

daily Essential Nutrients

CLINICAL REFERENCE
for Healthcare Professionals





Dear Healthcare Professional,

Thank you for your interest in Hardy Nutritionals® **Daily Essential Nutrients (DEN)** – a unique technology-enhanced vitamin-mineral formulation for the treatment of mood, anxiety, and behavioral symptoms.

This clinical reference provides detailed information about **DEN** accumulated through extensive research and valuable feedback from healthcare professionals.

For your convenience, we've included Section 7, Treatment Guidelines, which is designed to simplify clinical use of **DEN** by putting information from other sections into clinical context.

We welcome any feedback, questions or concerns you may have. Please feel free to call us.

We appreciate working with you for your patients' health!

Sincerely,

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1 Description

Daily Essential Nutrients (DEN) is a micronutrient formula for oral administration. It consists of 17 minerals, 13 vitamins, 4 amino acids, and 4 antioxidants/botanicals. All minerals are chelated with a proprietary technology-enhanced process which combines specialized organic molecules with micronized minerals to maximize mineral absorption and delivery to cells.

DEN is a light brown powder and is enclosed in a white opaque gelatin capsule. The capsules are made from BSE-free bovine-derived gelatin.



Supplement Facts

Serving Size: 4 Veggie Capsules
Servings Per Container: 90

Amount Per Serving		%DV
Vitamin A (as retinyl palmitate)	1920 IU	38%
Vitamin C (as ascorbic acid)	200 mg	333%
Vitamin D (as cholecalciferol)	1000 IU	250%
Vitamin E (as d-alpha tocopheryl succinate)	120 IU	400%
Vitamin K (as 75% phyloquinone; 25% menaquinone-7)	40 mcg	50%
Thiamin (as thiamin mononitrate)	20 mg	1333%
Riboflavin	6 mg	353%
Niacin (as niacinamide)	30 mg	150%
Vitamin B ₆ (as pyridoxine hydrochloride)	23.3 mg	1167%
Folate (as calcium L-5 methyltetrahydrofolate)	267 mcg	67%
Vitamin B ₁₂ (as methylcobalamin & adenosylcobalamin)	300 mcg	5000%
Biotin	360 mcg	120%
Pantothenic acid (as d-calcium pantothenate)	10 mg	100%
Calcium (as NutraTek™ chelation complex)	440 mg	44%
Iron (as NutraTek™ chelation complex)	4.6 mg	25%
Phosphorus (as NutraTek™ chelation complex)	280 mg	28%
Iodine (as NutraTek™ chelation complex)	68 mcg	45%
Magnesium (as NutraTek™ chelation complex)	200 mg	50%
Zinc (as NutraTek™ chelation complex)	16 mg	107%
Selenium (as NutraTek™ chelation complex)	68 mcg	97%
Copper (as NutraTek™ chelation complex)	2.4 mg	120%
Manganese (as NutraTek™ chelation complex)	3.2 mg	160%
Chromium (as NutraTek™ chelation complex)	208 mcg	173%
Molybdenum (as NutraTek™ chelation complex)	48 mcg	64%
Potassium (as NutraTek™ chelation complex)	80 mg	2%

Proprietary blend 596 mg †
Choline bitartrate, alpha-lipoic acid, mineral wax, inositol, acetyl-L-carnitine, grape seed extract, ginkgo biloba leaf extract, N-acetyl-L-cysteine, L-methionine, trace minerals as NutraTek™ chelation complex: lithium orotate, boron, vanadium, nickel.

† Daily Value (%DV) not established.

Other ingredients: Vegetarian capsule (hypromellose), microcrystalline cellulose, glycine, citric acid, magnesium stearate, silicon dioxide, titanium dioxide.

Rev. 16-09

2 Clinical Pharmacology

2.1 Clinical trials

Daily Essential Nutrients (**DEN**) and similar broad-spectrum micronutrient formulations have been extensively researched as interventions for mental health symptoms. The study designs employed in the published articles range from double-blind research to case studies with years of historical information and two database analyses (see *Appendix A*).

Consistent research results have been found across scientists at more than a dozen independent institutions in several countries. None of the researchers have had financial ties to these formulations.

Significant double-blind research is currently underway using **DEN**.

2.2 Mechanism of action

The exact mechanism by which **DEN** exerts its therapeutic effect is not entirely understood. It is presumed to be linked to the various roles of vitamins and minerals in the synthesis²⁻⁸ and regulation⁹⁻¹⁶ of neurotransmitters in the brain.

In addition, genetic polymorphisms (variations) can often result in increased requirements for nutrients in enzyme pathways, and higher nutrient intakes have been shown to ameliorate the effects of many of these genetic conditions.¹⁷⁻¹⁹

2.3 Pharmacodynamics

In humans, **DEN** pharmacodynamics are presumed to be a complex interaction of individual nutrient pharmacodynamics, many of which have been studied extensively.²⁰⁻²⁵

In animal studies, accelerated structural and functional recovery of neurons were observed following experimentally-induced brain lesions when animals were supplemented with a micronutrient formula substantially similar to **DEN**.²⁶ Similar structural, chemical, and functional neuronal deficits exist in mood and cognitive regulation in humans²⁷⁻²⁹ which would presumably respond in a similar way to **DEN** therapy.

2.4 Absorption and metabolism

2.4.1 Systemic bioavailability

As yet, there are no publications regarding nutrient bioavailability of **DEN** after a single oral dose.

It is not known to what degree food affects the systemic bioavailability of **DEN**. Although food may decrease the rate of absorption, this effect does not appear to be clinically significant. Administering **DEN** with food is recommended.

2.4.2 Metabolism

The vitamins and minerals in **DEN** are presumed to be metabolized in the same way as those in foods and similar supplements.²⁰⁻²⁴ The complexity of **DEN** metabolism may affect medication use (see 4.2 *Drug interactions*).

The effect of age upon the metabolism of **DEN** has not been systematically investigated. No unusual age-associated pattern of adverse events has been observed in children, adolescents, or the elderly.¹

It is not known how renal or liver impairment can affect the metabolism of **DEN**.

3 Indications & Dosage

3.1 Indications

Daily Essential Nutrients (DEN) is indicated for the treatment of mood, anxiety, and behavioral symptoms.

Significant evidence exists to indicate that a wide range of mood, anxiety, and behavioral symptoms can result from inadequate intake of vitamins and minerals and/or poor nutrient status,¹⁹ and that broad-spectrum micronutrient interventions substantially similar to **DEN** can significantly alleviate these symptoms.¹

3.2 Dosage

In general, the recommended therapeutic dose of Daily Essential Nutrients (DEN) is 4 capsules three times daily with food. One level scoop of DEN Powder is equivalent to 4 DEN capsules.

In published research, both adults and children have responded well when broad-spectrum micronutrient formulas substantially similar to DEN have been administered at levels comparable to this therapeutic dosage (see Appendix A).

Based on clinical experience, young children (generally ages 2-5) diagnosed with psychiatric conditions may require lower doses of DEN (often about 4-8 capsules/day).

Maintenance requires an adequate dose of DEN that preserves symptom remission. Optimal maintenance dosage will vary with individual needs.

For additional DEN dosage considerations, including initial dosage titration, see 7 Treatment Guidelines.

3.2.1 Biological safety data

Biological safety data from 144 children and adults were available from eight datasets of broad-spectrum micronutrient formulas substantially similar to **DEN** which were administered at comparable therapeutic dosages. In these reports, there was not a single reported occurrence of a clinically meaningful negative outcome/effect or an abnormal blood test that could be attributed to toxicity.¹

Testing included routine blood samples, heart rate and blood pressure measurements. One dataset included a full laboratory panel at baseline, completion, and at the end of open label extension. In addition, a smaller safety panel (hematology, potassium, calcium, alanine aminotransaminase, creatinine and estimated glomerular filtration rate (eGFR)) was performed every two weeks during each study phase.

For each dataset, no significant changes were noted and all values remained within normal clinical reference ranges.¹

4 Side Effects & Drug Interactions

4.1 Side effects

Side-effect-free intake ranges for vitamins and minerals have been established by the United States Institute of Medicine and similar authorities around the world based on a comprehensive review of relevant data in adults and children.²⁰⁻²⁵

According to these intake ranges established by the Institute of Medicine, the most important clinically relevant side-effect of the therapeutic dosage of **Daily Essential Nutrients (DEN)** is mild diarrhea and other mild gastrointestinal complaints in a small

percentage of patients who are sensitive to therapeutic magnesium doses.

Regarding this effect, the Institute of Medicine states, “Although a few studies have noted mild diarrhea and other mild gastrointestinal complaints in a small percentage of patients at levels of 360 to 380 mg (15.0 to 15.8 mmol) per day, it is noteworthy that many other individuals have not encountered such effects even when receiving substantially more than this [level] of supplementary magnesium.”²⁰

The following treatment-emergent adverse events have been observed in patients with bipolar disorder, depression, ADHD, generalized anxiety disorder, mood lability and explosive rage, oppositional defiant disorder, Asperger syndrome, and Prader Willi syndrome:¹

4.1.1 Body as a Whole

Infrequent: headache

4.1.2 Digestive System

Frequent: change in urine color (a fluorescent yellow color due to riboflavin).

Infrequent: loose stools, nausea.

Rare: flatulence, diarrhea, stomach ache, vomiting.

4.2 Drug interactions

4.2.1 Anticoagulant medications

DEN contains vitamin K, which promotes blood clotting function. Caution is advised when administering **DEN** to patients on warfarin-type anticoagulant therapy, as vitamin K may alter the hypoprothrombinemic response to anticoagulant drugs.

Periodic monitoring of prothrombin time is essential in determining the appropriate dosage of anticoagulant medications during **DEN** therapy. Dosage adjustments to anticoagulant medications may be required.

4.2.2 Psychoactive drugs

Interactions have been observed in clinical experience when **DEN** is administered together with psychoactive drugs, including lithium. On this issue, researchers commented, “use of multi-nutrient formulations as an adjunct should be monitored closely and with full attention to the possibility that optimum dosing of psychotropic agents may require significant adjustments.”¹ Treatment guidelines for patients taking psychiatric drugs are found in 7.2 *Psychiatric medications*.

Based on initial clinical evaluations, **DEN** has shown much milder interactions with psychoactive medications than previously researched citrus bioflavonoid-containing micronutrient formulas. Furanocoumarins and related compounds in citrus bioflavonoids are known to impede hepatic clearance of many medications by inhibiting various cytochrome p450 enzymes, including CYP3A4, CYP1A2, CYP2C19, and CYP2C9.³⁰

However, **DEN** appears to show significant interactions with lithium, presumably because lithium is metabolized differently than other central nervous system (CNS)-active medications. Treatment guidelines for patients taking lithium are found in 7.2 *Psychiatric medications*.

Because interactions of **DEN** with psychiatric medications, including lithium, have not been systematically evaluated, caution is warranted. Any agent with CNS activ-

ity has the potential to interact with **DEN** and complicate the management of micronutrient treatments. These include psychiatric medications, medical drugs with CNS actions (antihistamines, medications for ‘colds’, theophylline, etc.), recreational agents (alcohol, marijuana, heroin, etc.), other commonly used substances that are not necessarily thought of as recreational agents (caffeine, nicotine), and certain hormones (e.g., glucocorticoids, thyroid hormones).

5 Warnings & Precautions

5.1 Warnings

All patient medication doses should be monitored by a physician while taking **Daily Essential Nutrients (DEN)**. Research indicates that psychoactive drugs may need to be gradually reduced or eliminated during nutrient therapy to avoid over-medication effects, with the recognition that abrupt medication discontinuation can be associated with adverse symptoms (see 4.2 *Drug interactions*).

5.2 Precautions

5.2.1 Citrus bioflavonoids

Patients who are currently taking a citrus bioflavonoid-containing supplement and are currently taking or have recently taken psychoactive medications should reduce the dose of citrus bioflavonoids gradually (by no more than 10% of the original dose per day) in order to minimize medication withdrawal effects (see 4.2 *Drug interactions*).

5.2.2 Clinical worsening

Patients being treated for any indication should be monitored closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of therapy, or at times of dose changes (either increases or decreases) in **DEN** or medications. Patients and/or caregivers should promptly report any adverse symptoms to a health professional, as medication dose changes may be required (see 8.1 *Psychiatric medication management*).

5.2.3 Iron

Although **DEN** contains a relatively low level of iron (about 1 mg per capsule), children should take **DEN** only under adult supervision. In cases documented by US Poison Control Centers, children who have died from iron supplements have taken more than 60 mg of iron/kg (27.2 mg of iron/lb) of body weight.

6 Overdose & Contraindications

6.1 Overdose

6.1.1 Human experience

No cases of overdose with **Daily Essential Nutrients (DEN)** have been documented.

6.1.2 Management of overdose

Management of overdose should consist of general measures employed in the management of overdose with similar nutritional formulations. Reduction or discontinuation of treatment is of fundamental importance.

6.2 Contraindications

Treatment with **DEN** should not be introduced if the patient is diagnosed with a condition where specific nutritional factors are contraindicated (e.g. Wilson’s disease), or if the patient has known hypersensitivity or allergy to any ingredients of **DEN**.

7 Treatment Guidelines

7.1 Using Daily Essential Nutrients (DEN)

Unless contraindications (see 6.2 *Contraindications*) or precautions (see 5.2 *Precautions*) direct otherwise, **DEN** can generally be administered to patients as outlined in this section. Individual patient characteristics may require adaptations according to clinical judgment.

7.1.1 Initial dosing

Generally, **DEN** can be titrated up to an appropriate therapeutic dose (see 3 *Indications & Dosage*) within 4 days (see *Figure 1*).

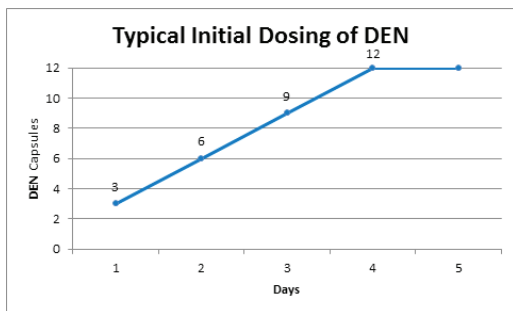


Figure 1 Typical initial dosing for **DEN**

7.1.2 Instructions for DEN use

Generally, patients should take **DEN** as directed on the label:

Suggested Use: “Consistently take 4 capsules 3 times daily, or a level recommended by your health professional. If desired, start with 1 capsule 3 times daily and increase gradually. Take with food.”

The most sensitive patients may benefit from starting with 1 capsule per day and increase to therapeutic levels as they are comfortable. Patients who have difficulty falling asleep should take **DEN** prior to 6 pm (see 8.7.2 *Inadequate sleep*).

Taking **DEN** with food helps to avoid potential gastrointestinal side effects (see 4.1 *Side effects*). Children should take **DEN** under adult supervision (see 5.2 *Precautions*).

7.2 Psychiatric medications

Psychiatric medication doses, including lithium, should be monitored carefully during **DEN** therapy (see 5.1 *Warnings*).

If psychiatric medication side effects emerge, gradually reduce medication dosages (see 4.2 *Drug interactions*). Ideal psychiatric medication tapering minimizes patient symptoms by avoiding both adverse interaction and withdrawal effects (see 8.1 *Psychiatric medication management*). **Figure 2** illustrates the importance of minimizing drug-related symptoms during the psychiatric medication reduction process.

Hardy Nutritionals® Balanced Free-Form Aminos or protein powders can help ameliorate drug-related symptoms until medication reductions are optimized, perhaps by binding to pharmacologically active drug metabolites and diminishing their pharmacologic effects. Absorption of protein products will be expedited if taken between meals.

7.2.1 Polypharmacy

Multiple psychiatric medications are often prescribed together to manage symptoms for which one medication alone may not be effective. These medications should be reduced at the same rate in order to maintain the balance that they exert together on the central nervous system.

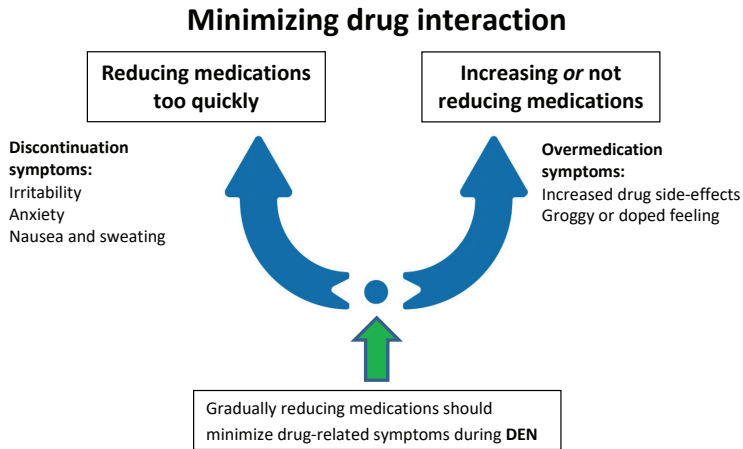


Figure 2 Psychotropic medication reduction guide

7.3 Other medications

All medication doses should be monitored by a physician during **DEN** therapy (see 5 *Warnings & Precautions*).

Medications for health conditions such as thyroid irregularities, insulin irregularities, heart issues, high blood pressure, high cholesterol, and cancer need to be monitored closely. Medication dosages may require adjustment.

Non-psychiatric medications that may limit a patient's response to **DEN** are listed in 8.2 *Non-psychiatric medications*.

7.4 Gastrointestinal issues

Healthy gastrointestinal function is critical for optimal digestion and absorption of nutrients from foods and supplements. Various gastrointestinal issues, such as bowel disorders, constipation, diarrhea, and gut microflora imbalance can limit response to **DEN** therapy. For detailed recommendations, see 8.5 *Gastrointestinal problems*.

7.5 Other considerations

Additional patient characteristics that can influence the use of **DEN** and/or adjunct treatments include the following:

- Patient history (see 8.6 *Patient history*).
- Lifestyle factors (see 8.7 *Lifestyle factors*).
- Recreational drug use (see 8.3 *Recreational drugs*).
- Supplement use (see 8.4 *Supplements*).
- Other factors influencing nutritional requirements (see 8.8 *Physical health and life stage factors*).

7.6 Addressing residual symptoms

DEN doses may need to be adjusted over time according to patient response and factors that limit the effectiveness of **DEN** therapy (see 8 *Possible Limiting Factors*). Adjunct treatments may also be useful.

7.6.1 Physical symptoms of anxiety and stress

Physical symptoms of anxiety may include light-headedness, muscle tension, and ‘butterflies’ in the stomach, which may be accompanied by excessive worrying, poor concentration, and distractibility. Patients who continue to experience symptoms of physical anxiety or stress while taking a therapeutic dose of **DEN** may benefit from added inositol (such as **Hardy Nutritionals® Inositol Powder**).

7.6.2 Racing or obsessive thoughts

Patients who continue to exhibit rage, aggression, racing thoughts or obsessive thoughts while taking a therapeutic dose of **DEN** may benefit from added choline (such as choline bitartrate or **Hardy Nutritionals® Phosphatidyl Choline**).

8 Possible Limiting Factors

Since 1996, we have observed that various factors can significantly limit responses to nutrient therapy, such as medications, lifestyle, and gastrointestinal health. Recognizing these factors and taking appropriate steps can make a significant difference to **Daily Essential Nutrients (DEN)** treatment response.

8.1 Psychiatric medication management

Changing psychiatric medications inappropriately during **DEN** therapy can be a significant limiting factor. Improper medication dosages can affect neurotransmitter systems in various ways and lead to fluctuations in brain chemistry that complicate symptom management.

8.1.1 Discontinuation

Gradually tapering off psychiatric medications generally provides the greatest stability for patients during treatment with **DEN**. We do not recommend abrupt discontinuation of any psychiatric medications during **DEN** therapy.

To prevent pronounced discontinuation symptoms as well as rebound (a significant return of the original symptoms), psychiatric medications should be reduced gradually. The rate at which medications are terminated and the duration of the pharmacological treatment are key factors that influence discontinuation symptoms. Discontinuation effects are typically more acute with drugs that have a relatively short half-life.

8.1.2 Increasing dose

Increasing psychiatric medication dosages while using **DEN** may increase the possibility of drug-nutrient interactions (see 4.2.2 *Psychoactive drugs*).

8.2 Non-psychiatric medications

Worsening of symptoms has been observed when various medications have been used together with **DEN**. These effects have been most pronounced with the following medications:

8.2.1 Anesthetics

Anesthetics have potential interactions with psychiatric medications. Psychiatric medication status is an important consideration in the management of the patient about to undergo anesthesia and surgery.³¹⁻³³ For example, benzodiazepines are commonly administered for many surgical procedures to sedate and relax patients. This may be considered increasing or changing medications (see 8.1 *Psychiatric medication management*).

Some unmedicated individuals taking previous formulations of **DEN** have reported withdrawal or post-withdrawal symptoms following surgery which have responded to standard post-withdrawal drug symptom alleviation measures (see 8.6.2 *Psychiatric drug use*).

8.2.2 Antacids

Antacids (such as Zantac, Prilosec, Tagamet, etc.) neutralize or inhibit the production of stomach acid which is necessary for digestion. Acidic denaturation is a major step in the process of extracting nutrients. Inhibiting this step of the digestive process can reduce the bioavailability of critical nutrients during the absorption phase.

8.2.3 Antibiotics

Antibiotics have saved countless lives. However, antibiotic use can cause collateral damage to the intestinal microbiome.³⁴ Oral antibiotics may vastly impact both good and pathogenic gut microflora, resulting in reduced nutrient absorption.

Individuals who take antibiotics during **DEN** therapy may experience a worsening of symptoms. This effect has not been observed with intravenous antibiotics, suggesting that the interaction occurs in the gastrointestinal system.

A temporary 50% increase in micronutrient dose for the duration of the antibiotic treatment generally compensates. Adding a probiotic-prebiotic combination (such as **Hardy Nutritionals® Greens & Probiotics**) during the course of antibiotic treatment, plus one to two weeks after completion, is also recommended.

A natural antibiotic/anti-fungal agent is also recommended for the duration of the antibiotic treatment, especially if the individual has a history of fungal/microbial infections. Possibilities include olive leaf extract (such as **Hardy Nutritionals® Olive Leaf Extract**), caprylic acid, garlic capsules, and oil of oregano.

8.2.4 Antihistamines

Antihistamines have been observed to cause clinically significant increases in psychiatric symptoms when used together with **DEN**. Cautious use is warranted.

8.2.5 Birth control

Hormone-containing birth control medications may worsen depression, alter mood, and/or increase nervousness and irritability when used together with **DEN**. Cautious use is warranted.

8.2.6 Hormone replacement therapy (HRT)

HRT may worsen depression, alter mood, and/or increase nervousness and irritability when used together with **DEN**. Cautious use is warranted.

8.2.7 Opioid Analgesics

Opioid analgesics may cause clinically significant increases in psychiatric symptoms when used together with DEN. Cautious use is warranted. (see 4.2.2 *Psychoactive drugs*).

8.3 Recreational drugs

8.3.1 Street drugs

Street drugs can cause a definite psychotropic effect, and the potential interaction with **DEN** may cause mood and mind altering effects (see *Appendix A*, reference 7). Keep in mind that many individuals who are addicted to street drugs try to conceal their addictive behaviors, and a patient's lack of progress or unexplained symptoms may be the result of consuming street drugs. Specialized nutrient therapy has been used to successfully treat addictions.³⁵

8.3.2 Alcohol

Alcohol abuse can significantly interfere with **DEN** therapy. Ideally, alcohol use should be minimized.

8.4 Supplements

8.4.1 Vitamins

Although taking extra vitamins while taking **DEN** is not usually necessary, adding individual vitamins for specific clinical purposes may be useful. For example, where long-standing specific vitamin deficiencies or genetic conditions predisposing individuals to higher vitamin needs exist, it may be necessary to add therapeutic amounts of specific vitamins in order to optimize therapeutic response to **DEN**.

8.4.2 Minerals

Additional iron may be added to **DEN** therapy without any issue. Generally, we recommend that the minerals copper, zinc, calcium and magnesium should not be added to **DEN** therapy, as they can alter critical mineral balances of the **DEN** formulation and render it less effective. Whole foods containing these minerals are not a problem.

8.4.3 Psychoactive supplements

Any psychoactive supplement has the potential to interfere with **DEN** effects. These include (but are not limited to) SAM-e, 5-Hydroxytryptophan (5-HTP), St. John's wort, ginseng, kava kava, skullcap, and valerian root. If patients choose to use psychoactive supplements during **DEN** therapy, advise cautious dosing and monitor their responses carefully.

8.5 Gastrointestinal problems

Diarrhea or constipation can reduce the absorption of essential vitamins and minerals. If either condition becomes an issue, whole foods and probiotics are often useful. Adequate hydration and a healthy diet with plenty of fiber from fruit and vegetables prevent many problems.

8.5.1 Bowel disorders

Irritation and inflammation of the intestinal lining is a common occurrence in chronic bowel disorders. These disorders may improve in time while using **DEN**, but can significantly reduce the absorption of key nutritional elements until they are corrected. Restriction diets, probiotics, digestive enzymes, certain oils, fatty acids, and

various other supplements may be beneficial in restoring and maintaining more normal bowel function.

8.5.2 Constipation

Constipation can be a critical limiting factor of **DEN** treatment by severely reducing absorption of essential vitamins and minerals. Root causes of constipation are varied. Depending on the cause of constipation, different measures may be appropriate to rectify the problem according to clinical judgment.

Treatment experience with **DEN** has shown that a few simple measures can often help constipation. Adequate hydration is essential. Fiber-rich whole foods like prunes, raw fruits and vegetables often help. In addition, patients with constipation benefit long-term from a probiotic-prebiotic combination (such as **Hardy Nutritionals® Greens & Probiotics**), which can help restore intestinal microflora balance.

8.5.3 Diarrhea

Diarrhea can severely limit the effectiveness of **DEN** treatment by preventing absorption of essential vitamins and minerals. Causes of diarrhea are varied. Depending on the cause of diarrhea, different measures may be appropriate to rectify the problem according to clinical judgment.

Treatment experience with **DEN** has shown that certain foods like unripe bananas, peanut butter, cheddar cheese often helped rectify diarrhea related to initiating nutrient therapy. In addition, many patients with chronic diarrhea benefit long-term from a probiotic-prebiotic combination (such as **Hardy Nutritionals® Greens & Probiotics**), which can help restore intestinal microflora balance.

8.5.4 Microflora imbalance

Gut microflora may become imbalanced due to factors such as antibiotic use, infections, and diet patterns. Restorative measures should be taken to ensure optimal absorption of micronutrient treatments.

A probiotic-prebiotic combination product (such as **Hardy Nutritionals® Greens & Probiotics**) may be beneficial in restoring healthy gut function in individuals with mild microflora imbalance.

If this is not sufficient and symptoms do not improve, then a natural antibiotic/antifungal agent (such as **Hardy Nutritionals® Olive Leaf Extract**) may be warranted. In particular, patients with a history of extensive or chronic antibiotic use are often highly susceptible to severe microflora imbalances (see *Appendix B* for indicative questionnaire).

Note: Antibiotic/antifungal agents like **Hardy Nutritionals® Olive Leaf Extract** may cause a die-off response, known as the Herxheimer reaction, which presents as flu-like symptoms and can arise anywhere from the first day to the first couple of weeks after beginning the product. If vomiting occurs, reduce the dosage or introduce an alternate antibiotic/antifungal agent (e.g. caprylic acid, garlic capsules, or oil of oregano). Changing antibiotic/anti-fungal products periodically may prevent organisms from adjusting to a single product. If there is no Herxheimer reaction, complete the course at recommended levels.

8.6 Patient history

8.6.1 Antibiotic use

If an individual has had a lengthy history of oral antibiotic use, particularly as a child, a probiotic (such as **Hardy Nutritionals® Greens & Probiotics**) is recommended. Normally, probiotics do not need to be taken on a continual basis. Once the probiotic has had its effect, it may only need to be taken periodically thereafter.

If symptoms do not improve with probiotic use, additional measures may be needed (see 8.5.4 *Microflora imbalance*).

8.6.2 Psychiatric drug use

Residual medication-related symptoms can appear for months and in some cases even years after psychiatric medications have been discontinued.^{36,37} Post-withdrawal medication symptoms are often triggered by such things as physical exertion, weight loss, stress, prolonged sun exposure, and liver or bowel cleanses. To a lesser extent, post-withdrawal drug symptoms may also be triggered by massage, chiropractic, or acupuncture therapies.

Some symptoms of post-withdrawal include insomnia, anxiety, depression, crying jags, agitation, and irritability. Individuals often report they feel medicated again. Post-withdrawal symptoms can often be mistaken for a return of psychiatric symptoms.

Suggestions for treatment of post-withdrawal drug symptoms include avoiding or moderating ‘trigger’ activities and/or temporarily adding protein isolate or free-form amino acids (such as **Hardy Nutritionals® Balanced Free-Form Aminos**) to the patient’s treatment regimen.

8.6.3 Sensitivities

Sensitive individuals may require and/or tolerate lower doses of **DEN**. Sensitive individuals may be identified by their history or by low medication tolerance. They may become restless, agitated, or irritable within hours or several days of starting micronutrient products.

8.6.4 Special nutrient needs

Where long-standing specific vitamin or mineral deficiencies exist, including genetic conditions that predispose individuals to higher vitamin or mineral needs, it may be necessary to add therapeutic amounts of specific vitamins or minerals in order to optimize therapeutic response.

8.7 Lifestyle factors

8.7.1 Inadequate diet

DEN is designed to add vitamin and mineral density to an existing diet. Thus, it is still very important for patients to eat regular, well balanced meals each day. There are many important nutritional factors that are best obtained from whole foods. Individuals taking **DEN** should avoid diet extremes and over-consumption of refined foods, especially if they are susceptible to gastrointestinal microflora imbalance (see 8.5.4 *Microflora imbalance*).

8.7.2 Inadequate sleep

Poor sleep quality and/or sleeplessness significantly exacerbates mania and psychosis issues. Adequate sleep is a significant factor in psychiatric health. Doses of **DEN** late in the day (after 6 pm) may contribute to wakefulness in some people.

8.7.3 Inadequate hydration

It is important to drink an adequate amount of water. Eight cups (approximately 2 quarts or 2 liters) of fluids per day are typically recommended. Water assists in moving nutrients into and flushing wastes out of the body.

8.7.4 Non-compliance

Inconsistent or “as needed” dosing of **DEN** is not recommended. The best results come from regular, steady dosing. It may be helpful to think of **DEN** as food for a starving brain. Non-compliance may indicate that the individual may require additional education and/or assistance.

8.7.5 Weight loss

Weight loss can trigger post-withdrawal drug symptoms, presumably by facilitating the release of sequestered medication residues from poorly perfused tissues. For measures that may alleviate post-withdrawal drug symptoms, see 8.6.2 *Psychiatric drug use*.

8.8 Physical health and life stage factors

8.8.1 Menstrual cycle

Psychiatric symptoms may increase during the menstrual cycle. This is likely due, in part, to changing hormone levels and increasing nutrient demands. Should symptoms become apparent during this time, **DEN** should be increased by at least one full dose of 4 capsules/day for about one week. In subsequent cycles, additional **DEN** taken a few days prior to menstruation may be preventative.

8.8.2 Physical illness

Additional **DEN** may be beneficial when a person becomes ill with a cold, flu, or other illness. Recurrent illness and infections are a sign of a weakened immune system. Increasing **DEN** by 4 capsules daily to support the immune system through illness may lead to faster recovery.

8.8.3 Pregnancy and breastfeeding

Nutritional requirements are significantly increased during pregnancy and breastfeeding. The daily dose of **DEN** should be increased in relative proportion to daily caloric intake, particularly in individuals with psychiatric symptoms. An additional dose of 4 **DEN** capsules per day may be useful.

8.8.4 Puberty

Puberty is a time when hormones are changing and the body's nutritional demands may be changing as a result. The onset of many psychiatric symptoms often corresponds with this period of development. For these reasons, additional **DEN** may be beneficial during puberty.

9 Appendix A

Research

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[†]Refers to pre-2013 versions of Truehope EMPowerplus which were co-formulated by David Hardy before he founded Hardy Nutritional®. Truehope EMPowerplus is a registered trademark of The Synergy Group of Canada Inc.

10 Appendix B

Microflora Imbalance Questionnaire

Section A: History

Circle the score to the right of each question when a response is “yes”, then total the circled numbers and write the total at the bottom of the section.

- 1. Have you taken tetracycline (Sumycin®, Panmycin®, Vibramycin®, Minocin®, etc.) or other antibiotics for acne for 1 month or longer? 25
- 2. Have you at any time in your life, taken other “broad spectrum” antibiotics for respiratory, urinary or other infections for 2 months or longer, or for shorter periods, 4 or more times in a 1 year span? 20
- 3. Have you recently taken a broad spectrum antibiotic drug? 6
- 4. Have you taken prednisone, Decadron® or other cortisone-type drugs by mouth or inhalation...
 - for more than 2 weeks? 15
 - for 2 weeks or less? 6
- 5. If you have ever had thrush, athlete’s foot, ringworm, jock itch or other chronic fungus infections of the skin or nails, have such infections been...
 - severe or persistent? 20
 - mild or moderate? 10
- 6. Do you crave sugar/ sweets? 10
- 7. Do you crave breads? 10
- 8. Do you crave alcoholic beverages? 10

Section A: Total Score _____

Section B: Secondary Indicators

For each symptom that is present, enter the appropriate number in the Point Score column:

- If a symptom is occasional or mild: 3 points
- If a symptom is frequent or moderately severe: 6 points
- If a symptom is severe and/or disabling: 9 points

Total the scores for this section and record them at the end of this section.

- Fatigue or lethargy _____
- Feeling of being “drained” _____
- Drowsiness _____
- Feeling “foggy” or “spacey” _____
- Inability to make decisions. _____
- Inability to concentrate _____
- Poor memory _____
- Frequent mood swings _____
- Attacks of anxiety or crying _____
- Headaches. _____

Abdominal pain	_____
Constipation.	_____
Diarrhea	_____
Bloating, belching or intestinal gas	_____
Indigestion or heartburn	_____
Chronic rashes or itching.	_____
Psoriasis or recurrent hives	_____
Rectal itching	_____

Section B: Total Score _____

Section C: Minor Indicators

For each symptom that is present, enter the appropriate number in the Point Score column:

- *If a symptom is occasional or mild:* 1 points
- *If a symptom is frequent or moderately severe:* 3 points
- *If a symptom is severe and/or disabling:* 5 points

Total the scores for this section and record them at the end of this section.

Irritability or jitteriness.	_____
Dizziness/loss of balance.	_____
Pressure above eyes or in ears...feeling of head swelling	_____
Tendency to bruise easily	_____
Food sensitivity or intolerance	_____
Dry mouth or throat	_____
Bad breath.	_____
Foot, hair or body odor not relieved by washing.	_____
Nasal congestion or post-nasal drip.	_____
Nasal itching	_____
Sore throat	_____
Laryngitis, loss of voice.	_____
Cough or recurrent bronchitis	_____
Burning or tearing of eyes	_____
Recurrent infections or fluid in ears.	_____
Ear pain or deafness	_____
Numbness, burning or tingling	_____
Muscle aches	_____
Muscle weakness or paralysis	_____
Pain and/or swelling in joints	_____
Impotence.	_____

Urinary frequency, urgency or incontinence _____
Burning on urination _____
Loss of sexual desire or feeling _____

Section C: Total Score _____

Female-Specific History

Questions 1-3 circle the score, 4-7 use scoring points below:

- *If a symptom is occasional or mild:* 3 points
- *If a symptom is frequent or moderately severe:* 6 points
- *If a symptom is severe and/or disabling:* 9 points

Total the scores for this section and record them at the end of this section.

1. Have you at any time in your life, been bothered by persistent vaginitis or other problems affecting your reproductive organs? **25**
2. Have you been pregnant...
 - 2 or more times? **5**
 - 1 time? **3**
3. Have you taken birth control pills for...
 - more than 2 years? **15**
 - 6 months to 2 years? **6**
4. Do you experience troublesome vaginal burning, itching or discharge? _____
5. Do you experience endometriosis or infertility? _____
6. Do you experience severe cramps and/or other menstrual irregularities? _____
7. Do you experience premenstrual tension? _____

Female-Specific History Score _____

Combined Score

Section A: _____/116
Section B: _____/162
Section C: _____/120
Female-specific: _____/81

Total Score: _____

Women	Men	Recommendation	
0-90	0-78	Unlikely an issue	
90-229	78-196	Possibly present	Probiotic
229-479	196-398	Likely present	OLE + Probiotic

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