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The Role of the Crohn's Disease Exclusion Diet in Treatment and Management of Crohn's Disease


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The increasing incidence of inflammatory bowel disease underscores the importance of environmental factors, particularly nutrition, in disease development. Diet plays a key role in shaping the gut microbiome, modulating immune responses, and maintaining intestinal barrier integrity, making nutritional therapy a valuable approach in management. Exclusive enteral nutrition is effective for inducing remission in pediatric Crohn's disease, with outcomes comparable to corticosteroids and added benefits for growth, nutritional status, and mucosal healing. However, its limited palatability, restrictive nature, and scarce adult data hinder widespread use. The Crohn's Disease Exclusion Diet, especially when combined with partial enteral nutrition, has demonstrated efficacy in inducing remission in mild-to-moderate Crohn's disease and may help maintain remission, although long-term data remain limited. This review outlines current advances in the diet in treatment of both pediatric and adult Crohn's disease.

BACKGROUND

The dramatic increase in inflammatory bowel disease (IBD) in industrialized countries and those adopting a Western diet suggest that environmental factors, including diet, are key contributors to the etiology of this disease. It is well established that dietary intake drives the gut microbiome, the intestinal immune response, and the intestinal barrier function. Nutritional interventions can play a significant role in managing Crohn's disease (CD) by targeting inflammation and thereby alleviating symptoms.

Exclusive enteral nutrition (EEN) was the

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first nutritional therapy shown to be effective in the treatment of CD. It involves the use of a nutritionally complete liquid formula as the sole source of nutrition for a defined period, typically 6–12 weeks, to induce remission.[1] Although introduced in the 1970s, it was not until the late 1990s and early 2000s that randomized controlled trials and subsequent meta-analyses established its efficacy as a first-line therapy for children with active CD. These studies demonstrated that EEN is at least as effective as corticosteroids for inducing clinical remission, with additional benefits of improved growth, nutritional status, and mucosal healing, and without the steroid-related adverse effects.[2]

Although effective, EEN adherence is often limited to its poor palatability and strict regimen. This prompted further studies leading to the development of partial enteral nutrition (PEN), a nutritional therapy where a patient receives from 35% to up to 80% of their daily caloric needs via a nutrient-rich formula. Early attempts in the early 2000s to use PEN in conjunction with whole foods failed to induce remission, highlighting that the benefits of EEN arise not only from the formula's composition but also from the exclusion of specific inflammatory dietary components.[3,4] Recent evidence supports PEN as an adjunct therapy in CD, particularly for maintenance of remission and in alongside combination therapies. It demonstrated a dose-dependent benefit in reducing relapse risk, with higher caloric intake associated with greater efficacy. Emerging data also suggests PEN may enhance outcomes when combined with biologics, including improved short-term clinical response and sustained endoscopic remission with anti-tumor necrosis factor (TNF) therapy.[5,6]

More recently, research has shifted toward combining PEN with anti-inflammatory dietary interventions. Compared with EEN, the Crohn's Disease Exclusion Diet (CDED) with PEN offers a structured anti-inflammatory approach that incorporates whole foods that is less restrictive for inducing remission in pediatric and adult patients with mild-to-moderate CD.[7] This review summarizes the diet phases and the evidence supporting the use of CDED in both pediatric and adult populations.

The Phases of the CDED

CDED is indicated for induction and maintenance of remission in pediatric and adult patients with mild-to-moderate luminal CD, particularly those with relatively short disease duration.[8,9] The diet may also be useful in patients with loss of response to biologic therapy as a bridge, rescue, or adjunctive therapy (See Table 1). Caution is advised in patients who are underweight. Relative contraindications to CDED include strictures, severe malnutrition, and patients with avoidant/restrictive food intake disorder (ARFID) or other eating disorders.[7,10]

Phase 1 (Week 0-6)[7,11-13]

- Is the induction phase
- 50% of total energy needs are provided by whole foods and the remaining 50% of energy and protein requirements are supplied through PEN
- In this phase, there is an increased risk of weight loss, malnutrition, and micronutrient deficiencies if patients are not properly monitored

Phase 2 (Week 7-12)

- It is the transition phase with gradual diet liberalization
- Intake of whole foods is increased to provide 75% of total energy and protein requirements, while PEN is reduced to 25%

Phase 3 (Week >12)[10,14]

- Is the maintenance phase. Some patients may continue to use PEN, but the overall goal is full transition to a long-term whole-food diet.
- This phase allows up to four "free meals" per week; ongoing studies are evaluating outcomes in both pediatric and adult populations

The standard CDED protocol requires mandatory intake of two boiled and cooled potatoes, two bananas, and one peeled apple as sources of resistant starches and chicken breast, fish, and eggs as protein sources during the first two phases of the

Table 1. Phases of Crohn's Disease Exclusion Diet

	Phase 1 (Induction Phase): Weeks 0-6	Phase 2 (Transition Phase): Weeks 7-12	Phase 3: Maintenance Phase
Phase Overview	• Increase soluble fiber • Increase prebiotic fiber • Increase resistant starch • Decrease insoluble fiber • Decrease fermentable fiber • Gluten/dairy-free • Rice/rice flour is the only grain allowed	• Increase soluble fiber • Increase insoluble fiber • Increase fermentable fiber • Continues to be dairy-free • Gradual reintroduction of legumes, gluten as whole grain bread, and other grains such as oatmeal and quinoa • Increase in variety of other fruits and vegetables	• Expand and diversify intake of recommended foods based on tolerance and preference • Reintroduction of yogurt as primary form of dairy • All fibers allowed • Mandatory foods by choice now • Diet is for 5 days per week, allows 2 "skip days"* *Encourage homemade food over processed foods for the skip days
Foods Allowed	**Mandatory** Chicken breast Egg Two potatoes (boiled/cooled, ok to reheat) Two bananas One peeled apple **Allowed** Lean fish, rice (white) avocado, strawberries, melon, tomatoes, cucumbers, carrot, spinach, lettuce **Condiments** Olive/canola oil, fresh herbs (parsley, basil, etc.), lemon juice, garlic, ginger, salt, pepper, cumin, turmeric **Sweeteners** Honey, table sugar **Drinks** Water, sparkling water, home-squeezed orange juice, herbal teas (lemon, mint)	**Additions from Phase 1** Tuna, lean beef (up to 7 oz) per week (1 slice/day) whole-grain bread daily, oats, quinoa, legumes, other fruits and vegetables (e.g., red pepper, blueberry, sweet potato, broccoli, kiwi) nuts- walnuts and almonds (small quantity, unsalted, unroasted, unprocessed)	**All foods are allowed except:** Processed, precooked or smoked meats and fish (sausages, luncheon meats, salami, fish sticks), soy products, persimmons, pomegranate, cactus fruits, passion fruit, dried fruits (sulphate-free dried fruits allowed on weekends), canned fruit, large portions of kale, leeks, asparagus, artichokes, soft drinks, instant coffee, alcohol
Partial Enteral Nutrition	50% of calorie needs	25% of calorie needs	PEN is optional or can be used to promote weight gain

diet. In vegetarian and vegan patients, maintaining adequate intake of protein and key micronutrients (e.g., vitamin B12) is essential. The standard CDED protocol has not been formally studied or validated in these populations, and adaptations would require substituting the animal protein sources, which are limited by the exclusion of plant protein sources in Phase 1 of the diet. The use of PEN can help meet protein and caloric needs and plant-based formulas can be used as alternatives.

Enteral nutrition formulas used in CDED

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(See Table 2) are available over the counter or by prescription, with potential insurance coverage. These formulas may be purchased without a prescription from pharmacies, grocery stores, and online retailers; however, this represents a potential significant out-of-pocket expense for many. For insurance coverage, formulas may be reimbursed when prescribed by a physician for medical nutrition therapy in CD, particularly in pediatric patients receiving EEN and who may require enteral feeding tube support. As coverage varies widely across insurance plans, patients should work with their gastroenterologist to obtain a prescription with appropriate diagnostic codes and the provider's office must submit medical documentation that highlights and justifies the formula's therapeutic role in treatment of CD.

The Role of the Gut Microbiome

Several dietary components influence the impact of the complex regulation of intestinal permeability, which is influenced by mucosal integrity, microbiome disbalances, and inflammatory changes in the epithelium.

In patients treated with CDED combined with PEN, diet-induced remission was associated with a correction of dysbiosis and change in both, the

Table 2. Options for Enteral Formulas

Formula Type	Macronutrients	Pros	Cons	Examples*
Polymeric (intact nutrients)	• Milk-based (whey, lactose free) or plant-based (pea protein)	• Ready to drink • Variety of flavors • Caloric density 0.6-2.4 calories per milliliter	• Cost • Some brands not available in retail stores • Plant-based contain fiber	**Pediatric** PediaSure®, Boost Kids Essentials®; Kate Farms Pediatric Standard 1.2® **Adult** Ensure Plus®, Boost Plus®, Kate Farms Standard®
Semi-elemental (hydrolyzed peptide-based)	• Milk-based (whey, lactose free) or plant-based (pea protein) • Maltodextrin, corn starch • Medium-chain triglycerides, soybean oil	• Ready to drink • Caloric density 1.0-1.5 calories per milliliter	• Cost • Access/availability • Less flavor options • Taste • Plant-based contain fiber	**Pediatric** PediaSure® Peptide®, Peptamen Jr®; Kate Farms Pediatric Peptide Standard 1.2® **Adult** Vital®, Peptamen®, Kate Farms Peptide®
Elemental (amino acid-based)	• Free amino acids • Maltodextrin, modified corn starch • Medium-chain triglycerides, soybean oil	• Caloric density is 1.0 calorie per milliliter – can be adjusted for higher calorie needs	• Cost • Access/availability • Most brands only have powder • Taste • Micronutrient needs may not be met in older patients	**Pediatric** Elecare Jr®, Alfamino Junior®; Neocate Junior® **Adult** Vivonex RTF®

*Names of formula are for educational purposes and do not endorse any brand

composition of the microbiome, as well as its metabolic pathways towards that of the microbial community in healthy controls.[15]

CDED has been shown to improve intestinal barrier integrity and induce distinct microbiome modifications, characterized by a reduction in Proteobacteria, and an increase in Firmicutes and Bacteroidetes—changes that correlate with clinical remission.[11,15-17]

CDED has also been associated with a more diverse gut microbiome compared with EEN, which may confer greater long-term benefit.[11] Despite these microbial shifts, diet-induced remission has not been consistently associated with sustained changes in short-chain fatty acids (SCFAs) or bile acids (BAs).[15]

A broader metabolomic analysis has shown that both the CDED combined with PEN, and EEN, are associated with significant changes in IBD-related metabolites, including kynurenine, ceramides, and amino acids. Reductions in specific kynurenine pathway metabolites (the primary route of tryptophan metabolism) and increases in serotonin pathway metabolites, have been associated with diet-induced and sustained remission.[18,19] Importantly, in samples from patients who failed to maintain remission, these metabolic changes were not observed.

Table 3. Comparison of EEN and CDED with PEN Therapies

	EEN[29,30]	CDED with PEN[11,26,27]
Population	Pediatric and adult Crohn's disease	
Disease Activity	Mild to moderate disease activity	
Disease Phenotype	Inflammatory: Primary treatment in mild to moderate disease Fistulizing: Not recommended as primary treatment Stricturing: EEN used as preoperative nutrition optimization; CDED with PEN is not used as primary treatment	
Therapeutic Use	Primary therapy: Yes Adjunctive therapy: Yes Salvage therapy: Yes, but not well-established or routinely used	
Evidence Source	• Randomized controlled trials • Systematic reviews • Meta-analyses • Cohort studies • Clinical guidelines	• Randomized controlled trials • Systematic reviews
Results	• Clinical remission: up to 80% pediatric cases • Endoscopic remission: 89% at week 8	• Clinical remission 75-80% at 25 weeks • Endoscopic remission 35% at 24 weeks
Structure	• 100% liquid diet • 100% energy and protein intake from enteral formula • Polymeric (intact nutrient formula) can be used. Elemental (hydrolyzed) formulas are not indicated unless polymeric formulas are not tolerated well	• A whole-food diet with enteral formula to supplement the diet
Phases	• Use for 4-12 weeks for induction of remission	• Phase 1: Week 0-6 50% CDED whole foods + 50% PEN • Phase 2: Week 7-12 75% CDED whole foods + 25% PEN • Phase 3: Week ≥12 75% CDED whole foods + 25% PEN

Pediatric Evidence with the CDED

There is strong evidence that CDED, particularly in combination with PEN, can induce remission in pediatric CD (See Table 3).

A pivotal study by Sigall-Boneh et al. found that 70% of children with active, mild-to-moderate luminal CD achieved clinical remission after six weeks with CDED plus 50% of calories coming from PEN.[8] Notably, six of seven patients adhering to CDED without PEN also achieved clinical remission, underscoring the significant therapeutic potential of diet alone. These findings were further validated by Levine et al. in the first multinational randomized controlled trial comparing CDED plus PEN with EEN in 74 children with mild-to-moderate luminal CD.[11] Although both approaches were similarly effective in inducing remission at week 6 (75% vs. 59%, p = 0.38), use of the CDED plus PEN resulted in significantly higher sustained remission rates than EEN (76% vs. 45%, p = 0.01). A subsequent study by Sigall-Boneh et al. showed that both EEN and CDED plus PEN lead to a rapid clinical response by week 3, which may help identify patients likely to achieve remission by week 6 with continued adherence.[20] In addition, CDED plus PEN, has been shown to lead to a significant decrease in fecal calprotectin levels in children with active mild to moderate CD.[21]

Beyond induction, several studies also support the role of CDED with PEN for maintaining remission. In the randomized controlled trial by Levine et al., children assigned to the CDED plus PEN maintained significantly higher rates of remission at 12 weeks compared to those who transitioned from EEN to a free diet with PEN.[11] Observational studies from Israel and Italy have also reported sustained remission beyond one year with CDED plus PEN, along with evidence of mucosal healing. Positive outcomes have been observed in both biologic-naïve and biologic-exposed patients.[22,23] A retrospective Croatian study of 61 pediatric patients showed a significantly higher weight gain (p= 0.002) and increases in body mass index (BMI) z-score (p=0.001) in patients receiving CDED and PEN compared to patients who received EEN alone.[24]

CDED with PEN may also serve as a useful salvage regimen for patients with inadequate response to biologic therapy. In a prospective cohort study of pediatric and adult patients with loss of response to biologics despite dose escalation or combination therapy, treatment with CDED with PEN for 12 weeks resulted in clinical remission at 6 weeks in 61.9% of patients.[17] Additional case series from Israel and Italy have also documented the benefits of CDED with PEN in refractory CD, including fistulizing and perianal phenotypes.[22, 23]

Adult Evidence with the CDED

Several observational studies and randomized controlled trials support the use of CDED in adults.[9,25]

The efficacy of CDED with PEN versus CDED monotherapy has been examined in biologic-naïve patients with early, mild-to-moderate CD. At weeks 6 and 12, a greater proportion of patients in the combination therapy arm achieved remission compared with those on diet alone. By week 24, nearly half of the cohort maintained both clinical and endoscopic remission, with a numerical advantage for CDED in combination with PEN (63% vs. 38%; p = 0.11). Improvements were also observed in inflammatory markers and quality-of-life indices, supporting the feasibility of CDED, either alone or with PEN, as a strategy for remission induction and mucosal healing.[26] CDED has also been studied in patients with limited therapeutic options. In a mixed pediatric–adult cohort that included 11 adults who had failed at least two biologics or combination regimens, remission was achieved most frequently in those with isolated ileal disease (83.3%).[26]

CDED has also demonstrated higher remission rates compared with a Mediterranean diet control in a randomized trial of 24 adults with mild-to-moderate disease.[27] This open-label study assessed symptomatic remission using the Harvey-Bradshaw Index (HBI), alongside fecal calprotectin and serum inflammatory indices at baseline, 12 weeks, and 24 weeks. The CDED demonstrated significantly higher remission rates at both time points: 70.8% vs. 38.1% at 12 weeks (p = .027) and 79.2% vs. 42.9% at 24 weeks (p < .0001). In addition, the CDED was associated with favorable changes in body composition, including a decrease in fat mass while maintaining or increasing fat-free mass and cellular mass.

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In pouchitis, CDED has been shown to improve clinical, biochemical, and endoscopic manifestations. Clinical remission rates were as high as 66.7% at week 6 and were maintained at week 24 among 46.7% of participants despite addition of diverse variety of foods and free meals as allowed in the maintenance phase of the diet. By week 12, patients experienced significant reductions in symptoms—particularly stool frequency and urgency—as well as decreases in serum CRP levels, with the most pronounced improvements observed in those with full dietary adherence.[28]

Role of the Dietitian

The involvement of an IBD-specialized Registered Dietitian (RD) is crucial. RDs evaluate indications and contraindications to determine patient suitability for the CDED and provide guidance for its safe and effective implementation, helping to minimize the risk of malnutrition while optimizing clinical outcomes.

With specialized training in nutritional assessment and management, RDs tailor macronutrient and micronutrient intake to individual needs, and monitor for deficiencies that may arise during dietary restriction or progression through the CDED phases.[7,29] The effectiveness of the CDED should be evaluated over time through assessment of gastrointestinal symptoms, nutritional status, and laboratory markers. In addition, RDs play a central role in tailoring the diet to cultural food practices by offering individualized recipes and counseling, while also helping patients manage limited food access, navigate social settings, and enhance family eating patterns.

Adherence to the CDED and any necessary adjustments can be assessed during follow-up appointments using tools such as dietary recalls. If remission is not achieved or sustained, or if nutritional deficiencies develop, the diet should be re-evaluated, and alternative therapies considered. Close coordination among the RD, the gastroenterologist, and patient is also essential to ensure alignment of nutrition care.

Laboratory Monitoring

Routine screening for nutritional deficiencies is essential. As no CDED-specific micronutrient monitoring guidelines currently exist, the following recommendations are adapted from standard IBD guidelines, with CDED-specific considerations noted where applicable (See Table 4).

The American Gastroenterological Association (AGA) recommends that all patients with IBD be monitored for vitamin D and iron deficiency, and that patients with extensive ileal disease or prior ileal resection be monitored for vitamin B12 deficiency.[29] Serum micronutrient levels should ideally be assessed during periods of disease quiescence, as many are acute-phase reactants that may fluctuate in the setting of active inflammation.

CDED with PEN has been shown to be nutritionally adequate, meeting more than 80% of the recommended daily intake for key micronutrients in adults. Patients receiving CDED without PEN, or those who are malnourished, may be at increased risk for micronutrient deficiencies and warrant closer monitoring. For patients on CDED for 12 weeks or with specific risk factors, monitoring and repletion of zinc, copper, folate, and fat-soluble vitamins should be considered. Magnesium, zinc, selenium, and folate deficiencies are particularly common due to reduced intake and increased gastrointestinal losses. In contrast, selenium, vitamin B12, vitamin D, and vitamin B9 levels may be affected by both dietary restriction and impaired absorption, particularly in patients with ileal involvement or prior intestinal surgery.[29]

Additional considerations apply to patients receiving CDED in combination with aminosalicylates (5-ASAs) or immunomodulators. Those treated with methotrexate or sulfasalazine should receive folic acid supplementation and be monitored for anemia. Monitoring of vitamin A, vitamin C, vitamin B6, and β-carotene may also be appropriate in selected patients, as low intake and serum levels have been reported in adults with active CD on exclusion diets.[26,29]

Strengths, Barriers, and Opportunities

The CDED offers several distinct strengths as a non-pharmacologic approach to CD management. Unlike pharmacologic therapies, the CDED directly targets nutrition, with the potential to improve

Table 4. Micronutrient Monitoring

Test	Recommendations	Considerations
The following screening recommendations are adapted from American Gastroenterological Association (AGA)[29] and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guidelines for IBD[31]		
Complete blood count with iron studies	At diagnosis and every 6–12 months in patients in remission; every 3 months in those with active disease	Consider IV iron infusions when inflammation is active
Vitamin B12	At diagnosis and annually in all patients; every 3–6 months in higher-risk groups	Higher-risk groups include patients with ileal disease or resection and those following a vegan diet
Vitamin B9	At diagnosis and annually	Patients receiving methotrexate or sulfasalazine should receive folic acid supplementation
Vitamin D (25-OH)	At diagnosis and every 6–12 months	Supplementation based on level and age
Calcium	Assess dietary intake and supplements as needed	Patients on CDED without PEN may need calcium supplementation, particularly during Phases 1 and 2
Vitamin C	Consider monitoring in selected patients	Deficiency is rare but may occur in patients consuming highly restrictive or poor-quality diets, including some patients on CDED without PEN
Zinc	At diagnosis and annually	Attempt for higher levels as it is involved in wound healing, tissue repair and immune function
Magnesium	At diagnosis and depending on clinical symptoms	Recommended in patients with chronic or severe diarrhea, extensive small bowel disease, or high-output states

Table 5. Resources for CDED Tools

ModuLife www.mymodulife.com	The ModuLife website and its app focus on CDED food lists and recipes, but access is only available through a healthcare provider who has been trained in the ModuLife program.
Crohn's and Colitis Foundation www.crohnscolitisfoundation.org	A platform called "Gut Friendly Recipes" is available where CDED recipes for all diet phases can be accessed using filters.
GI Nutrition Foundation www.ginutritionfoundation.com	CDED recipes for all phases of the diet are accessible through its online recipe database. The platform also provides updates on research related to the CDED.

overall dietary quality, supports growth in pediatric patients, and promotes beneficial changes in the gut microbiome. The structured phase of the diet also encourages family engagement, as dietary changes are often implemented at the household level, fostering shared investment in the patient's care.[7,29]

Implementation of the CDED may pose challenges due to hunger, social aspects of eating, dietary monotony, and the psychological strain of restriction. Adherence may be improved through support from healthcare teams, family, and peers and use of palatable supplements.[12,23]

Strategies such as offering different formula options, varying temperatures, or using overnight nasogastric feeding can also help reduce formula fatigue and improve tolerability. Tools, such as recipes to support implementation of the CDED are available, although they remain limited (See Table 5).

Although use of the CDED in clinical practice is growing, implementation remains inconsistent and further education is needed for patients and healthcare providers. When used as a treatment strategy, either alone or alongside other therapies, clinicians should clearly explain the monitoring plan

over a defined period, including expected response targets and when to reassess effectiveness or begin reintroducing foods or food groups. The strongest evidence supports its use in children and adults with mild-to-moderate Crohn's disease. Expanding the evidence base in more complex disease phenotypes and underrepresented populations, such as pregnant individuals, patients with stricturing or penetrating disease, and J-pouch patients, remains an important area for future research.

CONCLUSION

CDED is an established dietary treatment for mild-moderate CD in the pediatric and adult population. Its three-phase structured approach emphasizes whole, anti-inflammatory foods that may aid to restore microbiome balance, reduce inflammation, support epithelial function and therefore mucosal immune response. Evidence demonstrates that CDED, particularly when combined with PEN, can induce and sustain remission, improve inflammatory biomarkers and enhance quality of life, and may be beneficial in complex settings such as biologic failure, pregnancy, and pouchitis. While generally better tolerated than EEN and associated with improved adherence in some studies, adherence to the CDED can be limited by dietary monotony, psychosocial burden, financial challenges, and nutritional deficiency risks. Success is improved with structured healthcare and social support, palatable supplements, and access to an IBD-specialized dietitian who can tailor the diet to lifestyle and cultural practices. Further research is needed to clarify its role in complex disease phenotypes and long-term outcomes. ■

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