

Evidence-Based Systematic Review of Selenium (Se)

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INTRODUCTION

While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. This monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

RELATED TERMS

- Atomic number 34, Na₂SeO₃, selenium dioxide, selenized yeast, L-selenomethionine, Se, Sele-Pak, selenate, selenite, selenious acid, selenium sulfide, selenocysteine, selenomethionine (Semet), selepen, Se-methylselenocysteine (SeMCYS).

BACKGROUND

- Selenium is a trace mineral found in soil, water, and some

foods. It is an essential element in several metabolic pathways, including the glutathione-peroxidase pathway. Selenium appears to promote antioxidant activity in the body via glutathione peroxidase (GPX), a selenium-dependent enzyme.

- Selenium deficiency can occur in areas where soil content of selenium is low, and may cause conditions such as Keshan disease and affect thyroid function. Selenium deficiency is also commonly seen in patients on total parenteral nutrition (TPN) as their sole source of nutrition. Gastrointestinal disorders may decrease the absorption of selenium resulting in depletion or deficiency. Selenium may be destroyed when foods are refined or processed.
- Specific dietary sources of selenium include brewer's yeast, wheat germ, butter, garlic, grains, sunflower seeds, Brazil nuts, walnuts, raisins, liver, kidney, shellfish (lobster, oyster, shrimp, scallops), fresh-water and salt-water fish (red snapper, salmon, swordfish, tuna, mackerel, halibut, flounder, herring, smelts). Selenium is also found in alfalfa, burdock root, catnip, fennel seed, ginseng, raspberry leaf, radish, horseradish, onion, chives, medicinal mushrooms (reishi, shiitake), and yarrow.
- The role of selenium in cancer prevention has been the subject of recent study and debate. Initial evidence from the Nutritional Prevention of Cancer (NPC) trial suggests that selenium supplementation reduces the risk of prostate cancer among men with normal baseline PSA (prostate specific antigen) levels, and low selenium blood levels. However, in this study selenium did not reduce the risk of lung, colorectal, or basal cell carcinoma of the skin, and actually *increased* the risk of squamous cell skin carcinoma. The ongoing Selenium and Vitamin E Cancer Prevention Trial (SELECT) aims to definitively address the role of selenium in prostate cancer prevention.

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EVIDENCE

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A: Strong scientific evidence for this use; B: Good scientific evidence for this use;

C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work);

F: Strong scientific evidence against this use (it likely does not work).

<p>Uses based on scientific evidence</p> <p><i>These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.</i></p>	<p>GRADE*</p>
<p>Antioxidant</p> <p>Selenium is a component of glutathione peroxidase, which possesses antioxidant activity, and demonstrates antioxidant properties in humans. Long-term clinical benefits remain controversial.</p>	<p>B</p>
<p>Prostate cancer prevention</p> <p>Initial evidence has suggested that selenium supplementation reduces the risk of developing prostate cancer in men with normal baseline PSA (prostate specific antigen) levels, and low selenium blood levels. This is the subject of large well-designed studies, including the Nutritional Prevention of Cancer Trial (NPC), and the ongoing Selenium and Vitamin E Cancer Prevention Trial (SELECT),¹⁻¹⁷ as well as prior population and case-control studies.^{18;19}</p> <p>The NPC was conducted in 1312 Americans, and reported that 200mcg of daily selenium reduces the overall incidence of prostate cancer – although these protective effects only occurred in men with baseline PSA levels less than or equal to 4 ng/mL, and those with low baseline blood selenium levels (<123.2 ng/mL).^{6;11;20;21} The NPC trial was primarily designed to measure the development of non-melanoma skin cancers, not other types of cancers, and therefore these prostate cancer results cannot be considered definitive. To settle this question, further study is underway: The SELECT trial is in progress, with a goal to include 32,400 men with serum PSA levels less than or equal to 4 ng/mL. SELECT was started in 2001, with results expected in 2013.</p> <p>Laboratory studies have reported several potential mechanisms for selenium’s beneficial effects in prostate cancer, including decrease in androgen receptors and PSA production,^{22;23} antioxidant effects, angiogenesis inhibition, or apoptosis.²⁴⁻²⁹</p> <p>It is not known if selenium is helpful in men who already have been diagnosed with prostate cancer to prevent progression or recurrence of disease.³⁰ It does appear that selenium may not be beneficial in those with elevated PSA levels, or with normal/high selenium levels. It remains unclear whether men at risk (or all men) should have their serum selenium values measured; results of the SELECT study may provide additional guidance. There is evidence that low selenium levels are associated with an increased risk of prostate cancer,¹⁸ and several mechanisms for the beneficial effects of selenium supplementation have been suggested.^{24;31;32}</p> <p>In the NPC trial, no benefits were seen in reducing the risk of colorectal or lung cancers. Although an overall reduction in cancer risk was observed, it is not clear which specific types of cancer besides prostate cancer prevention may benefit.</p>	<p>B</p>
<p>Keshan disease</p> <p>Keshan disease is a cardiomyopathy (heart disease) restricted to areas of China in people having an extremely low selenium status. Prophylactic administration of sodium selenite has been shown to significantly decrease the incidence of this disorder.^{33;34}</p> <p>Selenium is used to treat and prevent selenium deficiency (for example in those with HIV or receiving enteral feedings).³⁵⁻⁴⁴</p>	<p>B</p>

<p>Asthma</p> <p>Preliminary research reports that selenium supplementation may help improve asthma symptoms.^{45;46} Further research is needed to confirm these results</p>	<p>C</p>
<p>Intracranial pressure symptoms</p> <p>Preliminary research shows a decrease of symptoms of elevated intracranial pressure (headaches, nausea, emesis, vertigo, unsteady gait, speech disorders, and Jacksonian seizures).^{47;48} More research is needed before a recommendation can be made.</p>	<p>C</p>
<p>Burns</p> <p>Early study results suggest that supplementation with selenium and other trace elements (copper, zinc) may increase the rate of burn wound healing.^{49;50} Additional research is necessary before a clear recommendation can be made.</p>	<p>C</p>
<p>Cancer treatment</p> <p>Several studies suggest that low levels of selenium (measured in the blood or in tissues such as toenail clippings), may be a risk factor for developing cancer,^{18;51-55} particularly prostate cancer.¹⁸ Population studies suggest that people with cancer are more likely to have low selenium levels than healthy matched individuals, but in most cases it is not clear if the low selenium levels are a cause or merely a consequence of disease. It remains unclear if selenium is beneficial in the treatment of any type of cancer.</p>	<p>C</p>
<p>Cardiomyopathy</p> <p>Low selenium levels have been associated with the development of cardiomyopathy,^{34;43;56-61} and selenium supplementation is likely of benefit in such cases (for example in Keshan disease.^{33;34} However, most cases of cardiomyopathy are not due to low selenium levels, and therefore selenium may not be helpful.</p> <p>It has been suggested that low selenium levels may be a risk for coronary heart disease, although this remains unclear.⁶²</p>	<p>C</p>
<p>Cataracts</p> <p>Preliminary research reports that selenium supplementation may affect the development of cataracts.^{63;64} Further research is needed before a clear conclusion can be drawn.</p>	<p>C</p>
<p>Chemotherapy side effects</p> <p>Study results of selenium supplementation during chemotherapy are mixed.⁶⁴⁻⁶⁶ General concern has been raised that antioxidants may interfere with radiation therapy or some chemotherapy agents (such as alkylating agents, anthracyclines, or platinums), which themselves can depend on oxidative damage to tumor cells for anti-cancer activity. Therefore, patients undergoing cancer treatment should speak with their oncologist before taking selenium.</p>	<p>C</p>
<p>Cystic fibrosis</p> <p>Preliminary research of selenium supplementation in CF patients yields indeterminate results.^{67;68} Further research is needed in this area before a conclusion can be drawn.</p>	<p>C</p>

<p>Dandruff</p> <p>Studies report that selenium-containing shampoos may help improve dandruff, and selenium is included in some commercially available products.</p>	<p>C</p>
<p>Dialysis</p> <p>The benefits of selenium supplementation in dialysis patients remain unclear.^{38;69-71} Some methods of dialysis may lower plasma selenium levels.</p>	<p>C</p>
<p>Fatigue</p> <p>Evidence of benefit is inconclusive in this area.</p>	<p>C</p>
<p>Malabsorption</p> <p>Low selenium status has been demonstrated in several malabsorptive syndromes and in some digestive and gastrointestinal allergic conditions. There is some evidence that children with food allergies have a higher risk of selenium deficiency. There is no clear benefit of selenium supplementation as a therapy for malabsorptive syndromes, although vitamin supplementation in general may be warranted.</p>	<p>C</p>
<p>Liver disease</p> <p>Selenium supplementation has been studied in various liver disorders, including hepatitis, with mixed results.</p>	<p>C</p>
<p>HIV/AIDS</p> <p>Selenium supplementation has been studied in HIV/AIDS patients, and some reports associate low selenium levels with complications such as cardiomyopathy. It remains unclear if selenium supplementation is beneficial in patients with HIV, particularly during antiretroviral therapy.^{36;37;39;40;72-79}</p>	<p>C</p>
<p>Infection prevention</p> <p>Preliminary research reports that selenium can be beneficial in the prevention of several types of infection, including recurrence of erysipelas (bacterial skin infection associated with lymphedema) or <i>Mycoplasma pneumoniae</i>. Further research is needed to confirm these results before a clear recommendation can be made.</p>	<p>C</p>
<p>Infertility</p> <p>Selenium supplementation has been studied for male infertility and sperm motility with mixed results.⁸⁰ Evidence is lacking regarding potential effects on female infertility.</p>	<p>C</p>
<p>Low birth weight</p> <p>Selenium supplementation has been studied in low birth weight infants. Additional evidence is warranted in this area before a clear conclusion can be drawn.⁸¹⁻⁸³</p>	<p>C</p>
<p>Lymphedema</p> <p>Preliminary research reports that selenium supplementation may decrease lymphedema.⁸⁴ Further research is needed to confirm these results before a clear recommendation can be made.</p>	<p>C</p>

<p>Myotonic dystrophy</p> <p>Selenium and vitamin supplementation has been studied in myotonic dystrophy with mixed results.^{85;86}</p>	C
<p>Pancreatitis</p> <p>There is inconclusive evidence regarding the use of selenium in pancreatitis.⁸⁷⁻⁸⁹</p>	C
<p>Pre-eclampsia</p> <p>Preliminary study in women with pregnancy induced hypertension has reported reduced edema, without significant impact on birth outcomes.⁹⁰ No clear conclusion can be drawn in the absence of additional well designed research.</p>	C
<p>Psoriasis</p> <p>Research is inconclusive in this area.^{91;92}</p>	C
<p>Rheumatoid arthritis</p> <p>Selenium supplementation has been studied in rheumatoid arthritis patients with mixed results.⁹³⁻⁹⁹ Additional research is necessary before a clear conclusion can be drawn.</p>	C
<p>Sepsis</p> <p>Study results of selenium supplementation in septic patients are mixed.¹⁰⁰⁻¹⁰⁴</p>	C
<p>Sunburn prevention</p> <p>Photoprotection was initially observed in preliminary research using selenium supplementation and other antioxidants, although there is some evidence of ineffectiveness in preventing light-induced erythema (skin redness).</p>	C
<p>Thyroid conditions</p> <p>An early toxic effect of selenium is disruption of endocrine function, including synthesis of thyroid hormones (T3). Selenium has been suggested to improve inflammatory activity in chronic autoimmune thyroiditis or Grave's disease.^{42;70;105-113} Further research is needed before a clear conclusion can be drawn.</p>	C
<p>Tinea capitis</p> <p>Commercially available 1% selenium sulfide shampoo has been reported as equivalent to sporicidal therapy in the adjunctive treatment of tinea capitis infection, although further high quality evidence is warranted.¹¹⁴</p>	C
<p>Tinea versicolor</p> <p>Preliminary study of topical selenium (selenium sulfide shampoo) is inconclusive.^{115;116}</p>	C

<p>Colorectal cancer prevention</p> <p>Evidence from the Nutritional Prevention of Cancer (NPC) trial suggests that selenium supplementation does not significantly reduce the risk of developing colorectal cancer.²¹ This randomized study was conducted in 1312 Americans over a 13 year period, and compared the effects of 200mcg of daily selenium versus placebo. Although initial (interim) analysis suggested possible benefits, a later analysis found a lack of statistical significance.</p>	D
<p>Kashin-beck osteoarthropathy</p> <p>Kashin-Beck disease is an osteoarthropathy endemic in selenium- and iodine-deficient areas. Preliminary evidence suggests that selenium supplementation does not significantly improve this disease.¹¹⁷</p>	D
<p>Lung cancer prevention</p> <p>Evidence from the Nutritional Prevention of Cancer (NPC) trial suggests that selenium supplementation does not significantly reduce the risk of developing lung cancer.^{13;21} This randomized study was conducted in 1312 Americans over a 13 year period, and compared the effects of 200mcg of daily selenium versus placebo. Although initial (interim) analysis suggested possible benefits, a later analysis found a lack of statistical significance. Other evidence is inconclusive.^{118;119}</p>	D
<p>Muscular dystrophy</p> <p>Preliminary studies suggest that selenium supplementation is not helpful in muscular dystrophy.¹²⁰⁻¹²²</p>	D
<p>Osteoarthritis</p> <p>Selenium-ACE, a formulation containing selenium with three vitamins, has been promoted for the treatment of arthritis. Research has failed to demonstrate significant benefits, with a possible excess of side-effects compared to placebo.</p>	D
<p>Skin cancer (nonmelanoma) prevention</p> <p>Results from the Nutritional Prevention of Cancer (NPC) trial, conducted among 1312 Americans over a 13 year period, suggest that selenium supplementation (200mcg daily) given to individuals at high risk of nonmelanoma skin cancer is ineffective at preventing basal cell carcinoma, and actually <i>increases</i> the risk of squamous cell carcinoma and total nonmelanoma skin cancer.^{11;16} Therefore, selenium supplementation should be avoided in individuals at risk or with a history of nonmelanoma skin cancer.</p>	D

***Key to grades:**

A: Strong scientific evidence for this use; B: Good scientific evidence for this use;

C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work);

F: Strong scientific evidence against this use (it likely does not work).

Uses based on tradition, theory or limited scientific evidence

The below uses are based on tradition or scientific theories. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

Abnormal pap smears, acne, alcoholic cirrhosis, alco-

holism, allergic rhinitis, altitude sickness, arsenic poisoning, atherosclerosis, chronic bronchitis, cognitive dysfunction; colitis, Cardiac arrhythmia, Error! Bookmark not defined. celiac disease, chdepression, dermatitis herpetiformis, diabetes mellitus, Downs Syndrome, Diabetic retinopathy, Error! Bookmark not defined,¹²³ gastric cancer prevention,¹²³ gray hair, helminth reinfection, highHepatitis, Error! Bookmark not defined. HIV/AIDS, hypothy cholesterol, hypersensitivity to electricity,

immune disorders, immune stimulation, inflammatory bowel disease, inflammation, lupus, macular degeneration, metabolic enhancement, meMacular degeneration, Error! Bookmark not defined. male impotency, menopausal symptoms, miscarriage prevention, mood disorders, mood enhancement, muscle weakness, neonatal disorders, organ dysfunction, Osgood-Schlatter disease, otitis media, pain, childhood growth promotion, photoprotection, Phenylketonuria, Error! Bookmark not defined. poor elasticity of poison prophylaxis, aging, fetal development, Prostate cancer Error! Bookmark not defined. risk, Psoriasis, re vaccine adjunct, Raynaud's phenomenon, strength enhancement, stroke, sudden infant death syndrome (SIDS), ulcerative colitis, vasculitis.

DOSING

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

ADULTS (18 years and older):

- **U.S. Recommended Dietary Allowance (RDA) for adults (oral):** 80-200 mcg. Specifically: 55 mcg for female adults; 70 mcg for male adults; 40-70 mcg for adolescent males, 45-55 mcg for adolescent females; 65 mcg for pregnant females; 75 mcg for breast-feeding females.
- **Prostate cancer prevention (oral):** The dose of selenium associated with reduced risk of prostate cancer in the NPC trial is 200 mcg daily.^{6:11;13:21}
- **Maximum Daily Dose (oral):** 400 mcg per day for those older than 14 years old (including adults and the elderly).
- **Intravenous (should only be used when oral therapy is not feasible, and under the direction of a qualified healthcare professional):** For treatment of selenium deficiency in adults, 100 mcg of elemental selenium daily for 24-31 days has been suggested. For prevention of selenium deficiency in adults, 20-40 mcg of elemental selenium daily has been suggested.
- **Other:** The following doses have been reported in research or practice, although efficacy is not necessarily proven. **Asthma:** 100 mcg daily. **Cancer prevention:** 200mcg daily. **Erysipelas infection:** 300-1000mg daily as selenium selenite. **HIV positive status:** 80 mcg daily. **Infertility (male):** 100 mcg daily. **Keshan disease:** 30 mcg daily. **Myocardial infarction (heart attack):** 100 mcg daily. **Rheumatoid arthritis:** 200 mcg daily.

CHILDREN (younger than 18 years):

- **U.S. Recommended Dietary Allowance (RDA) for infants and children (oral):** 10 mcg for 0-6 months; 15mcg daily for 6-12 months; 20 mcg for 1-6 years; 30 mcg for 7-10 years; 45 mcg for 11-14 years; 50 mcg for 5-18 years. Adequate Intake for infants up to 6 months old may be 2.1 mcg/kg/day, and for infants 7-12 months may be 2.2 mcg/kg/day.
- **Maximum Daily Dose (oral):** 45 mcg for 0- 6 months; 60 mcg for 7-12 months; 90 mcg for 1-3 years; 150 mcg for 4-8 years; 280 mcg for 9-13 years.
- **Intravenous (should only be used when oral therapy is not feasible, and under the direction of a qualified healthcare professional):** 3 mcg of elemental selenium/kg/day intravenously for the treatment or prevention of selenium deficiency has been noted.
- **Other:** To treat selenium deficiency in premature infants, 5 mcg per day of selenized yeast has been given by a nasogastric tube.

SAFETY

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

ALLERGIES

Selenium is a trace element, and hypersensitivity is unlikely. Avoid if known allergy/hypersensitivity to products containing selenium.

Side Effects and Warnings

- **Chronic toxicity:** The level of selenium exposure that will cause chronic toxicity is not known, although doses 4-5 times normal dietary intake have been implicated (1 gram per day for two years has produced signs of toxicity in women).¹²⁴⁻¹²⁶ Selenium toxicity may cause gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhea, garlic-like breath odor, metallic taste), neuromuscular-psychiatric disturbances (weakness/fatigue, lightheadedness, irritability, hyperreflexia, muscle tenderness, tremor, peripheral neuropathy), dermatologic changes (skin rash/dermatitis/flushing, fingernail loss/thickening/blotching/streaking/paronychia, hair changes/loss), liver dysfunction, kidney dysfunction, thrombocytopenia (low blood platelets), immune alterations (natural killer cell impairment), thyroid dysfunction (decreased T3), reduced sperm motility, or growth retardation. Blood

selenium levels may be used to assess the degree of toxicity, with levels below 1000 mcg/L usually not associated with serious toxicity, and levels above 2000 mcg/L predictive of potential serious toxicity. Chronic selenium toxicity may resemble arsenic toxicity.

- **Acute overdose (selenosis):** Acute selenium poisoning may cause fever, gastrointestinal symptoms (nausea, vomiting, pain, anorexia), liver or kidney functional impairment, respiratory distress, cardiac complications (EKG changes, increased creatine kinase levels, heart damage), and even death if levels are high enough.^{67;126-129} Other symptoms similar to chronic selenium toxicity may also occur.
- **Cardiovascular:** Chronic low selenium levels are associated with the development of cardiomyopathy,^{34;36;43;56-61;130;131} and possibly with coronary artery disease.⁶²
- **Endocrine:** An early toxic effect of selenium is disruption of endocrine function, including synthesis of thyroid hormones (T3),^{42;70;106;107;110;111;113;132} with unclear effects on growth hormone and insulin-like growth factor. Selenium deficiency may also worsen thyroid disorders related to iodine-deficiency.^{42;108;133;134}
- **Renal:** Kidney failure and dialysis are associated with low selenium levels,^{38;69-71} and kidney transplant appears to correct selenium levels.¹³⁵
- **Genitourinary:** Chronic high selenium levels may decrease sperm motility,^{80;136} although effects on fertility are not known.
- **Oncologic:** Results from the Nutritional Prevention of Cancer (NPC) trial, conducted among 1312 Americans over a 13 year period, suggest that selenium supplementation (200mcg daily) given to individuals at high risk of nonmelanoma skin cancer is ineffective at preventing basal cell carcinoma, and actually *increases* the risk of squamous cell carcinoma and total nonmelanoma skin cancer.¹¹ Therefore, selenium supplementation should be avoided in individuals at risk or with a history of non-melanoma skin cancer.
- **Psychiatric:** Researchers have reported high levels of selenium in children with behavioral problems, although causality has not been established. Chronic selenium toxicity has been associated with irritability or fatigue.

PREGNANCY AND BREASTFEEDING

- No pregnancy category has been established for supplemental selenium intake although it is generally believed to be safe during pregnancy when consumed in amounts normally found in foods. Animal research reports that large doses of selenium may contribute to birth defects.^{126;137}
- Selenium is excreted in breastmilk,^{138;139} but is generally believed to be safe to consume during lactation in amounts commonly found in foods.

INTERACTIONS

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

INTERACTIONS WITH DRUGS

- **HMG-CoA reductase inhibitors ("Statins"):** Concomitant use of selenium in combination with beta-carotene and vitamins C and E appears to decrease the effectiveness of the combination of simvastatin (Zocor®) and niacin, although long-term effects are not known. This may be due to antioxidant effects associated with selenium use. Theoretically, selenium could reduce the effectiveness of other HMG-CoA reductase inhibitors such as atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®), and pravastatin (Pravachol®).
- **Niacin:** Concomitant use of selenium in combination with beta-carotene, vitamin C, and vitamin E appears to decrease the effectiveness of the combination of niacin and simvastatin (Zocor®). This may be due to antioxidant effects associated with selenium use.
- **Corticosteroids:** High-dose steroid therapy may decrease plasma selenium levels.
- **Chemotherapy/Radiation Therapy:** Concern has been raised that antioxidants may interfere with radiation therapy or some chemotherapy agents (such as alkylating agents, anthracyclines, or platinum), which themselves can depend on oxidative damage to tumor cells for anti-tumor effects. Studies of the effects of antioxidants on cancer therapies yield mixed results, with some reporting antagonistic effects (interference), others noting synergism (benefit), and most suggesting no significant interaction. This remains an area of study and controversy. In particular, selenium may reduce toxic side effects associated with chemotherapy drugs including cisplatin, doxorubicin, or bleomycin. However, until better evidence is available, selenium supplementation is not recommended during chemotherapy or radiation therapy due to potential interference. Patients considering use of selenium during chemotherapy or radiation therapy should discuss this choice with their medical and radiation oncologists.
- **Antacids:** Agents that alter the pH of the stomach may decrease absorption of selenium.
- **Oral contraceptives:** Selenium levels may be decreased in patients taking oral contraceptives.
- **Erythropoietin (EPO):** Selenium has been suggested to increase the effects of erythropoietin in hemodialysis patients.

- **Clozapine:** It has been suggested that cardiac side effects associated with clozapine use may be related to low selenium concentrations. It is not clear if assessment of selenium levels or selenium supplementation should be routine in patients taking this drug.

INTERACTIONS WITH HERBS AND DIETARY SUPPLEMENTS

- **Antioxidants:** Selenium is a component of glutathione peroxidase, which possesses antioxidant activity, and demonstrates antioxidant properties in humans. Long-term clinical benefits remain controversial. Selenium may add to the effect of other antioxidants in the body, such as vitamins A, C, and E, lycopene, green tea, soy, grape seed extract, or melatonin.
- **Vitamin C:** There is preliminary evidence that vitamin C may be necessary for maintaining selenium levels in the body.

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For each therapy covered by Natural Standard, a research team systematically gathers scientific data and expert opinions. Validated rating scales are used to evaluate the quality of available evidence. Information is incorporated into comprehensive monographs which are designed to facilitate clinical decision making. All monographs undergo blinded editorial and peer review prior to inclusion in Natural Standard databases.

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SELECTED REFERENCES:

Natural Standard developed the above evidence-based information based on a systematic review of more than 2600 articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com.

1. Combs GF. Status of selenium in prostate cancer prevention. *Br J Cancer* 2004 (e-publication released June 22, 2004).
2. Huff J. Re: Selenium supplementation and secondary prevention of nonmelanoma skin cancer in a randomized trial. *J Natl Cancer Inst* 2004;96(4):333-334.
3. Whanger PD. Selenium and its relationship to cancer: an update dagger. *Br J Nutr* 2004;91(1):11-28.
4. Finley JW. Reduction of cancer risk by consumption of selenium-enriched plants: enrichment of broccoli with selenium increases the anticarcinogenic properties of broccoli. *J Med Food* 2003;6(1):19-26.
5. Klein EA, Lippman SM, Thompson IM, et al. The selenium and vitamin e cancer prevention trial. *World J Urol* 2003;21(1):21-27.
6. Duffield-Lillico AJ, Dalkin BL, Reid ME, et al. Selenium supplementation, baseline plasma selenium status and incidence of prostate cancer: an analysis of the complete treatment period of the Nutritional Prevention of Cancer Trial. *BJU Int* 2003;91(7):608-612.
7. Klein EA, Thompson IM, Lippman SM, et al. SELECT: the selenium and vitamin E cancer prevention trial. *Urol Oncol* 2003;21(1):59-65.
8. Vinceti M, Malagoli C, Bergomi M, et al. Correspondence re: Duffield-Lillico et al., Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: a summary report of the Nutritional Prevention of Cancer Trial. 11: 630-639, 2002. *Cancer Epidemiol Biomarkers Prev* 2003;12(1):77.
9. Klein EA, Lippman SM, Thompson IM, et al. The selenium and vitamin E cancer prevention trial. *World J Urol* 2003;21(1):21-27.
10. Klein EA. Clinical models for testing chemopreventative agents in prostate cancer and overview of SELECT: the Selenium and Vitamin E Cancer Prevention Trial. *Recent Results Cancer Res* 2003;163:212-225.
11. Duffield-Lillico AJ, Slate EH, Reid ME, et al. Selenium supplementation and secondary prevention of nonmelanoma skin cancer in a randomized trial. *J Natl Cancer Inst* 2003;95(19):1477-1481.
12. Moyad MA. Selenium and vitamin E supplements for prostate cancer: evidence or embellishment? *Urology* 2002;59(4 Suppl 1):9-19.
13. Reid ME, Duffield-Lillico AJ, Garland L, et al. Selenium supplementation and lung cancer incidence: an update of the nutritional prevention of cancer trial. *Cancer Epidemiol Biomarkers Prev* 2002;11(11):1285-1291.
14. Combs GF, Jr., Clark LC, Turnbull BW. An analysis of cancer prevention by selenium. *Biofactors* 2001;14(1-4):153-159.
15. Clark LC, Dalkin B, Krongrad A, et al. Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. *Br J Urol* 1998;81(5):730-734.
16. Clark LC, Combs GF, Jr., Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with

- carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *JAMA* 1996;276(24):1957-1963.
17. Clark LC, Dalkin B, Krongrad A. Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. *Journal of the American Nutraceutical Association* 1999;2(1):14-18.
 18. Li H, Stampfer MJ, Giovannucci EL, et al. A prospective study of plasma selenium levels and prostate cancer risk. *J Natl Cancer Inst* 2004;96(9):696-703.
 19. Hartman TJ, Albanes D, Pietinen P, et al. The association between baseline vitamin E, selenium, and prostate cancer in the alpha-tocopherol, beta-carotene cancer prevention study. *Cancer Epidemiol Biomarkers Prev* 1998;7(4):335-340.
 20. Combs GF. Status of selenium in prostate cancer prevention. *Br J Cancer* 2004;
 21. Duffield-Lillico AJ, Reid ME, Turnbull BW, et al. Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: a summary report of the nutritional prevention of cancer trial. *Cancer Epidemiol Biomarkers Prev* 2002;11(7):630-639.
 22. Dong Y, Zhang H, Hawthorn L, et al. Delineation of the molecular basis for selenium-induced growth arrest in human prostate cancer cells by oligonucleotide array. *Cancer Res* 2003;63(1):52-59.
 23. Dong Y, Lee SO, Zhang H, et al. Prostate specific antigen expression is down-regulated by selenium through disruption of androgen receptor signaling. *Cancer Res* 2004;64(1):19-22.
 24. Fleming J, Ghose A, Harrison PR. Molecular mechanisms of cancer prevention by selenium compounds. *Nutr Cancer* 2001;40(1):42-49.
 25. Zu K, Ip C. Synergy between selenium and vitamin E in apoptosis induction is associated with activation of distinctive initiator caspases in human prostate cancer cells. *Cancer Res* 2003;63(20):6988-6995.
 26. Kim YS, Milner J. Molecular targets for selenium in cancer prevention. *Nutr Cancer* 2001;40(1):50-54.
 27. Lu J. Apoptosis and angiogenesis in cancer prevention 28. Stewart MS, Spallholz JE, Neldner KH, et al. Selenium compounds have disparate abilities to impose oxidative stress and induce apoptosis. *Free Radic Biol Med* 1999;26(1-2):42-48.
 29. Tapiero H, Townsend DM, Tew KD. The antioxidant role of selenium and seleno-compounds. *Biomed Pharmacother* 2003;57(3-4):134-144.
 30. Stratton MS, Reid ME, Schwartzberg G, et al. Selenium and inhibition of disease progression in men diagnosed with prostate carcinoma: study design and baseline characteristics of the 'Watchful Waiting' Study. *Anticancer Drugs* 2003;14(8):595-600.
 31. Ganther HE. Selenium metabolism and mechanisms of cancer prevention. *Adv Exp Med Biol* 2001;492:119-130.
 32. Lamson DW, Brignall MS. Antioxidants in cancer therapy; their actions and interactions with oncologic therapies. *Altern Med Rev* 1999;4(5):304-329.
 33. Keshan Disease Research Group. Observation on effect of sodium selenite in prevention of Keshan disease. *Chinese Medical Journal* 1979;471-476.
 34. Li GS, Wang F, Kang D, et al. Keshan disease: an endemic cardiomyopathy in China. *Hum Pathol* 1985;16(6):602-609.
 35. Abrams CK, Siram SM, Galsim C, et al. Selenium deficiency in long-term total parenteral nutrition. *Nutr Clin Pract* 1992;7(4):175-178.
 36. Barbaro G. Selenium deficiency and HIV-associated cardiomyopathy. *J R Soc Med* 2002;95(1):57.
 37. Baum MK, Shor-Posner G, Lai S, et al. High risk of HIV-related mortality is associated with selenium deficiency. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;15(5):370-374.
 38. Bogye G, Tompos G, Alftan G. Selenium depletion in hemodialysis patients treated with polysulfone membranes. *Nephron* 2000;84(2):119-123.
 39. Campa A, Shor-Posner G, Baum M. Selenium status and the human immunodeficiency virus. *J Am Diet Assoc* 2000;100(4):418.
 40. Cirelli A, Ciardi M, de Simone C, et al. Serum selenium concentration and disease progress in patients with HIV infection. *Clin Biochem* 1991;24(2):211-214.
 41. Constans J, Delmas-Beauvieux MC, Sergeant C, et al. One-year antioxidant supplementation with beta-carotene or selenium for patients infected with human immunodeficiency virus: a pilot study. *Clin Infect Dis* 1996;23(3):654-656.
 42. Contempre B, Dumont JE, Ngo B, et al. Effect of selenium supplementation in hypothyroid subjects of an iodine and selenium deficient area: the possible danger of indiscriminate supplementation of iodine-deficient subjects with selenium. *J Clin Endocrinol Metab* 1991;73(1):213-215.
 43. Kavanaugh-McHugh AL, Ruff A, Perlman E, et al. Selenium deficiency and cardiomyopathy in acquired immunodeficiency syndrome. *JPEN J Parenter Enteral Nutr* 1991;15(3):347-349.
 44. Kuroki F, Matsumoto T, Iida M. Selenium is depleted in Crohn's disease on enteral nutrition. *Dig Dis* 2003;21(3):266-270.
 45. Allam MF, Lucane RA. Selenium supplementation for asthma. *Cochrane Database Syst Rev* 2004;(2):CD003538.
 46. Hasselmark L, Malmgren R, Zetterstrom O, et al. Selenium supplementation in intrinsic asthma. *Allergy* 1993;48(1):30-36.
 47. Chen J, Berry MJ. Selenium and selenoproteins in the brain and brain diseases. *J Neurochem* 2003;86(1):1-12.
 48. Schweizer U, Brauer AU, Kohrle J, et al. Selenium and brain function: a poorly recognized liaison. *Brain Res Brain Res Rev* 2004;45(3):164-178.
 49. Gartner R, Albrich W, Angstwurm MW. The effect of a selenium supplementation on the outcome of patients with severe systemic inflammation, burn and trauma. *Biofactors* 2001;14(1-4):199-204.

50. Borner J, Zimmermann T, Albrecht S, et al. [Selenium administration in severe inflammatory surgical diseases and burns in childhood]. *Med Klin* 1997;92 Suppl 3:17-19.
51. Garland M, Morris JS, Stampfer MJ, et al. Prospective study of toenail selenium levels and cancer among women. *J Natl Cancer Inst* 1995;87(7):497-505.
52. Mark SD, Qiao YL, Dawsey SM, et al. Prospective study of serum selenium levels and incident esophageal and gastric cancers. *J Natl Cancer Inst* 2000;92(21):1753-1763.
53. Postovsky S, Arush MW, Diamond E, et al. The prevalence of low selenium levels in newly diagnosed pediatric cancer patients. *Pediatr Hematol Oncol* 2003;20(4):273-280.
54. Yoshizawa K, Willett WC, Morris SJ, et al. Study of prediagnostic selenium level in toenails and the risk of advanced prostate cancer. *J Natl Cancer Inst* 1998;90(16):1219-1224.
55. Yu S, Chu Y, Gong X, et al. Regional variation of cancer mortality incidence and its relation to selenium levels in China. *Biological Trace Element Research* 1985;7:21-29.
56. Constans J, Sire S, Sergeant C, et al. [Dilated cardiomyopathy and selenium deficiency in AIDS. Apropos of a case]. *Rev Med Interne* 1997;18(8):642-645.
57. Derejczyk J, Jendryczko A, Bratek A. Selenium in dilated cardiomyopathy - a case of six-month-old child effectively treated by immunosuppression enriched with selenium and other antioxidants. *Pediatrics Polska* 1994;69(10):865-871.
58. Johnson RA, Baker SS, Fallon JT, et al. An occidental case of cardiomyopathy and selenium deficiency. *N Engl J Med* 1981;304(20):1210-1212.
59. Marcus RW. Myopathy and cardiomyopathy associated with selenium deficiency: case report, literature review, and hypothesis. *Md Med J* 1993;42(7):669-674.
60. Reeves WC, Marcuard SP, Willis SE, et al. Reversible cardiomyopathy due to selenium deficiency. *JPEN J Parenter Enteral Nutr* 1989;13(6):663-665.
61. Yang GQ, Ge KY, Chen JS, et al. Selenium-related endemic diseases and the daily selenium requirement of humans. *World Rev Nutr Diet* 1988;55:98-152.
62. Yoshizawa K, Ascherio A, Morris JS, et al. Prospective study of selenium levels in toenails and risk of coronary heart disease in men. *Am J Epidemiol* 2003;158(9):852-860.
63. Karakucuk S, Ertugrul MG, Faruk EO, et al. Selenium concentrations in serum, lens and aqueous humour of patients with senile cataract. *Acta Ophthalmol Scand* 1995;73(4):329-332.
64. Naziroglu M, Karaoglu A, Aksoy AO. Selenium and high dose vitamin E administration protects cisplatin-induced oxidative damage to renal, liver and lens tissues in rats. *Toxicology* 2004;195(2-3):221-230.
65. Sieja K. Protective role of selenium against the toxicity of multi-drug chemotherapy in patients with ovarian cancer. *Pharmazie* 2000;55(12):958-959.
66. Sundstrom H, Korpela H, Sajanti E, et al. Supplementation with selenium, vitamin E and their combination in gynaecological cancer during cytotoxic chemotherapy. *Carcinogenesis* 1989;10(2):273-278.
67. Snodgrass W, Rumack BH, Sullivan JB, Jr., et al. Selenium: childhood poisoning and cystic fibrosis. *Clin Toxicol* 1981;18(2):211-220.
68. Watson RD, Cannon RA, Kurland GS, et al. Selenium responsive myositis during prolonged home total parenteral nutrition in cystic fibrosis. *JPEN J Parenter Enteral Nutr* 1985;9(1):58-60.
69. Bonomini M, Forster S, De Risio F, et al. Effects of selenium supplementation on immune parameters in chronic uraemic patients on haemodialysis. *Nephrol Dial Transplant* 1995;10(9):1654-1661.
70. Napolitano G, Bonomini M, Bomba G, et al. Thyroid function and plasma selenium in chronic uremic patients on hemodialysis treatment. *Biol Trace Elem Res* 1996;55(3):221-230.
71. Sperschneider H, Schroder K, Winnefeld K, et al. Influence of selenium substitution on left ventricular hypertrophy in hemodialysis patients. *Nieren-und Hochdruckkrankheiten* 1998;27(5):223-230.
72. Baeten JM, Mostad SB, Hughes MP, et al. Selenium deficiency is associated with shedding of HIV-1--infected cells in the female genital tract. *J Acquir Immune Defic Syndr* 2001;26(4):360-364.
73. Baum MK, Miguez-Burbano MJ, Campa A, et al. Selenium and interleukins in persons infected with human immunodeficiency virus type 1. *J Infect.Dis* 2000;182 Suppl 1:S69-S73.
74. Campa A, Shor-Posner G, Indacochea F, et al. Mortality risk in selenium-deficient HIV-positive children. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999;20(5):508-513.
75. Chariot P, Bignani O. Skeletal muscle disorders associated with selenium deficiency in humans. *Muscle Nerve* 2003;27(6):662-668.
76. Constans J, Pellegrin JL, Sergeant C, et al. Serum selenium predicts outcome in HIV infection. *J Acquir Immune Defic Syndr Hum Retrovirol* 1995;10(3):392.
77. Constans J, Seigneur M, Blann AD, et al. Effect of the antioxidants selenium and beta-carotene on HIV-related endothelium dysfunction. *Thromb Haemost* 1998;80(6):1015-1017.
78. Dworkin BM. Selenium deficiency in HIV infection and the acquired immunodeficiency syndrome (AIDS). *Chem Biol Interact* 1994;91(2-3):181-186.
79. Schrauzer GN, Sacher J. Selenium in the maintenance and therapy of HIV-infected patients. *Chem Biol Interact* 1994;91(2-3):199-205.
80. Scott R, MacPherson A, Yates RW, et al. The effect of oral selenium supplementation on human sperm motility. *Br J Urol* 1998;82(1):76-80.
81. Darlow BA, Winterbourn CC, Inder TE, et al. The effect of selenium supplementation on outcome in very low birth weight infants: a randomized controlled trial. The New Zealand Neonatal Study Group. *J Pediatr* 2000;136(4):473-480.

82. Darlow BA, Austin NC. Selenium supplementation to prevent short-term morbidity in preterm neonates. *Cochrane Database Syst Rev* 2003;(4):CD003312.
83. Huston RK, Jelen BJ, Vidgoff J. Selenium supplementation in low-birthweight premature infants: relationship to trace metals and antioxidant enzymes. *JPEN J Parenter Enteral Nutr* 1991;15(5):556-559.
84. Kasseroller R. [Administration of selenium in lymphedema]. *Med Klin* 1997;92 Suppl 3:50-51.
85. Orndahl G, Grimby G, Grimby A, et al. Functional deterioration and selenium-vitamin E treatment in myotonic dystrophy. A placebo-controlled study. *J Intern Med* 1994;235(3):205-210.
86. Orndahl G, Sellden U, Hallin S, et al. Myotonic dystrophy treated with selenium and vitamin E. *Acta Med Scand* 1986;219(4):407-414.
87. Uomo G, Talamini G, Rabitti PG. Antioxidant treatment in hereditary pancreatitis. A pilot study on three young patients. *Dig Liver Dis* 2001;33(1):58-62.
88. Wereszczynska-Siemiakowska U, Mroczko B, Siemiakowski A, et al. The importance of interleukin 18, glutathione peroxidase, and selenium concentration changes in acute pancreatitis. *Dig Dis Sci* 2004;49(4):642-650.
89. Wollschlager S, Ludwig K, Meissner D, et al. [Effect of selenium administration on various laboratory parameters in patients with acute pancreatitis]. *Med Klin* 1997;92 Suppl 3:22-24.
90. Han L, Zhou SM. Selenium supplement in the prevention of pregnancy induced hypertension. *Chin Med J (Engl)* 1994;107(11):870-871.
91. Fairris GM, Lloyd B, Hinks L, et al. The effect of supplementation with selenium and vitamin E in psoriasis. *Ann Clin Biochem* 1989;26 (Pt 1):83-88.
92. Michaelsson G, Berne B, Carlmark B, et al. Selenium in whole blood and plasma is decreased in patients with moderate and severe psoriasis. *Acta Derm Venereol* 1989;69(1):29-34.
93. Aaseth J, Haugen M, Forre O. Rheumatoid arthritis and metal compounds--perspectives on the role of oxygen radical detoxification. *Analyst* 1998;123(1):3-6.
94. Gaby AR. Alternative treatments for rheumatoid arthritis. *Altern Med Rev* 1999;4(6):392-402.
95. Heinle K, Adam A, Gradl M, et al. [Selenium concentration in erythrocytes of patients with rheumatoid arthritis. Clinical and laboratory chemistry infection markers during administration of selenium]. *Med Klin* 1997;92 Suppl 3:29-31.
96. Heliövaara M, Knekt P, Aho K, et al. Serum antioxidants and risk of rheumatoid arthritis. *Ann Rheum Dis* 1994;53(1):51-53.
97. Peretz A, Neve J, Duchateau J, et al. Adjuvant treatment of recent onset rheumatoid arthritis by selenium supplementation: preliminary observations. *Br J Rheumatol* 1992;31(4):281-282.
98. Peretz A, Siderova V, Neve J. Selenium supplementation in rheumatoid arthritis investigated in a double blind, placebo-controlled trial. *Scand J Rheumatol* 2001;30(4):208-212.
99. Tarp U. Selenium in rheumatoid arthritis. A review. *Analyst* 1995;120(3):877-881.
100. Forceville X, Vitoux D, Gauzit R, et al. Selenium, systemic immune response syndrome, sepsis, and outcome in critically ill patients. *Crit Care Med* 1998;26(9):1536-1544.
101. Gartner R, Angstwurm MW, Schottdorf J. [Selenium administration in sepsis patients]. *Med Klin* 1997;92 Suppl 3:12-14.
102. Hohmann C. Selenium is effective in sepsis. *Pharmazeutische Zeitung* 2002;147(18):31.
103. Lehmann C, Egerer K, Weber M, et al. [Effect of selenium administration on various laboratory parameters of patients at risk for sepsis syndrome]. *Med Klin* 1997;92 Suppl 3:14-16.
104. Zimmermann T, Albrecht S, Kuhne H, et al. [Selenium administration in patients with sepsis syndrome. A prospective randomized study]. *Med Klin* 1997;92 Suppl 3:3-4.
105. Berger MM, Reymond MJ, Shenkin A, et al. Influence of selenium supplements on the post-traumatic alterations of the thyroid axis: a placebo-controlled trial. *Intensive Care Med* 2001;27(1):91-100.
106. Bouvier N, Millart H. [Relationships between selenium deficiency and 3,5,3'-triiodothyronine (T3) synthesis]. *Ann Endocrinol (Paris)* 1997;58(4):310-315.
107. Bratter P, Negretti dB, V. Influence of high dietary selenium intake on the thyroid hormone level in human serum. *J Trace Elem Med Biol* 1996;10(3):163-166.
108. Contempre B, Duale NL, Dumont JE, et al. Effect of selenium supplementation on thyroid hormone metabolism in an iodine and selenium deficient population. *Clin Endocrinol (Oxf)* 1992;36(6):579-583.
109. Gartner R, Gasnier BC, Dietrich JW, et al. Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibodies concentrations. *J Clin Endocrinol Metab* 2002;87(4):1687-1691.
110. Hofbauer LC, Spitzweg C, Magerstadt RA, et al. Selenium-induced thyroid dysfunction. *Postgrad Med* 1997;73(856):103-104.
111. Makropoulos W, Heintz B, Stefanidis I. Selenium deficiency and thyroid function in acute renal failure. *Ren Fail* 1997;19(1):129-136.
112. Olivieri O, Girelli D, Stanzial AM, et al. Selenium, zinc, and thyroid hormones in healthy subjects: low T3/T4 ratio in the elderly is related to impaired selenium status. *Biol Trace Elem Res* 1996;51(1):31-41.
113. Strain JJ, Bokje E, van't Veer P, et al. Thyroid hormones and selenium status in breast cancer. *Nutr Cancer* 1997;27(1):48-52.
114. Givens TG, Murray MM, Baker RC. Comparison of 1% and 2.5% selenium sulfide in the treatment of tinea capitis. *Arch Pediatr Adolesc Med* 1995;149(7):808-811.
115. Hull CA, Johnson SM. A double-blind comparative study of sodium sulfacetamide lotion 10% versus selenium sulfide

- lotion 2.5% in the treatment of pityriasis (tinea) versicolor. *Cutis* 2004;73(6):425-429.
116. Katsambas A, Rigopoulos D, Antoniou C, et al. Econazole 1% shampoo versus selenium in the treatment of tinea versicolor: a single-blind randomized clinical study. *Int J Dermatol* 1996;35(9):667-668.
 117. Moreno-Reyes R, Suetens C, Mathieu F, et al. Kashin-Beck osteoarthropathy in rural Tibet in relation to selenium and iodine status. *N Engl J Med* 1998;339(16):1112-1120.
 118. Zhuo H, Smith AH, Steinmaus C. Selenium and lung cancer: a quantitative analysis of heterogeneity in the current epidemiological literature. *Cancer Epidemiol Biomarkers Prev* 2004;13(5):771-778.
 119. Yu SY, Mao BL, Xiao P, et al. Intervention trial with selenium for the prevention of lung cancer among tin miners in Yunnan, China. A pilot study. *Biol Trace Elem Res* 1990;24(2):105-108.
 120. Backman E, Nylander E, Johansson I, et al. Selenium and vitamin E treatment of Duchenne muscular dystrophy: no effect on muscle function. *Acta Neurol Scand* 1988;78(5):429-435.
 121. Gamstorp I, Gustavson KH, Hellstrom O, et al. A trial of selenium and vitamin E in boys with muscular dystrophy. *J Child Neurol* 1986;1(3):211-214.
 122. Kurihara M, Kumagai K, Nakae Y, et al. [Two sibling patients with non-Fukuyama type congenital muscular dystrophy with low serum selenium levels--therapeutic effects of oral selenium administration]. *No To Hattatsu* 2000;32(4):346-351.
 123. Wei WQ, Abnet CC, Qiao YL, et al. Prospective study of serum selenium concentrations and esophageal and gastric cardia cancer, heart disease, stroke, and total death. *Am J Clin Nutr* 2004;79(1):80-85.
 124. Martin A. Selenium toxicity. *Cahiers de Nutrition et de Dietetique* 1996;31(6):348-353.
 125. Therond P, Malvy D, Favier A. Potential toxicity of high dose selenium by the enteral route. *Nutrition Clinique et Metabolisme* 1997;11(2):91-101.
 126. Wilber CG. Toxicology of selenium: a review. *Clin Toxicol* 1980;17(2):171-230.
 127. Clark RF, Strukle E, Williams SR, et al. Selenium poisoning from a nutritional supplement. *JAMA* 1996;275(14):1087-1088.
 128. Gasmi A, Garnier R, Galliot-Guilley M, et al. Acute selenium poisoning. *Vet Hum Toxicol* 1997;39(5):304-308.
 129. Yang GQ, Wang SZ, Zhou RH, et al. Endemic selenium intoxication of humans in China. *Am J Clin Nutr* 1983;37(5):872-881.
 130. Dworkin BM, Antonecchia PP, Smith F, et al. Reduced cardiac selenium content in the acquired immunodeficiency syndrome. *JPEN J Parenter Enteral Nutr* 1989;13(6):644-647.
 131. Fryer MJ. Rationale for clinical trials of selenium as an antioxidant for the treatment of the cardiomyopathy of Friedreich's ataxia. *Med Hypotheses* 2002;58(2):127-132.
 132. Calomme MR, Vanderpas JB, Francois B, et al. Thyroid function parameters during a selenium repletion/depletion study in phenylketonuric subjects. *Experientia* 1995;51(12):1208-1215.
 133. Arthur JR, Beckett GJ, Mitchell JH. The interactions between selenium and iodine deficiencies in man and animals. *Nutrition Research Reviews* 1999;12(1):55-73.
 134. Foster HD. The iodine-selenium connection: its possible roles in intelligence, cretinism, sudden infant death syndrome, breast cancer and multiple sclerosis. *Med Hypotheses* 1993;40(1):61-65.
 135. Morris-Stiff GJ, Oleesky DA, Smith SC, et al. Sequential changes in plasma selenium concentration after cadaveric renal transplantation. *Br J Surg* 2004;91(3):339-343.
 136. Armstrong NC. Oral selenium supplementation increases sperm motility in subfertile. *Focus on Alternative and Complementary Therapies* 1999;4(1):28-29.
 137. Willhite CC. Selenium teratogenesis. Species-dependent response and influence on reproduction. *Ann N Y Acad Sci* 1993;678:169-177.
 138. Trafikowska U, Sobkowiak E, Butler JA, et al. Organic and inorganic selenium supplementation to lactating mothers increase the blood and milk Se concentrations and Se intake by breast-fed infants. *J Trace Elem Med Biol* 1998;12(2):77-85.
 139. Gathwala G, Yadav OP, Sangwan K, et al. A study on plasma selenium level among pregnant women at Rohtak, Haryana. *Indian J Public Health* 2003;47(2):45-48.