The Use of Dietary Supplements in Diabetic Peripheral Neuropathy

These products can be used to treat this frequent complication of diabetes.

Objectives

1) To examine the significant role of dietary supplements in the treatment of painful diabetic peripheral neuropathy.

2) To understand the Dietary Supplement Health and Education Act.

3) To identify both the benefits and risks of specific dietary supplements when treating painful diabetic peripheral neuropathy.

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*Following this article, an answer sheet and full set of instructions are provided (p. 202).—**Editor***

By Robert G. Smith DPM, MSc, RPh

Introduction

Polyneuropathy is a major complication of both insulin-dependent and non-insulin-dependent diabetes mellitus, and is the most common form of neuropathy in the developed world. In the United States, the American Diabetes Association reports that 23.6 million children and adults (8% of the population) have diabetes.[1] Although estimates of the prevalence of diabetic peripheral neuropathy vary substantially depending on diagnostic criteria and the intensity of investigation, most studies suggest that about 30-50% of all diabetic people are affected.[2] Backonja[3] stated that approximately 45% of diabetic patients will experience neuropathy during the course of the disease. Backonja[3] also stated that 4% to 5% of all diabetic patients will have painful neuropathy.

Peripheral neuropathy is characterized by a progressive loss of nerve fibers that predisposes the patient to pain or insensitivity in the extremities as well as neuropathic ulcerations; it can also result in amputation. Neuropathic pain results from primary lesions or dysfunction of the peripheral or central nervous system (Figure 1). This pain encompasses a variety of sensory, motor, and autonomic symptoms.[4,5]

Despite its many etiologies, neuropathic pain is usually spontaneous, continuous, burning, paroxysmal, and evoked by various mechanical or thermal stimuli.[6] Long-term elevation of plasma glucose levels has been established as the definitive cause of diabetic peripheral neuropathy.[7] Currently, the only treatment that addresses the

Continued on page 196

Supplements...

underlying cause of painful diabetic neuropathy is improved control of blood glucose levels.[5]

Glucose Control and Diabetic Neuropathy

There is strong evidence for the importance of tight glucose control in delaying, and possibly preventing diabetic peripheral neuropathy. Tesfaye noted that the same cannot be said for diabetic peripheral neuropathic pain.[2] In the absence of a curative therapy for painful diabetic neuropathy, pharmacologic or nonpharmacologic tools, or combination of both, should be used to provide control of symptoms. Pharmacological interventions, as well as advances in the management of painful diabetic peripheral neuropathy, have been thoroughly reviewed.[2,5]

Lack of response and unwanted side-effects of conventional pharmacological treatments force many suffers of painful diabetic neuropathy to explore alternative herbal and dietary supplements.[8]

This article reviews dietary supplements currently used to manage painful diabetic neuropathy. First, the history of dietary supplements and the Dietary Supplement Health and Education Act (DSHEA) legislation are presented as a foundation. Second, the dietary supplement properties used to treat painful diabetic neuropathy are described. Finally, comparisons of these supplements with regard to the dosages, frequencies, and adverse effects described in the medical literature are offered to help with selection of the most appropriate supplement for each individual patient.

Supplement Use and Legislation

The word "vitamin", short for vital amines, was coined in 1912 as an abbreviated term meant to capture the notion of important factors in the diet. In 1913, the first vitamin, thiamine, was isolated; deficiency of thiamine caused beriberi. Thirteen vitamins and 15 essential minerals have now been identified as important to human nutrition.

Large-scale fortification of diets began in the United States with the addition of iodine to table salt in 1924 to prevent goiter, followed by the addition of thiamine, riboflavin, niacin, and iron to flour in 1941. Multivitamin and multimineral products providing more than vitamins A and D became available in pharmacies and grocery stores in the mid-1930s.

In the early 1940s, the first multivitamin and mineral tablet was introduced. Annual sales of supplements to Americans are now reported at about $23 billion, a substantial share of which is spent on vitamins and minerals.[9] The most common type of dietary supplement reported in the United States is the multivitamin supplement.[10]

Dietary supplement use is increasingly common in the general population of the United States, and usage may be even more common in some subpopulations (e.g., patients with diabetes).[11] More than half of American adults take dietary supplements in the belief that the supplements will make them feel better, have greater energy, improve their health, and prevent and treat disease.

DSHEA

In 1994, the Dietary Supplement Health and Education Act (DSHEA) defined a dietary supplement as a vitamin, mineral, herb or other botanical, amino acid, or other substance (e.g., coenzyme, organ tissue, glandular, or metabolite).[12] The DSHEA assumed that the history of use of a given supplement was evidence for its safety, thus grandfathering in all supplements on the market before the legislation. The current level of public assurance of the safety and quality of multivitamin and minerals products is inadequate.

Currently, manufacturers of these products are not required to report adverse events and the FDA has no regulatory authority to require labeling changes or to help inform the public of these issues and concerns. Further, the FDA has insufficient resources and legislative authority to require specific safety data from dietary supplement manufacturers or distributors before or after their products are made available to the public. These unregulated supplement products would be subject to premarket approval if they were marketed as food additives.

Notably, the ingredients in some cases possess biological activities similar, if not identical, to those found in medications.[10] Use of nutrients in foods and supplements in the United States is changing, and the NIH is concerned that public safety cannot be assured.[10]

Adverse events from multivitamin/multimineral supplements appear with some frequency in both the reports of the American Association of Poison Control Centers and the FDA's MedWatch system.[10]

Finally, the NIH position is that the present evidence is insufficient to recommend either for or against the use of multivitamin/multimineral supplements by the American public to prevent chronic disease.[10] Further, Bardia et al. examined the extent to which US adults used herbal supplements in accordance with evidence-based indications.[13] Of the 30, 617 adults surveyed, 5,787 (18.9%) had consumed herbal supplements in the past 12 months. Of these, 3,315 (57.3%) used herbs to treat a specific health condition.

It was concluded that roughly two-thirds of adults using commonly consumed herbs did not do so in accordance with evidence-based indications. For this reason, it is essential that practicing podiatric physicians acutely evaluate current medical literature on the subject of

Continued on page 197

TABLE 1
Mechanisms of Neuropathic Pain

Peripheral mechanisms	Central mechanisms
Changes in sodium channel distribution and expression	Central sensitization
Altered neuropeptide expression	AB fibre sprouting into lamina II of dorsal horn
Sympathetic sprouting	Reduced inhibition of descending pathyways
Peripheral sensitization	
Altered peripheral blood flow	
Axonal atrophy, degeneration or regeneration	
Damage to small fibers	
Glycaemic flux	

Adapted from Tesfaye S. Advances in the management of diabetic peripheral neuropathy Curr Opin Support Palliat Care 3: 136, 2009

Supplements...

botanicals and supplements to treat diabetic neuropathic pain.

Challenges in Standardizing Herbal and Supplemental Products

Goldman identified several challenges in standardizing herbal medicines.[14] The first such challenge is that bioassays must be based on biological models, which are not available for the health claims made for many popular herbs.[14] Secondly, chemical analysis has limited value when the ingredients responsible for a plant's activity have not been identified.[14] Also, if the active ingredient of an herb is known, it remains unclear whether the crude herb would be preferable to its purified active component.[14]

When the active principle ingredient of an herbal preparation is not known and there is no accepted method of standardization, a clinical trial offers an attractive approach to evaluate the activity.[14] Two important requirements necessary for successful clinical herbal trials include a consistent herbal formulation and a large study sample.[14]

Although the methodology of herbal trials has improved, some studies cited in specific herbal compendia have a specific limitation. Many results of herbal trials often do not reach statistical significance because these studies enroll fewer participants than trials of conventional medications. Other limitations (e.g., poorly designed clinical trials or incomplete reports) make it difficult to evaluate published studies.[14]

One method of resolving these limitations is to pool data from individual trials by using a meta-analysis to reach an interpretation of the results of a group of inconclusive trials.[14]

Herbal and Dietary Supplements used in Diabetes Mellitus and Diabetic Peripheral Neuropathy

Diabetes mellitus is a chronic condition affecting millions of Americans. Podiatric physicians are very familiar with conventional medical treatments available to treat both diabetes mellitus and painful diabetic peripheral neuropathy. Many of the podiatric physician's patients solicit a professional podiatric opinion on the use of complementary and alternative medicine therapies, including dietary supplements to treat their diabetic and neuropathic symptoms (Figure 2).

The main motivations for patients to use these dietary supplements are to improve blood glucose, manage their symptoms, and lessen the risk of developing serious complications.

Yeh, et al. conducted an electronic literature search as well as a follow-up physical search of 108 trials examining 36 herbs and 9 vitamin and mineral supplements that involved 4,565 patients with diabetes or impaired glucose tolerance.[15] Upon analysis, 58 controlled clinical trials (42 randomized and 16 non-randomized trials) involving persons with diabetes or impaired glucose tolerance were discovered.[15]

These investigators present both a well-written narrative and a descriptive graphic table illustrating the study design, sample size, intervention, control group, outcomes, and adverse effects.[15] Two interesting points of inclusion in this table were the "quality of evidence" and "Jadad" scores.[15] Of these 58 trials, the direction of evidence for improved glucose control was positive in 76% (44 of 58 trials).[15]

It was concluded that there is still insufficient evidence to draw definitive conclusions regarding the efficiency of individual herbs and supplements for diabetes. Chromium has been the most widely studied supplement, but other supplements with positive preliminary results include: gymnema sylvestre, aloe vera, vanadium, momordic charantia, and nopal.[15]

Finally, it was noted that the available data suggest that several supplements may warrant further study.[15]

Alpha-Lipoic Acid

Alpha-lipoic acid, also known as thioctic acid, is an endogenous, sulfur-containing free radical scavenger found in mitochondria.[8] Treatment with alpha-lipoic acid improves nerve blood flow and distal nerve conduction and increases endoneurial glucose uptake and energy metabolism in animals.[8,16,17] Alpha-lipoic acid also recycles other antioxidants (e.g., vitamin E

Continued on page 198

TABLE 2
Dietary Supplements Treating Diabetic Peripheral Neuropathy

Supplement	Mechanisms	Daily Dose	Possible Adverse Effects
Alpha-Lipoic acid	Reduces oxidation throughout body	600 mg	May Lower Blood Glucose
Acetl-L-carnitine	Uptake and oxidation of long fatty acids	1000 mg (IM)	Nausea and Diarrhea
Benfotiamine	Increase transketolase activity	300-450 mg	No reports of toxicity
Capsaicin	Depletes neurotransmitter stores	Topical 3 to 4 times	Hot sensation may cause discontinuation
Vitamin B-6	Inhibits glycoslation of proteins	Inconclusive	Avoid doses larges dose with levodopa without taking carbidopa
Vitamin B-12	Reduces homocysteine	Unknown	Not to used with Leber's opyic atropy
L-methylfolate Pyridoxal 5'-phosphate Methylcobalamin	Methlation of homocsteine Prosthetic group for enzymes Biological active Vitamin B-12	Twice a day	Co-administration with certain drugs will alter folate plasma levels Antibiotics may alter intestinal microflora resulting decrease absorption of methycobalamine
Vitamin E	Powerful antioxidant reducing free radicals	900 IU	Possible drug interaction with Warfarin alteration in vitamin K stores Use in caution of liver failure

and vitamin C) but can chelate transition metals, like iron and copper.[8] Alpha-lipoic acid reduces oxidation throughout the body because it is both fat-soluble and water-soluble.[8]

According to Halat and Dennehy, clinical trials have demonstrated symptomatic improvements after short-term parenteral use rather than long-term use of alpha-lipoic acid.[8] Because oral formulations are more convenient for patients to maintain adherence, more economical, and easier to obtain, the scope of alpha-lipoic acid trials discussed here will be limited to recent trials using oral alpha lipoic acid. One clinical trial reported significant improvements in nerve conduction velocity with oral doses of 600 to 1, 200 mg per day for two years.[18]

Another trial observed that symptoms improved using 1,800 mg per day for 21 days.[19] A final investigation demonstrated that oral treatment with alpha-lipoic acid for five weeks improved neuropathic symptoms and deficits in patients with diabetic peripheral neuropathy. Further, the study established that an oral dose of 600 mg once daily provided the optimum risk-to-benefit ratio.[20]

Currently, alpha-lipoic acid is already approved in Germany for diabetic neuropathy.[8] When more research on the long-term benefits of alpha-lipoic acid become available, it is hoped that statements concerning the long-term safety and clinical effectiveness will allow the practicing podiatric physician to evaluate the benefits of this supplement for treating diabetic peripheral neuropathy.

The podiatric physician may need to advise the patient who initiates alpha-lipoic acid treatment to monitor their blood glucose levels frequently because lipoic acid may lower blood glucose levels unexpectedly.

Acetyl-L-carnitine

Acetyl-L-carnitine is an endogenous substance similar in structure to acetylcholine, and is involved in the uptake and oxidation of long-chain fatty acids in mitochondria.[8,21] One of the first human randomized controlled trials examined 20 patients with symptomatic neuropathy during a 15-day period.[21]

The subjects of this investigation received either intramuscular acetyl-L-carnitine or a placebo at 1000 mg per day.[21] Those patients who received intramuscular acetyl-L-carnitine showed a significant decrease in neuropathic symptoms as compared to the placebo group, but no change in vibratory perception threshold was noted.[21]

De Grandis and Minardi assessed the efficacy and tolerability of acetyl-L-carnitine versus placebo in the treatment of diabetic neuropathy, mainly by evaluating the effects of treatment on electrophysiological parameters and pain symptoms.[22] The main efficacy parameter was the effect of treatment on 6- and 12-month changes from baseline in nerve conduction velocity (NCV) and amplitude in the sensory (ulnar, sural and median) and motor (median, ulnar and peroneal) nerves.

The effect of treatment on pain was also evaluated by means of a visual analog scale (VAS).[22] Acetyl-L-carnitine was effective and well-tolerated for both improving neurophysiological parameters and reducing pain over a one-year period. Therefore, it was concluded that acetyl-L-carnitine offers a promising treatment option for patients with diabetic neuropathy.[22]

The podiatric clinician will obtain valuable information by reading De Grandis's recent review on the use of acetyl-L-carnitine in chemotherapy-induced peripheral neuropathy and applying this knowledge to diabetes-induced peripheral neuropathy.[23] Preliminary results have confirmed the reasonably good tolerability profile and efficacy of acetyl-L-carnitine in chemotherapy-induced peripheral neuropathy.[23]

De Grandis suggested that these studies support the use of acetyl-L-carnitine in cancer patients with persisting neurotoxicity induced by paclitaxel or cisplatin treatment.[23] Acetyl-L-carnitine can cause gastrointestinal symptoms such as nausea and diarrhea.

Benfotiamine

The fat-soluble form of vitamin B1, called benfotiamine, has been used effectively to treat alcoholic and diabetic neuropathies. Unlike that of thiamine, the structure of benfotiamine contains an open thiazole ring that closes once it is absorbed to produce biologically active thiamine. Benfotiamine is absorbed via passive diffusion through the intestinal mucosa and is rapidly converted to biologically active thiamine. Peak plasma concentrations of thiamine after oral benfotiamine administration are at least five times greater than those observed after oral administration of water-soluble thiamine salts.

Benfotiamine exerts its beneficial effects through a number of mechanisms. In the case of diabetes, benfotiamine increases transketolase activity, and thereby blocks three of the major molecular pathways leading to hyperglycemic damage. Benfotiamine prevents the increase in UDP-N-acetylglucosamine (UDP-GlcNAc), and enhances the hexosamine pathway activity to decrease the buildup of detrimental glucose metabolites that can lead to advanced glycation end products (AGE).

In addition, benfotiamine corrects imbalances in the polyol pathway by decreasing aldose reductase activity, sorbitol concentrations, and intracellular glucose, thereby protecting endothelial cells from glucose-induced damage.[24]

The efficacy and safety of benfotiamine in the treatment of diabetic polyneuropathy have been recently reported.[25] Stracke, et al. utilized a randomized double blind, placebo-controlled, phase-III study of 181 patients with symmetrical, distal diabetic polyneuropathy.[25]

After six weeks of treatment with 600 mg of benfotiamine per day, 300 mg of benfotiamine per day, or placebo, the primary outcome parameter "neuropathy symptom scored" differed significantly between the treatment groups.[25] The improvement was more pronounced at the higher benfotiamine dose and increased with treatment duration.[25]

Realm Laboratories has recently made Neuremedy™ available in the U.S.A. The active ingredient in Neuremedy™ is 150 mg of benfotiamine. There are no reports of benfotiamine drug interactions.[25] Benfotiamine administration appears to be safe with no reports of toxicity in the scientific literature.[26] Based on clinical studies to date, daily doses of oral benfotiamine range from 300-450 mg daily, in divided doses.[26]

Capsaicin

Capsaicin directly affects sensory fibers, especially C-fibers.[8,27] Initial application of capsaicin stimulates these fibers and deletes endogenous neurotransmitter stores associated with pain transmission (e.g., substance P, vasoactive intestinal peptide, cholecystokinin, and somatostatin).[28] This can result in a burning sensation

Continued on page 199

within the first few weeks of use.

This sensation might affect patient compliance, and patients should be advised to continue use, since it may take four to six weeks before benefits are appreciated.[8] Capsaicin is available without a prescription in strengths ranging from 0.025% to 0.25%. Clinical trials have demonstrated that application of capsaicin must take place three to four times a day for symptom improvement. There have been hundreds of studies on using capsaicin for the treatment of diabetic neuropathy. Unlike many other herbal food-based products, capsaicin is regulated as an over-the-counter product by the Food and Drug Administration; and therefore, it meets manufacturing, safety, and clinical efficacy standards for over-the-counter products.[8]

Zostrix® Neuropathy Cream is made with topical purified natural capsaicin (0.25%) that is far stronger than any other capsaicin cream currently available without a prescription. The product's unique patented cream formulation, which includes lidocaine, improves the tolerance of high strength capsaicin.

Zostrix® Neuropathy Cream can be used alone, or as a highly effective adjunctive therapy as a systemic pain medication to effectively relieve diabetic neuropathy pain. The formulation has proven efficacy with continued use for the treatment of localized neuropathic pain and a low risk of systemic side effects, adverse events, or drug interactions.

Clinically proven results demonstrated that Zostrix Neuropathy Cream significantly increased pain relief. Overall, 90% of Painful Diabetic Neuropathy patients reported improvement and by week six patients' pain was reduced by 50%.**

Vitamin B6 and Vitamin B12

Low levels of vitamin B6 have been reported in patients with diabetic neuropathy, but not in diabetic patients with neuropathy.[8,29] Vitamin B6 inhibits the glycosylation of proteins. Jones and Gonzalez conducted a small-scale, six-week trial of 10 diabetic patients using an open-study design to evaluate the effect of 25 mg of oral vitamin B6 on diabetic peripheral neuropathy.[30]

This trial observed symptomatic improvement in all patients; however, subsequent randomized, double-blind and placebo-controlled trials failed to demonstrate similar results.[8] Individuals being treated with levodopa without taking carbidopa at the same time should avoid daily doses of 5 milligrams or greater of vitamin B6.

Neuropathy caused by vitamin B12 deficiency is successfully treated with supplementation to restore normal vitamin B12 levels. The most common forms of supplemental B12 are cyanocobalamin and hydroxcobalamin. The natural form of B12 found in food is methylcobalamin.

The chemical structure of B12 is very complex, with numerous methyl groups attached. Methyl groups are used in beneficial methylation reactions such as those that reduce homocysteine. Methylcobalamin appears to be the most effective form of vitamin B12 for protection of nerves. Patients should be advised not to take cyanocobalamin if they have Leber's optic atrophy.

L-methylfolate, Pyridoxal 5′-phosphate, Methylcobalamin combination

L-methylfolate is the primary biologically active isomer of folate and the primary form of folate in the circulation. L-methylfolate is used in the methylation of homocysteine to form methionine and tetrahydrofolate. Pyridoxal 5′-phosphate is the active form of vitamin B6 and is used as the prosthetic group for many enzymes that depend on this vitamin.

Methylcobalamin is one of the two forms of biologically active vitamin B12. Commercial prescription products of L-methylfolate 2.8 mg, Pyridoxal 5′-phosphate 25 mg, and Methylcobalamin 2 mg are available under the name Metanx®.[31] These products are indicated for the distinct nutritional requirements of diabetic patients with endothelial dysfunction, who present with loss of protective sensation as well as neuropathic pain associated with diabetic peripheral neuropathy.[31]

Additionally, it is indicated for the distinct nutritional requirements of patients with endothelial dysfunction and/or hyperhomocysteinemia, who present with lower extremity ulcerations.[31] The recommended dose is one tablet twice daily or as directed by a physician.

Adverse reactions reported with Metanx® include: paresthesia, somnolence, nausea and headaches, mild transient diarrhea, polycythemia vera, itching, transitory exanthema and the feeling of swelling of the entire body.[31] When the podiatric physician elects to prescribe this combination of medication, caution may need to be exercised with antibiotics since alteration of the intestinal microflora may decrease the absorption of methylcobalamine.

The co-adminstration of Metanx® with either metformin, para aminosalicylic acid, or potassium chloride may decrease the absorption of methylcobalamin.[31] Because several drugs are associated with lowering serum folate levels or reduction of active folate available, monitoring of folate plasma levels may be advised when a patient's medication includes anticonvulsants, methotrexate, sulfasalazine, cholestyramine, colchicine, high dose NSAIDs, triamterene, trimethoprim, or in the presence of excessive alcohol intake or smoking.[31]

Vitamin E

Vitamin E is a powerful antioxidant that reduces levels of free radicals and oxidative stress. The effect of vitamin E on nerve function was evaluated in a randomized, double-blind, placebo-controlled trial with 21 type-2 diabetic patients diagnosed with mild-to-moderate neuropathy.[8,32]

The primary outcome evaluated large doses of vitamin E (900 IU) and the ability to reduce neuropathy over a six-month period.[32] There were no changes in glycemic indices, but both median and tibial motor nerve conduction velocities were significantly improved in the vitamin E group as compared to the placebo group.[32] These findings suggest that patients with neuropathy might experience a reduction of symptoms.[32]

Patients who begin to take vitamin E should consult their primary care providers before taking the vitamin if they are also taking warfarin, or if they have a vitamin K deficiency or history of liver failure.

Homeopathic Alternative

Neuragen PN® is a topical homeopathic drug designed for effective, temporary relief from pain that is described as shooting, burning, tingling, or stabbing, especially in the hands

Continued on page 200

Continuing Medical Education

Supplements...

and feet. Neuragen PN is a clinically-proven treatment for nerve pain caused by diabetes (foot and hand nerve pain)** Neuragen PN's® listed homeopathic ingredients include: hypericum 12C, aconitum napellus 12C, lycopodium 12C, phosphorus 12C, rhus toxicodendron 12C, and secale cornutum 12C. Neuragen PN® is concentrated and requires application of only a few drops.

Application of more than a few drops at a time may not improve effectiveness. The time period of relief varies from less than an hour to several days, depending on the type and extent of pain. Neuragen PN® does not numb the area of application and can be applied up to four times per day. Neuragen PN® is not recommended for muscular pain or arthritis.

Conclusion

Pain relief is one of the most challenging issues in diabetic neuropathy. Adequate glucose control is the mainstay of treatment for diabetic neuropathy, and conventional FDA-approved pharmaceuticals may be prescribed and used by neuropathic patients if symptom relief is not adequate. The podiatric physician will come to realize that the accessibility and advertising of dietary supplement products make these products attractive for many sufferers.

Additionally, shortcomings exist in the available dietary supplements because of the current governmental legislation. Specifically, there is no guarantee of efficacy, safety, or product content. This article reviewed dietary supplements currently used to manage painful diabetic neuropathy. ■

***Company will provide clinical information upon request to substantiate statements.*

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EXAMINATION

Continuing Medical Education

See answer sheet on page 203.

1) Backonja stated that ___to ____ of all diabetic patients will have painful neuropathy.
- A) 1%, 2%
- B) 2%, 3%
- C) 4%, 5%
- D) 6%, 10%

2) All of the following are peripheral mechanisms of neuropathic pain except:
- A) Damage to small fibers
- B) Reduced inhibition of descending pathways
- C) Glycemic flux
- D) Sympathetic sprouting

3) The word "vitamin" was coined in 1912 as an abbreviated term for _____.
- A) vital minerals
- B) vital proteins
- C) vital acids
- D) vital amines

4) Annual sales of supplements to Americans are reported at about_____.
- A) $ 16 million
- B) $ 50 thousand
- C) $ 23 billion
- D) $ 10 million

5) All of the following are challenges in standardizing herbal medicines identified by Goldman except:
- A) FDA safety data exists on all herbal products
- B) chemical analysis has limited value for many herbs
- C) whether the crude herb would be preferable to its purified active component
- D) bioassays must be based on biological models

6) Alpha-lipoic acid is an endogenous, sulfur-containing, free radical scavenger found in the_____.
- A) golgi body
- B) nucleus
- C) ribosomal RNA
- D) mitochondria

7) Acetyl-L-carnitine is involved in the uptake and oxidation of_____ in mitochondria?
- A) long-chain proteins
- B) omega-3 fatty acids
- C) long-chain fatty acids
- D) long-chain polysaccharides

8) The fat-soluble form of vitamin B1 is called_____.
- A) thiamine
- B) methylfolate
- C) benfotiamine
- D) tetrahydrofolate

9) Stracke, et al. found that improvement in diabetic polyneuropathy symptoms was more pronounced at _____
- A) a lower benfotiamine dose and decreased duration
- B) a higher benfotiamine dose and increased duration
- C) a lower benfotiamine dose and increased duration
- D) a higher benfotiamine dose and decreased duration

10) Based on clinical studies to date, daily doses of oral benfotiamine range from_____ daily, in divided doses.
- A) 25 mg—50 mg
- B) 100 mg—150 mg
- C) 500 mg—750 mg
- D) 300 mg—450 mg

11) The amount of purified natural capsaicin in proven Zostrix® Neuropathy Cream, the strongest available without a prescription, is:
- A) .0015
- B) .0025
- C) .25
- D) .025

12) The natural form of B12 found in food is_____.
- A) cyanocobalamin
- B) hydroxcobalamin
- C) methylcobalamin
- D) hexhydrocobalamin

13) According to this review, all of the following drugs are associated with reduction of serum folate levels except:_____.
- A) high doses of NSAIDs
- B) L-methylfolate
- C) anticonvulsants
- D) colchicine

14) According to ADA reports regarding US patients, 23.6 million children and adults or ____ of the population, have diabetes.
- A) 2%
- B) 5%
- C) 8%
- D) 15%

15) Select the homeopathic ingredient found in clinically-proven Neuragen® PN?
- A) Hypericum 12C, Aconitum
- B) Phosphorus 12C,
- C) Secale cornutum 12 C,
- D) All of the above are homeopathic ingredients

Continued on page 202

Continuing Medical Education

EXAMINATION

(cont'd)

16) According to this review, several studies have established long-term_____as the definitive cause of diabetic peripheral neuropathy.

A) elevation of plasma potassium
B) elevation of plasma glucose
C) elevation of plasma uric acid
D) elevation of plasma calcium

17) The current level of public assurance of safety and quality of multivitamin and minerals is _____.

A) adequate
B) acceptable
C) inadequate
D) sufficient

18) Yeh, et al. concluded that there is still _____ evidence to draw definitive conclusions regarding efficiency of herbs for diabetes.

A) insufficient
B) sufficient
C) satisfactory
D) enough

19) According to this review, vitamin E doses of _____may improve both median and tibial motor nerve conduction velocities when compared to placebo.

A) 200 IU
B) 400 IU
C) 900 IU
D) 300 IU

20) Despite its many etiologies, neuropathic pain is usually_____.

A) spontaneous
B) continuous
C) burning
D) all of the above are correct descriptions of neuropathic pain

See answer sheet on page 203.

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Continuing Medical Education

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Please print clearly...Certificate will be issued from information below.

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Charge to: _____Visa _____ MasterCard _____ American Express

Card #_____Exp. Date_____

Note: Credit card is the only method of payment. Checks are no longer accepted.

Signature_____Soc. Sec.#_____Daytime Phone_____

State License(s)_____Is this a new address? Yes_____ No_____

Check one: _____ I am currently enrolled. (If faxing or phoning in your answer form please note that $2.50 will be charged to your credit card.)

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Over, please

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ENROLLMENT FORM & ANSWER SHEET (cont'd)

EXAM #9/09
MRSA in the Diabetic Foot (Rogers and Bevilacqua)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

LESSON EVALUATION

Please indicate the date you completed this exam

_____

How much time did it take you to complete the lesson?

_____ hours _____minutes

How well did this lesson achieve its educational objectives?

_____Very well _____Well

_____Somewhat _____Not at all

What overall grade would you assign this lesson?

A B C D

Degree_____

Additional comments and suggestions for future exams:

_____

_____

_____

_____

_____

_____

EXAM #10/09
The Use of Dietary Supplements in Diabetic Peripheral Neuropathy (Smith)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

LESSON EVALUATION

Please indicate the date you completed this exam

_____

How much time did it take you to complete the lesson?

_____ hours _____minutes

How well did this lesson achieve its educational objectives?

_____Very well _____Well

_____Somewhat _____Not at all

What overall grade would you assign this lesson?

A B C D

Degree_____

Additional comments and suggestions for future exams:

_____

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