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Micronutrient Considerations for Celiac Disease

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While the benefit of a gluten-free diet to promote healing in individuals with celiac disease is clear, it is critical for providers to consider the micronutrient fluctuations that are associated with this condition and its dietary treatment. Nutritional deficiencies of micronutrients are frequently found in untreated or newly diagnosed celiac disease often as a byproduct of malabsorption. Deficiencies may persist even after strict adherence to a gluten-free diet related to lower nutrient profiles of gluten-free grains and gluten-free products and possibly concurrent dietary restrictions. Micronutrients of concern that may or may not require supplementation include vitamin D, calcium, vitamin B12, folate, and iron. A team approach, including a dietitian specializing in celiac disease, is necessary to ensure micronutrient needs are met on an ongoing basis. This review will summarize considerations for monitoring and supplementation of micronutrients of concern for those adherent to a gluten-free diet.

INTRODUCTION

Celiac disease (CeD) is a genetically-mediated autoimmune disease in which gluten causes damage to the small intestine, resulting in interference of nutrient absorption.[1] At this time, the only treatment for CeD is strict avoidance of gluten, a protein found in wheat, barley, and rye.[2] Gluten triggers a reversible inflammatory process in the small bowel mucosa, which may induce diarrhea, steatorrhea, constipation, bloating, nausea, vomiting, and/or weight loss in individuals with CeD.[1] Once a gluten-free diet (GFD) is initiated, the bowel begins to heal, and most individuals report resolution of symptoms. Despite symptom improvement, a strict GFD must be maintained for life to prevent ongoing damage.[3] A strict GFD can restore the histology of the small bowel in 95% of children within two years, whereas 34% and 66% of adults experience mucosal recovery after two and five years, respectively.[1]

Nutritional deficiencies of micronutrients are frequently found in untreated or newly diagnosed CeD.[2] Long-term consequences of mucosal damage and inflammation include malabsorption of nutrients such as calcium, vitamin D, iron,

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vitamin B12, folic acid, and zinc, which increases the risk for osteoporosis, anemia, and stunted growth.[1] The degree of malabsorption depends on the length of time before the CeD diagnosis and the degree of intestinal mucosal injury.[2] Moreover, development and/or persistence of symptoms, such as diarrhea and vomiting, may result in decreased total intake and may impact the quality of the diet, further increasing this risk. Parallel restrictions of lactose avoidance and vegan/vegetarian diets may exacerbate the risk for deficiencies and subsequent comorbidities. In a cross-sectional age and gender matched study of Spanish adults, the individuals with CeD on a GFD for >1 year had a deficient intake of folate, vitamin E, vitamin D, iodine, and calcium.[4] Women with CeD also had lower iron intake than the women in the control group.[4] Additionally, a cross-sectional study of 20 individuals with CeD and 39 healthy controls showed significant differences in serum and dietary folate levels.[5] Specifically, the folate, B6, and B12 values were lower in the diet of the individuals on a GFD compared to the healthy controls.[5]

Gluten free (GF) products tend to also have lower iron and B vitamins as well as other nutrients, such as calcium, zinc, and magnesium. As the FDA enriches wheat products back to the natural nutrient value of the wheat grain,[6] a wheat-based diet is inherently rich in iron, fiber, and B complex vitamins. Food products such as GF breads, pastas, and cereals are not required to be enriched by the FDA.[6] Lee and colleagues found that by adding only GF whole grains to a typical GFD, the overall nutrient value improved, specifically with increases in thiamin, iron, calcium, and folate.[7]

While the benefit of adhering to a GFD to promote healing in individuals with CeD is clear, it is critical for clinicians to consider the micronutrient fluctuations that are associated with this condition and its medically required dietary pattern. This review will summarize considerations for monitoring and supplementation of micronutrients of concern for those adherent to a GFD.

Nutrient-Specific Recommendations

Through discussions with our specialist providers at the Celiac Disease Center at Columbia University, we developed guidelines based on current evidence along with our clinical experience and judgment. Typically ordered nutrient labs include iron studies, folate, vitamin B12, and vitamin D. There is no consensus on the optimal timing for a dual x-ray absorptiometry (DEXA) scan to evaluate bone mineral density (BMD) in CeD, whether at diagnosis or during follow up.[2]

For a newly diagnosed CeD patient who just started a GFD:

- Pediatric: we recommend ordering the typical nutrient labs after 4-6 months on a GFD.
- Adult: we recommend ordering the typical nutrient labs at the CeD diagnosis and annually for monitoring. However, if nutrient labs are low at diagnosis, we generally recommend rechecking labs in 3-6 months.

If usual food intake shows nutritional inadequacies that cannot be alleviated through improved eating habits to meet the Recommended Dietary Allowances (RDA), the dietitian should recommend a GF multivitamin/mineral (MVM).[8] If nutrient deficiencies are found through lab work, clinicians should consider recommending a MVM or nutrient-specific supplementation (Table 1, Table 2). A prenatal MVM is recommended for all pregnant or lactating individuals.[9]

Vitamin D

Vitamin D plays an important role in promoting bone health, both through hormonal regulation of bone remodeling and calcium absorption.[2] Vitamin D deficiency is common in CeD, which may be due to villous atrophy, fat malabsorption, and possibly reduced dairy intake secondary to lactose intolerance.[2] In addition, much of the bone loss in CeD is related to secondary hyperparathyroidism, which is likely caused by vitamin D deficiency and can only be partially reversed with a GFD.[2] Verma studied 60 newly diagnosed pediatric patients and found a significant increase in vitamin D levels as well as BMD and bone mass content after 6 months on a GFD.[10]

Vitamin D can be obtained through sunlight, supplements, and food.[11] The skin makes vitamin D when it is exposed to sunlight; amounts vary based on the time of day, season, geographical

Table 1. Micronutrient Supplementation Guidelines for Celiac Disease

Micronutrient	Current Lab Reference Ranges	Consider Supplementation	
Multivitamin/ Mineral **Pediatric: Oral** **Adult: Oral**	N/A	Pediatric/Adult: If diet appears inadequate nutritionally, recommend MVM supplementation. If nutrient deficiencies are found through lab work, consider MVM or nutrient-specific supplementation. Pregnancy/Lactation: Recommend prenatal MVM for all pregnant or lactating individuals.	
Vitamin D **Pediatric: Oral** **Adult: Oral**	Optimal: 25 (OH) D: 30-50 ng/mL Insufficiency: 25 (OH) D: 20-29 ng/mL Deficiency: 25 (OH) D: < 20 ng/mL	Pediatric: *RDA:* Birth to 12 months: 10 mcg (400 IU) 1-70 years: 15 mcg (600 IU) *UL:* Birth to 6 months: 25 mcg (1000 IU) Infants 7-12 months: 38 mcg (1500 IU) Children 1-3 years: 63 mcg (2500 IU) Children 4-8 years: 75 mcg (3000 IU) > 9 years: 100 mcg (4000 IU) *Infants and Young Children:* The DGA recommends that fully and partially breastfed infants should receive a supplement of ~400 IU (~10 mcg)/day vitamin D beginning in the first week of life. The DGA, noting the difficulty of obtaining sufficient vitamin D from foods, advises that young children might need to continue a vitamin D supplement after age 12 months. If 25 (OH) D < 30 ng/mL, recommend age-specific vitamin D or MVM with vitamin D that meets age-specific RDA. *Children/Teens:* If 25 (OH) D 15-30 ng/mL, recommend 2000 IU/day for 3 months, then 800-1000 IU/day for 9 subsequent months. If 25 (OH) D < 15 ng/mL, noncompliant with vitamin supplement, and inadequate dietary intake, recommend 50,000 IU weekly for 4-6 weeks, then switch to 800-1000 IU/day. BMD: Rarely checked Adult: RDA: 1-70 years: 15 mcg (600 IU) 71 years and older: 20 mcg (800 IU) Although the optimal intake (diet plus supplement) has not been clearly established in premenopausal osteoporosis (or in males with osteoporosis), 600 IU vitamin D daily is generally suggested.	

	Consider Discontinuing Supplementation	Situations When Supplementation Would Not be Recommended
	Ongoing unless any vitamin or mineral reaches hazardous levels.	If there is any concern for overdose of any particular nutrient. Smokers and, possibly, former smokers should avoid MVM products providing large amounts of beta-carotene or vitamin A because 2 studies have linked these nutrients to an increased risk of lung cancer in smokers. Taking excess vitamin A (as retinol or other preformed forms of vitamin A but not beta-carotene) during pregnancy can increase the risk of birth defects in infants.
	Pediatric: If 25 (OH) D > 30 ng/mL and dietary intake is adequate. However, most patients need to continue vitamin D supplementation on an ongoing basis due to inadequate dietary intake. Consider recommending vitamin D supplements while students are in school and holding supplements while students are out of school. Adult: Decrease supplementation if 25 (OH) D > 50 ng/mL (unless PTH elevated and serum calcium low). If levels are considered hazardous: ≥ 80 ng/mL, consider discontinuing or decreasing supplementation. Near 100 ng/mL is considered toxic (more likely to occur in those who are taking 5000 IU/day or more).	*Medication interactions:* Orlistat Statins Steroids Thiazide diuretics Summer months may not be necessary to supplement with vitamin D.

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Table 1. Micronutrient Supplementation Guidelines for Celiac Disease *(continued from page 29)*

Micronutrient	Current Lab Reference Ranges	Consider Supplementation	
Vitamin D (continued) **Pediatric: Oral** **Adult: Oral**		*UL:* > 9 years: 100 mcg (4000 IU) If 25 (OH) D < 30 ng/mL, recommend vitamin D or MVM with vitamin D ~1000 IU/day. Recheck in 12 weeks and adjust supplementation as needed to bring levels to ≥ 30. For adults, increasing and maintaining the 25 (OH) D level consistently > 30 ng/mL may require >1000 IU/day (i.e. malabsorption, inadequate dietary vitamin D intake, inadequate sun exposure). If 25 (OH) D < 15 ng/mL, recommend 50,000 IU 1x/week for 8 weeks, then switch to ~2000 IU/day. If osteoporosis is present, discuss supplement recommendations with a bone endocrinologist. BMD: Regularly check Pregnancy/Lactation: *RDA:* Pregnant and breastfeeding individuals: 15 mcg (600 IU) *UL:* Pregnant and breastfeeding individuals: 100 mcg (4000 IU) Recommend prenatal MVM with 600 IU/day for all pregnant or lactating individuals. If 25 (OH) D < 30 ng/mL, then recommendations would be consistent with above for additional supplementation.	
Calcium **Pediatric: Oral** **Adult: Oral**	Total blood calcium: 8.5-10.5 mg/dL Ionized calcium: 4.65-5.2 mg/dL Urinary calcium: 100-300 mg/dL 2.5-7.5 mmol/24 hr	Absorption from calcium is highest with doses of 500mg or less. If supplementation of more than 500 mg is needed, doses should be divided and given every 4-6 hours. Pediatric: *RDA:* 0-6 months: 200 mg 7-12 months: 260 mg 1-3 years: 700 mg 4-8 years: 1000 mg 9-18 years: 1300 mg If dietary calcium intake is inadequate to meet age-specific RDA, recommend calcium supplementation to meet the deficit. Adult: *RDA:* 19-50 years: 1000 mg 51-70 years: 1000 mg male, 1200 mg female > 70+ years: 1200 mg The optimal intake (diet plus supplement) has not been clearly established in premenopausal osteoporosis (or in males with osteoporosis), 1000 mg of calcium total is generally suggested.	

	Consider Discontinuing Supplementation	Situations When Supplementation Would Not be Recommended
	If supplementation induces constipation or if calcium is elevated in blood or urine. In females if kidney stones are a risk or are present with high calcium intake (> 1200 mg).	Kidney issues. Post-menopausal females who take calcium supplements may be at risk for increased kidney stones. Chronic constipation. *Medication interactions:* Dolutegravir Levothyroxine Lithium Quinolone antibiotics

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Table 1. Micronutrient Supplementation Guidelines for Celiac Disease *(continued from page 31)*

Micronutrient	Current Lab Reference Ranges	Consider Supplementation	
Calcium (continued) **Pediatric: Oral** **Adult: Oral**		If dietary calcium intake is inadequate to meet age-specific RDA, recommend calcium supplementation to meet the deficit. Recommend additional calcium supplementation (up to 1500 mg daily in divided doses) if individual has met the RDA for at least 2-3 months and vitamin D is optimized, but albumin adjusted serum calcium is below normal, PTH is elevated above the upper limit of normal, or urine calcium is < 100 mg/24 hrs. Pregnancy/Lactation: Recommend prenatal MVM for all pregnant or lactating individuals. Additional calcium supplementation may be necessary to meet RDA.	
Vitamin B12 **Pediatric: Oral Sublingual Injection** **Adult: Oral Sublingual Injection**	Vitamin B12: 299-1054 pg/mL	Pediatric: *RDA:* Birth to 6 months: 0.4 mcg 7-12 months: 0.5 mcg 1-3 years: 0.9 mcg 4-8 years: 1.2 mcg 9-13 years: 1.8 mcg 14+years: 2.4 mcg *Infants* The DGA adds that infants fed human milk might also require a vitamin B12 supplement if the mother's vitamin B12 status is inadequate, which might occur, for example, if the mother follows a vegan diet. If ≤ 200-300 pg/mL, recommend 500 mcg/day. Adult: *RDA:* 14+years: 2.4 mcg If borderline (200-300 pg/mL), check MMA. If MMA WNL, vitamin B12 is acceptable, but oral or sublingual vitamin B12 can be offered: 1000 mcg/day. If < 200 pg/mL or within borderline range (200-300 pg/mL) and elevated MMA, recommend injection of 4 doses of 1000 mcg. Pregnancy/Lactation: *RDA:* Pregnancy 2.6 mcg Lactation 2.8 mcg Recommend prenatal MVM for all pregnant or lactating individuals.	
Folate/ Folic acid **Pediatric: Oral** **Adult: Oral**	Plasma folate: 2.5-20 ng/mL or 4.5-45.3 nmol/L **Commercial lab reference standards vary	Pediatric: *RDA:* Birth to 6 months: 65 mcg DFE 7-12 months: 80 mcg DFE 1-3 years: 150 mcg DFE 4-8 years: 200 mcg DFE 9-13 years: 300 mcg DFE 14+ years: 400 mcg DFE	

	Consider Discontinuing Supplementation	Situations When Supplementation Would Not be Recommended
	If vitamin B12 level is elevated above normal range, decrease supplementation.	*Medication interactions*: Gastric acid inhibitors Metformin
	If folate level normalizes outside of child-bearing years.	Contraindicated with Methotrexate, Xeloda, and 5-FU. *Medication interactions:* Antiepileptic medications Sulfasalazine *MTHFR:* Some of these individuals might benefit from supplementation with 5-MTHF. CDC recommends 400 mcg/day of folic acid, not 5-MTHF, for people who could become pregnant, even if they have a MTHFR.

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Table 1. Micronutrient Supplementation Guidelines for Celiac Disease *(continued from page 33)*

Micronutrient	Current Lab Reference Ranges	Consider Supplementation	
Folate/ Folic acid (continued) **Pediatric: Oral** **Adult: Oral**		*UL:* 1-3 years: 300 mcg DFE 4-8 years: 400 mcg DFE 9-13 years: 600 mcg DFE 14-18 years: 800 mcg DFE If folate is low, recommend an age-specific folic acid supplement. Track trends in folate levels. If levels remain borderline low, recommend MVM with folic acid or age-specific folic acid supplement. Adult: *RDA:* 14+ years: 400 mcg DFE *UL:* 14-18 years: 800 mcg DFE 19+ years: 1,000 mcg DFE If folate is low, recommend MVM with folic acid or ~400 mcg folic acid supplement. Pregnancy/Lactation: *RDA:* Pregnancy 600 mcg DFE Lactation 500 mcg DFE *UL:* 1,000 mcg DFE Recommend prenatal MVM for all females of child-bearing age through pregnancy and lactation. If folate is low, consider additional folic acid supplement in addition to prenatal MVM.	
Iron **Pediatric: Oral Infusion** **Adult: Oral Infusion**	Ferritin: Newborns: 25-200 ng/mL 1-month old: 200-600 ng/mL 2-5 months old: 50-200 ng/mL 6 months-15 years old: 7-140 ng/mL Adult males: 24-336 ng/mL Adult females: 24-307 ng/mL TSAT: 20-50%	Pediatric: *RDA:* Birth to 6 months: 0.27 mg 7-12 months: 11 mg 1-3 years: 7 mg 4-8 years: 10 mg 9-13 years: 8 mg 14-18 years: male 11 mg, female 15 mg For newly diagnosed individuals with CeD, if Hgb and Hct WNL and ferritin < 24 ng/mL, monitor levels to see if normalizes with GFD. If anemic (Hgb and Hct are low) and no risk for constipation, recommend iron supplement of 3-6 mg/kg/day up to 45 mg elemental iron. If ferritin is low or borderline anemic, and not currently taking a MVM, recommend MVM with iron. TSAT 17%-20%, optimize through diet. TSAT < 17%, recommend MVM with iron.	

	Consider Discontinuing Supplementation	Situations When Supplementation Would Not be Recommended
	Pediatric: If iron levels normalize then recommend a MVM with iron ongoing. If iron supplementation induces constipation or if ferritin levels reach triple digits. Adult: If etiology of iron deficiency resolves and levels normalize, can consider discontinuing (i.e. CeD, GI bleed). If iron supplementation induces constipation or if ferritin levels reach triple digits.	Chronic constipation. *Medication interactions:* Levodopa Levothyroxine Proton pump inhibitors

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Table 1. Micronutrient Supplementation Guidelines for Celiac Disease *(continued from page 35)*

Micronutrient	Current Lab Reference Ranges	Consider Supplementation	
Iron (continued) **Pediatric: Oral Infusion** **Adult: Oral Infusion**		Adult: *RDA:* 19-50 years: male 8 mg, female 18 mg 51+ years: 8 mg For newly diagnosed individuals with CeD, if Hgb and Hct WNL and ferritin < 24 ng/mL, monitor levels to see if normalizes with GFD. If ferritin < 24 ng/mL and/or TSAT < 20%, recommend MVM with iron. In a menstruating female with Hgb and Hct WNL, but ferritin 5 points below normal, only recommend MVM with iron. If TSAT 17%-20%, optimize through diet. If TSAT < 17%, recommend MVM with iron. If ferritin < 24 ng/mL and anemic (Hgb and Hct are low), recommend ~45 mg iron supplement daily, or every other day if intolerant, along with further evaluation. Iron infusion recommended if failure/intolerance of oral iron in the setting of persistent iron deficiency anemia. Repeat infusion until anemia is corrected. Pregnancy/Lactation: *RDA:* 14-18 years: pregnancy 27 mg, lactation 10 mg 19-50 years: pregnancy 27 mg, lactation 9 mg Recommend prenatal MVM for all pregnant or lactating individuals.	

Note: Prioritize nutrients from food first. Dietitians should evaluate patients' diets for lack of variety, inadequacies,

Legend:

RDA = Recommended Dietary Allowance, UL = Tolerable Upper Intake Level, MVM = Multivitamin/Mineral, WNL = Within Normal Limits, N/A = Not Applicable, BMD = Bone Mineral Density, DFE = Dietary Folate Equivalents, MTHFR = Methylenetetrahydrofolate Reductase, 5-MTHF = 5-methyltetrahydrofolate, Hgb = Hemoglobin, GI = Gastrointestinal, ng/mL = Nanograms per Milliliter, mcg = Micrograms, IU = International Unit, pg/mL = Picogram per Milliliter, nmol/L = Nanomole per Liter, g/dL = Gram per Deciliter

Legend: Folate

1 mcg DFE = 1 mcg food folate, 1 mcg DFE = 0.6 mcg folic acid from fortified foods or dietary supplements consumed with foods, 1 mcg DFE = 0.5 mcg folic acid from dietary supplements taken on an empty stomach

latitude, skin pigmentation, and other factors.[12] Food sources include fatty fish, such as salmon, mackerel, and tuna.[11,12] Vitamin D is added to milk and other dairy products, orange juice, and fortified cereals.[11,12] However, GF cereals may not be fortified. Cheese and egg yolks naturally contain small amounts of vitamin D.[11,12] Many of these sources are animal-based and therefore, individuals following vegan or vegetarian dietary plans must be counseled on strategies to incorporate plant-based vitamin D sources, such as fortified dairy alternatives.[11,12]

There are two types of vitamin D supplements: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol).[13] The primary source of vitamin D2 is plants, and D2 can be manufactured

	Consider Discontinuing Supplementation	Situations When Supplementation Would Not be Recommended

and risk factors such as lactose intolerance, veganism or vegetarianism and make recommendations accordingly.

DGA = The Dietary Guidelines for Americans 2020-2025, CeD = Celiac Disease, GFD = Gluten-Free Diet, 25 (OH) D = 25-hydroxy vitamin D, MMA = Methylmalonic Acid, RD = Registered Dietitian, Hct = Hematocrit, TSAT = Transferrin Saturation, CDC = Centers for Disease Control and Prevention, mg/dL = Milligrams per Deciliter, mmol/24 hr = Millimole per 24 hours, mg = Milligram, hr = Hour,

synthetically, whereas vitamin D3 is synthesized in the skin after exposure to the sun.[13] Both forms are well-absorbed in the small bowel.[11] Vitamin D supplements should ideally be taken with a meal and the full amount can be taken at one time.[12] Many calcium supplements also contain vitamin D. Although the body needs vitamin D to absorb calcium, a vitamin D supplement does not need to be taken at the same time as a calcium supplement.[12] Note that individuals may not need supplementation over the summer months if increased exposure to sunlight is expected.

Calcium

Calcium is an essential mineral for development and maintenance of bone integrity.[12] Calcium is

Table 2. Gluten-Free Supplement Brands

Nutrient Name	Pediatric	Adult

Multivitamin/Mineral (MVM)	• NaturesPlus® Animal Parade
	• L'il Critters™
	• Olly®
	• Renzo's®
	• Centrum Kids MultiGummies
	• Centrum Organic Kids MultiGummies
	• Rainbow Light Kid's One™ Multivitamin
		• Sundown®
		• Vitafusion™
		• Kirkland Signature MVM
		• One A Day® Women's Complete Multivitamin (tablets)
		• Centrum
		  ○ Centrum: Adults, Men, Women
		  ○ Centrum MultiGummies: Men, Women
		  ○ Centrum Organic MultiGummies: Men, Women
		  ○ Centrum Silver: Adults, Men, Women
		  ○ Centrum Minis: Men 50+, Women 50+
		  ○ Centrum Maternal Health: PreNatal Multivitamin Gummies, PostNatal Multivitamin Gummies

Vitamin D	• NaturesPlus® Animal Parade • L'il Critters™ • Carlson® Baby's Super Daily D3 • Renzo's® • Vitafusion™	• Nature Made® • Sundown® • Vitafusion™
Calcium	• NaturesPlus® Animal Parade • L'il Critters™ • Renzo's® • Vitafusion™ • Bluebonnet® (liquid & chewable)	• Nature Made® • Sundown® • Vitafusion™
Vitamin B12	• Nature Made® • Olly® Daily Energy (caffeine free)	• Nature Made® • Sundown® • Vitafusion™ • Vitacost® Liquid Vitamin B12 • Olly® Daily Energy (caffeine free)
Folate	• CanPrev Folate 5-MTHF Active Vitamin B9 drops • Sundown®	• Sundown® • Doctor's Best® Fully Active Folate
Iron	• NovaFerrum® • MaryRuth's® Vegan Liquid Iron • Renzo's® • Fusion Lifestyle Soft Chews	• NovaFerrum® • MaryRuth's® Vegan Liquid Iron • Nature Made® • Life Extension® Iron Protein Plus • Slow Fe® • Now® • MegaFood® Blood Builder

also part of teeth constitution and enables blood to clot, muscles to contract, and the heart to beat.[12] The body cannot produce its own calcium, so sufficient dietary intake is critical.[12] If calcium intake is insufficient, calcium is taken from the bones.[12] Additionally, mucosal damage in CeD impairs calcium absorption, which can lead to impaired bone health. Initially, lactose intolerance may occur related to impaired release of lactase enzyme from the damaged mucosa, which may further limit dairy intake. However, this lactose intolerance is likely to resolve with mucosal healing. Pediatric patients with untreated CeD are at risk of short stature and constitutional delay of puberty.[1] Nonetheless, a 2022 meta-analysis concluded that the GFD was associated with higher bone mineral content and BMD in children and adolescents with CeD.[14] Calcium-rich foods include dairy (milk, yogurt, cheese), fortified milk substitutes (soy, nut, pea), kale, and salmon.[15]

It is important to note that absorption from calcium is highest with doses of 500 mg or less.[15] Therefore, calcium intake, from food or supplements, should be spread out throughout the day for maximum absorption. The bioavailability of calcium from dairy products and fortified foods is 30%.[15] The presence of oxalic acid and phytic acid in plants reduces calcium absorption.[15] Foods such as milk, broccoli, kale, and cabbage have an absorption rate of 27% while spinach, collard greens, sweet potatoes, and beans have an absorption rate of 5%.[15] Nevertheless, when individuals consume a variety of foods, the interactions with oxalic or phytic acid likely have minimal or negligible nutritional consequences.[15] Absorption of dietary calcium is also reduced to a small extent by intakes of caffeine and phosphorus and to a greater extent by insufficient vitamin D status.[15]

Dietitians are necessary to assess dietary intake because serum calcium is an unreliable marker for calcium status.[15] Calcium supplementation may be recommended if dietary calcium is inadequate or if malabsorption is suspected. If supplementation is recommended, calcium citrate is often the supplement of choice. Calcium citrate can be taken with or without food, is more easily absorbed, and causes fewer symptoms of gas, bloating, and constipation than calcium carbonate.[15] Calcium citrate is also recommended for individuals who are taking acid suppressants as the calcium citrate is better absorbed even in a lower acid environment than calcium carbonate.[15] However, calcium citrate supplements only contain approximately 20% calcium.[15] Therefore, in order to reach daily requirements, individuals may need to take more of the calcium citrate supplement.

Vitamin B12

Vitamin B12 is required for proper red blood cell formation, neurological function, and DNA synthesis.[16] Vitamin B12 is absorbed primarily in the ileum.[2] Possible reasons for deficiency in CeD, although not well-established, include terminal ileal involvement, pancreatic insufficiency, and competition for vitamin B12 by undesirable bacteria in SIBO.[2]

Vitamin B12 is naturally found in animal products, including fish, meat, poultry, eggs, milk, and milk products.[16] Therefore, individuals following vegan diet plans must be counseled on strategies to incorporate plant-based vitamin B12 sources, such as fortified nutritional yeast and dairy alternatives.[16]

Absorption of vitamin B12 is dose dependent.[16] The estimated bioavailability from food varies because absorption decreases drastically when the availability of intrinsic factor is at capacity (at 1–2 mcg of vitamin B12).[16] Bioavailability also varies by the type of food source; it appears to be about three times higher in dairy products compared to meat, fish, and poultry.[16] The bioavailability from dietary supplements is about 50% higher than that from food sources.[16] Gastric acid inhibitors (proton pump inhibitors and histamine 2-receptor antagonists) used to treat gastroesophageal reflux disease and peptic ulcer disease may interfere with vitamin B12 absorption from food by slowing the release of gastric acid into the stomach.[16]

Vitamin B12 administered parenterally as a prescription medication through intramuscular injections may be considered for severe deficiency, neurologic features, or ongoing malabsorption.[2] Clinicians should assess for intake of supplements, herbals, and energy drinks, which may be sources of vitamin B12.

Folate

Folate is a B vitamin that is naturally present in some foods whereas folic acid is the form of vitamin B9 that is used in fortified foods and most dietary supplements.[17] Folate deficiency is common in CeD likely related to malabsorption, lower folate content of GF grains, and the lack of fortification/enrichment of GF products.[7] Folate is found in a wide variety of foods, including vegetables, especially dark green leafy vegetables, fruits and fruit juices, nuts, beans, peas, seafood, eggs, dairy products, meat, poultry, and grains.[17] Spinach, liver, asparagus, and Brussels sprouts are among the foods with the highest folate levels.[17] Dietitians should assess for a lack of variety and inadequate intake of GF whole grains in the diet as studies have shown improvement in folate levels with the inclusion of GF whole grains.[7]

At least 85% of folic acid is estimated to be bioavailable when taken with food, whereas only about 50% of folate naturally present in food is bioavailable.[17] When consumed without food, nearly 100% of supplemental folic acid is bioavailable.[17] Given the risk of neural tube defects related to low folate levels, a prenatal MVM with folic acid is recommended for all females of child-bearing age through pregnancy and lactation.[17]

Iron

Iron is an essential mineral for carrying oxygen in the hemoglobin of red blood cells.[18] Iron also supports the body's metabolism, growth, development, cellular functioning and synthesis of some hormones and connective tissue.[18] Iron deficiency is common in newly diagnosed CeD due to malabsorption, but iron deficiency discovered further along into the GFD warrants additional investigation to determine the etiology.

Dietary iron is in the form of heme or non-heme iron.[18] Heme iron comes from animal sources, such as meat, fish, and poultry and is most readily absorbed by the body.[18] Non-heme iron is found in plant-based foods, such as fruits, vegetables, beans and nuts and has a lower bioavailability.[18] Strategies to increase absorption of iron include cooking with a cast iron skillet and consuming heme iron sources or vitamin C along with non-heme iron sources to enhance the absorption of the non-heme iron.[18]

Fortified foods are recommended for children between ages 1-2 to ensure iron stores are repleted as prenatal iron stores are exhausted by 6 months.[18] Pediatric diets commonly fall short of adequate iron intake and most GF pediatric chewable supplements do not contain iron. Special attention should be paid to toddlers who drink milk in excess of 24 oz per day due to possible interference with iron absorption.

Frequently used forms of iron in supplements include ferrous and ferric iron salts, such as ferrous sulfate, ferrous gluconate, ferric citrate, and ferric sulfate.[18] Ferrous iron in dietary supplements is more bioavailable than ferric iron.[18] It is important to note that supplements containing 25 mg iron or more can reduce zinc absorption and plasma zinc concentrations so these levels should be monitored.[18] Calcium might interfere with the absorption of iron, although this effect has not been definitively established and the effect is expected to be mitigated by a typical mixed western diet.[18] Nevertheless, some experts suggest taking individual calcium and iron supplements at different times of the day to maximize absorption.[18]

Although high doses of supplemental iron (45 mg/day or more) are often used to replete iron stores in iron deficiency, it is important to consider that they may cause gastrointestinal side effects, such as nausea and constipation.[18] Other forms of supplemental iron, such as heme iron polypeptides, carbonyl iron, iron amino-acid chelates, and polysaccharide-iron complexes, might have fewer gastrointestinal side effects than ferrous or ferric salts.[18] Iron infusion is recommended if there is failure or intolerance of oral iron in the setting of persistent iron deficiency anemia. Because proton pump inhibitors reduce production of gastric acid, they can reduce iron absorption as well. Therefore, consider that individuals with iron deficiency on proton pump inhibitors can have suboptimal responses to iron supplementation.[18]

CONCLUSION

A GFD prescription should include standard nutritional guidance emphasizing naturally GF whole foods such as fruits, vegetables, dairy, meat, seafood, nuts, seeds, and legumes for a sound nutritional base.[2] The addition of naturally GF

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whole grains or pseudocereals, such as amaranth and quinoa, provides the fiber, B vitamins, and minerals (calcium, iron, magnesium) missing when gluten is removed.[2]

Research has indicated that micronutrient deficiencies are common at the time of diagnosis and even after initiation and adherence to a GFD. Deficiencies may be attributed to malabsorption from villous atrophy, lower nutrient profiles of GF grains and GF products, as well as additional dietary restrictions. Routine monitoring of at-risk vitamin and mineral levels should be part of comprehensive follow-up for patients with CeD. A patient-centered team approach including consultation and regular follow up with a specialist dietitian will ensure optimal outcomes. ■

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References

1. Aljada B, Zohni A, El-Matary W. The Gluten-Free Diet for Celiac Disease and Beyond. Nutrients. 2021; 13(11):3993.
2. Dennis M, Lee AR, Mccarthy T. Nutritional Considerations of the Gluten-Free Diet. Gastroenterology Clinics of North America. 2019;48(1):53–72.
3. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. Lancet. 2018;391(10115):70-81.
4. Ballestero-Fernández C, Varela-Moreiras G, Úbeda N, et.al. Nutritional Status in Spanish Adults with CD Following a Long-Term Gluten-Free Diet Is Similar to Non-Celiac. Nutrients. 2021;13(5):1626.
5. Valente FX, Campos Tdo N, Moraes LF, et. al. B vitamins related to homocysteine metabolism in adults celiac disease patients: a cross-sectional study. Nutr J. 2015;14:110.
6. FDA - National Research Council (US) Subcommittee on the Tenth Edition of the Recommended Dietary Allowances. Recommended Dietary Allowances: 10th Edition. Washington (DC): National Academies Press (US); 1989.
7. Lee AR, Ng DL, Dave E, et. al. The effect of substituting alternative grains in the diet on the nutritional profile of the gluten-free diet. J Hum Nutr Diet. 2009 Aug;22(4):359-63.
8. Academy of Nutrition and Dietetics. RECOMMENDATIONS SUMMARY. Evidence Analysis Library. https://www.andeal.org/template.cfm?template=guide_su12ry&key=2102. Published 2023. Accessed February 15, 2023.
9. Office of dietary supplements - multivitamin/mineral supplements. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/MVMS-HealthProfessional/. Published October 11, 2022. Accessed February 15, 2023.
10. Verma A, Lata K, Khanna A, et al. Study of effect of gluten-free diet on vitamin D levels and bone mineral density in celiac disease patients. J Family Med Prim Care. 2022;11(2):603-607.
11. Office of dietary supplements - vitamin D. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/vitamind-healthprofessional/#h2. Published August 12, 2022. Accessed February 15, 2023.
12. Calcium/vitamin D requirements, Recommended Foods & Supplements. Bone Health & Osteoporosis Foundation. May 24, 2023. Accessed July 30, 2023. https://www.bonehealthandosteoporosis.org/patients/treatment/calciumvitamin-d/.
13. Alayed Albarri EM, Sameer Alnuaimi A, Abdelghani D. Effectiveness of vitamin D2 compared with vitamin D3 replacement therapy in a primary healthcare setting: a retrospective cohort study. *Qatar Med J*. 2022;2022(3):29.
14. Oliveira DDC, da Silva DCG, Kawano MM, de Castro CT, Pereira M. Effect of a gluten-free diet on bone mineral density in children and adolescents with celiac disease: Systematic review and meta-analysis *Crit Rev Food Sci Nutr*. 2022;1-11.
15. Office of dietary supplements - calcium. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/#h2. Published October 6, 2022. Accessed February 15, 2023.
16. Office of dietary supplements - vitamin B12. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/#h2. Published December 22, 2022. Accessed February 15, 2023.
17. Office of dietary supplements - folate. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/. Published November 30, 2022. Accessed February 15, 2023.
18. Office of dietary supplements - iron. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/. Published April 5, 2022. Accessed February 15, 2023.

Answers to this month's crossword puzzle:

1 B	A	2 R	R	3 E	T	4 T	5 S	■	6 S	7 I	8 P	9 H	O	N
U	■	E	■	S	■	10 O	C	T	■	11 L	E	E	■	■
12 M	I	C	13 R	O	R	N	A	■	14 R	E	P	A	I	15 R
P	■	16 T	O	P	■	■	17 L	18 A	■	I	■	R	■	A
■	19 P	A	T	H	20 O	21 G	E	N	■	22 T	I	T	E	R
23 D	■	L	■	24 A	D	O	■	A	■	I	■	B	■	E
25 O	26 S	■	27 A	G	E	■	■	28 T	29 I	S	S	U	E	■
30 P	E	31 R	C	U	S	32 S	I	O	N	■	■	R	■	■
33 A	C	H	E	S	■	A	■	M	■	34 T	O	N	I	35 C
■	■	I	■	■	■	36 L	A	Y	■	H	■	■	■	O
37 V	A	G	U	38 S	■	I	■	■	39 S	Y	S	40 T	E	M
I	■	O	■	M	■	V	■	■	■	R	■	O	■	P
41 V	I	S	C	E	R	A	L	■	42 J	O	I	N	■	O
I	■	I	■	L	■	R	■	43 A	■	I	■	44 U	P	S
45 D	I	S	P	L	A	Y	■	46 S	O	D	A	S	■	E