3.1b The frequency of evaluation of children with CP for signs of impaired growth/ malnutrition should be every 3 to 6 months.		
3.2a Children with CP, with or without EPI, should receive a regular diet.		
3.2b Children who have both CP and T3cDM require specialized diabetic nutritional evaluation.		
3.3a Children with CP should have fat-soluble vitamin levels measured every 6 to 12 months.		
3.3b If supplemental vitamins are provided in CP, levels should be repeated 3 months after dose adjustment.		
3.3c There is no evidence to recommend routine monitoring of other vitamins, minerals or trace elements in CP unless their deficiencies are suspected clinically.		
3.4a BMD should be measured in children with CP and malnutrition, persistently low vitamin D or history of fractures, specifically in vertebrae, hip, or wrist.		
3.5a Children with CP should be screened for pancreatic exocrine insufficiency every 6 to 12 months utilizing fecal elastase or 72h fecal fat collection.		
3.5b In children with CP and EPI, PERT dosing should be similar to recommendations established for treating EPI in CF.		
3.5c Dosing of PERT should be followed clinically and via repeating tests of fat maldigestion/ malabsorption as necessary.		
3.5d In patients with T3cDM, strict adherence to glucose control should be maintained to prevent hypoglycemia, malnutrition and hyperglycemia-associated weight loss.		
3.5e Children with CP who develop EPI and/or T3cDM require more frequent follow-up for malnutrition, growth delay and vitamin deficiencies than the general CP population.		

AP = acute pancreatitis; ARP = acute recurrent pancreatitis; BMD = bone mineral density; BMI = body mass index; CP = chronic pancreatitis; EN = enteral nutrition; EPI = exocrine pancreatic insufficiency; NG = nasogastric tube; NJ = nasojejunal tube; PERT = pancreatic enzyme replacement therapy; PN = parenteral nutrition; SAP = severe acute pancreatitis; T3cDM = type 3c diabetes mellitus.

\*Only recommendation of Grade 1B support. All other recommendations within this table are Grade 1C.

involving nutrition in children with ARP. Special attention must be directed towards children with CP, who are at risk of developing complications such as EPI and T3cDM that will further affect their nutritional status. Review of the literature revealed lack of information and data in the area of nutrition in pediatric pancreatology—a limitation that led to most recommendations being expert recommendations rather than strongly evidence-based. This clinical report should serve as basis and stimulus for future research to expand the evidence for specific nutritional interventions in children with pancreatic diseases.

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