

Nutrition and Lupus: Myths and Realities

Jennifer H Anolik, MD, PhD
Division of Allergy, Immunology & Rheumatology
University of Rochester Medical Center
Rochester, New York
2009

Lupus at the University of Rochester

- The Lupus Clinic
- Autoimmunity Center of Excellence: Our Division currently provides the leadership for this University-wide NIH-funded multidisciplinary center, one of only 8 in the country. Ongoing Lupus projects in the division under this center (Sanz, Looney, Anolik) include:
 - Unraveling the mechanisms that underlie the breakdown of B-cell tolerance in SLE
 - Defining abnormalities in B cells in SLE
 - Delineating the role of cytokines like interferon and BAFF in SLE
 - Understanding the immunological consequence of B-cell depletion and other targeted therapies in the treatment of SLE
- Clinical Trials Program: Investigation of new, targeted biological interventions in SLE. The AIR unit has an active program in clinical trials in systemic lupus erythematosus supported in part by a grant from the Lupus Clinical Trials Consortium.

Topics for today

- Diet
 - Cardiovascular health: low sodium, low cholesterol, low saturated fat diet
 - Omega-3-fatty acids over omega-6
- Dietary supplements
 - Vitamins
 - Osteoporosis is common: Vitamin D and calcium
 - ?Value of other vitamins
 - Herbal supplements/other
 - Little data

Summary

NO SPECIFIC DIET FOR THE TREATMENT OF SLE EXISTS
However, based on animal studies and limited human studies...

- Possible adverse implications for SLE
 - Excess calories
 - Excess protein
 - High fat, especially saturated and omega-6-fatty acids
 - L-canavanine found in alfalfa
- Possible beneficial dietary compounds
 - Vitamin E
 - Vitamin A
 - Selenium
 - Fish oils (omega-3-polyunsaturated fatty acids)
 - Primrose oil
 - Flaxseed
 - Plant herb (*Tripterygium wilfordii*)
 - DHEA
 - Calcium and vitamin D

Complementary/alternative medicine

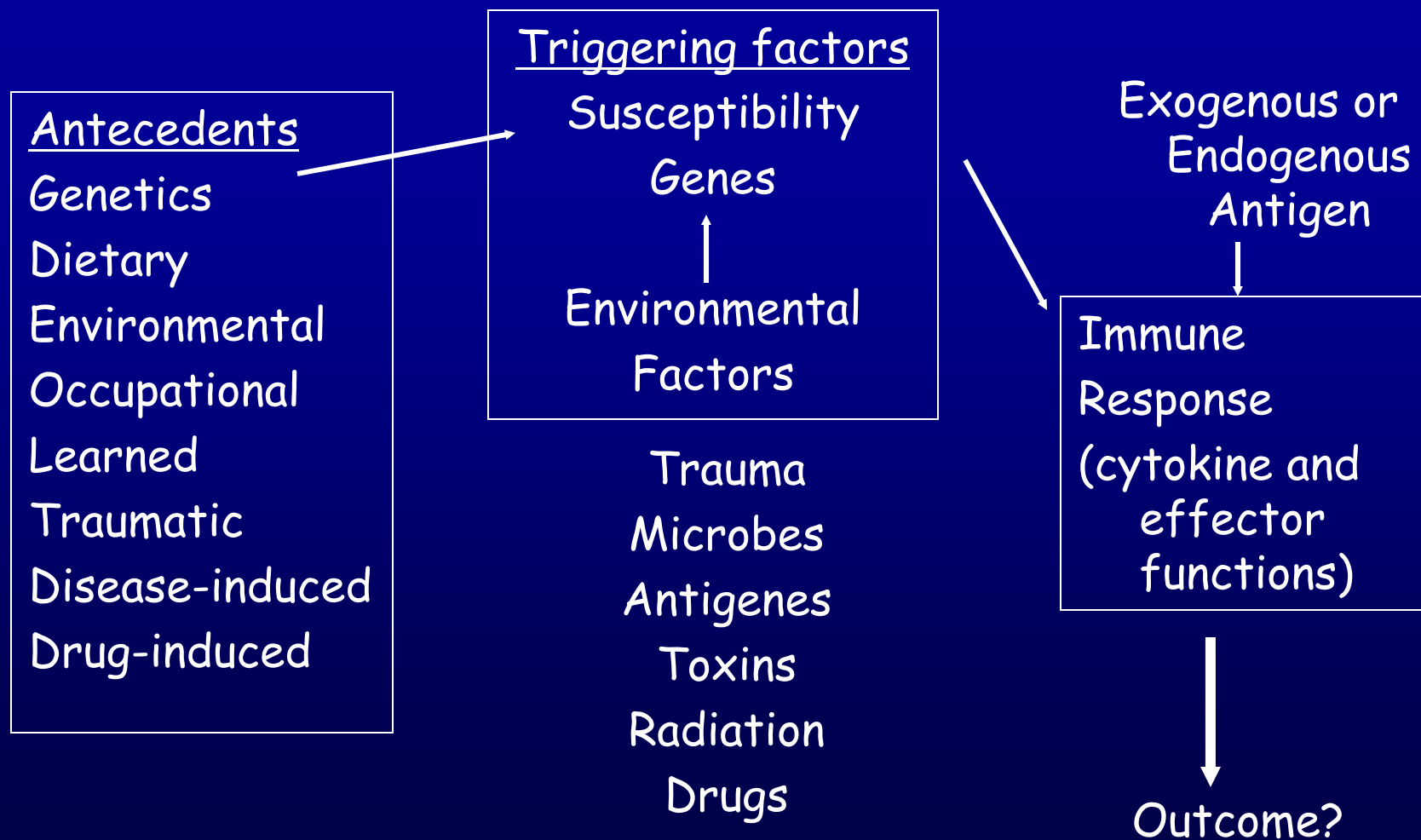
- Complementary and alternative medicine includes all those types of medicine that, when mentioned by a patient, elicit a blank look from their physicians, and cause the physician to leave the room in a hurry



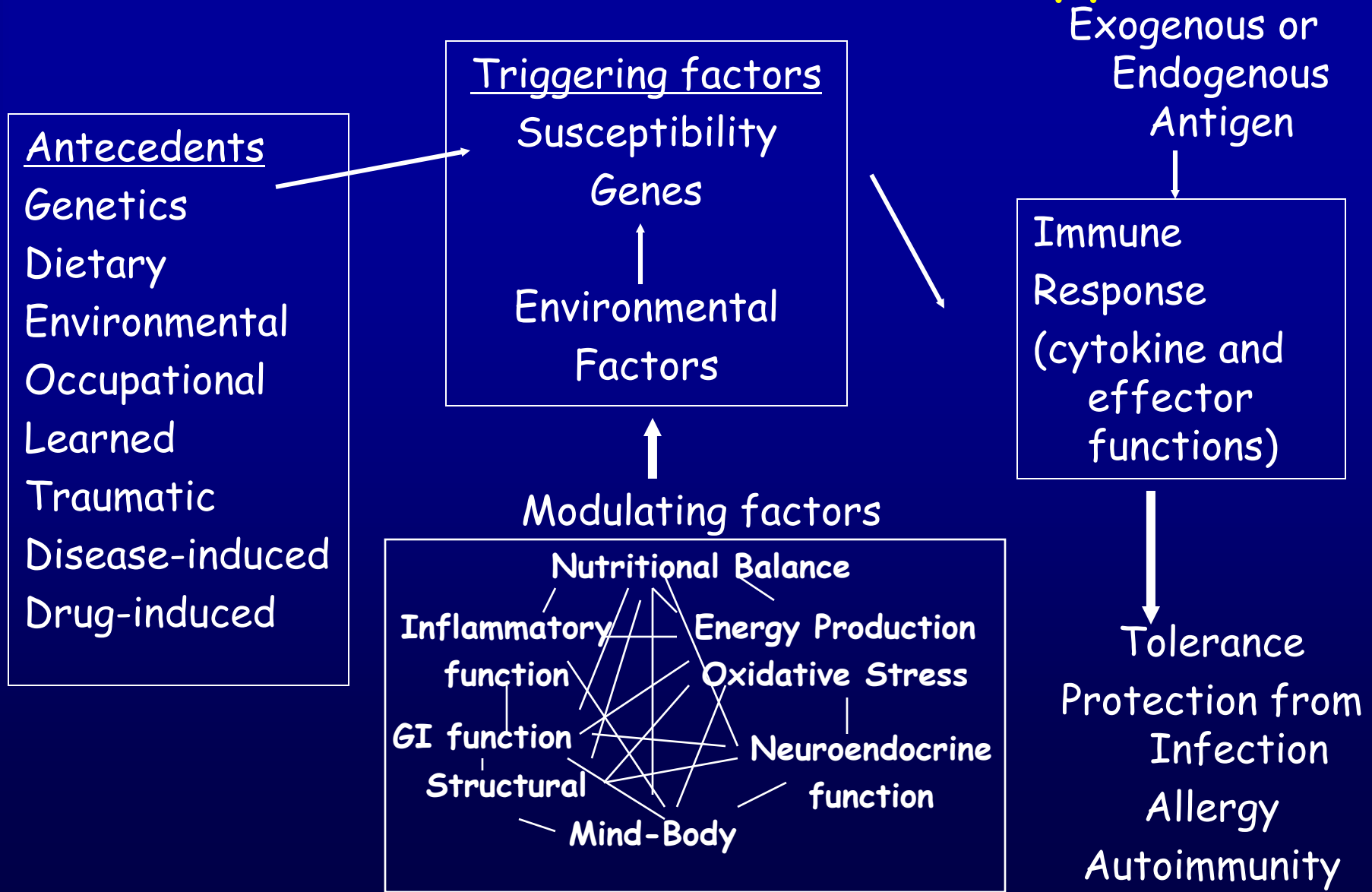
NCCAM Definition

- Complementary and alternative medicine, as defined by the National Center for Complementary and Alternative Medicine (NCCAM), is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.
- Also defined as 'diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine'.

Multifactorial nature of autoimmune disease



Needs a functional medicine approach



Usage of CAM is common

- 4 out of 10 Americans used CAM for chronic conditions
- 629 million visits with \$27 billion being spent each year
- Estimated that 60-90% of patients with arthritis have used CAM
- About 65% of SLE patients have been reported to have used CAM in some studies
- Lupus patients who use CAM tend to be younger and better educated

Usage of CAM in SLE

Table 1. Use of alternative medical therapies by SLE patients in Canada, the United States, and the United Kingdom*

	Canada (n = 229)	United States (n = 267)	United Kingdom (n = 211)
Relaxation techniques	51 (22.3)	71 (26.6)	45 (21.3)
Massage	36 (15.7)	52 (19.5)	40 (19)
Herbal medicine	28 (12.2)	28 (10.5)	32 (15.2)
Lifestyle diets	26 (11.4)	41 (15.4)	27 (12.8)
Self-help groups	21 (9.2)	29 (10.9)	10 (4.7)
Imagery	18 (7.9)	26 (9.7)	7 (3.3)
Folk remedies	18 (7.9)	10 (3.7)	4 (1.9)
Spiritual healing	16 (7)	39 (14.6)	14 (6.6)
Chiropractic	15 (6.6)	13 (4.9)	4 (1.9)
Megavitamin therapy	14 (6.1)	14 (5.2)	10 (4.7)
Homeopathy	14 (6.1)	6 (2.2)	13 (6.2)
Energy healing	11 (4.8)	6 (2.2)	6 (2.8)
Commercial weight loss	8 (3.5)	18 (6.7)	14 (6.6)
Biofeedback	8 (3.5)	10 (3.7)	0 (0)
Acupuncture	7 (3.1)	3 (1.1)	8 (3.8)
Hypnosis	3 (1.3)	3 (1.1)	3 (1.4)
Other	10 (4.4)	8 (3)	13 (6.2)
Total	116 (50.7)	134 (50.2)	102 (48.3)

* The total refers to all patients using at least 1 alternative therapy. Values are the number (%) of patients. SLE = systemic lupus erythematosus.

Evidence based medicine

- Grades of evidence
 - Case reports
 - Case series
 - Case controlled studies
 - Cohort studies
 - Randomized controlled trials
- Need to be cautious about products not approved by the FDA or the ACR. Considerations:
 - What is the proof? Is it effective in lupus?
 - Is it un-safe?
- Dietary supplements are regulated as foods, not drugs, so there could be quality issues in the manufacturing process

First do no harm!

- Supplements can interact with prescribed or over-the-counter medicines, and other supplements
- "Natural" does not necessarily mean "safe" or "effective." Overall, there is not much rigorous research available on the effectiveness and safety of botanical and other supplements

First do no harm

Examples of potentially harmful use of CAM:

- Many herbs can interfere with prescription drugs, or can be dangerous if taken in large quantities. Always check with your doctor before taking any herbal remedy or dietary supplement.
 - Some herbs contain undeclared pharmaceutical compounds- such as non-steroidal anti-inflammatories
 - Some contain estrogenic activity
 - Beware of 'stimulants of the immune system'
- Use of unproven remedies as a substitute for conventional therapy

Herbal remedies

- Herbal remedies promoted for the treatment of arthritis include ginger, Chinese Thunder God Vine, willow bark extract, feverfew, cat's claw and stinging nettle.
- Ginger and willow bark extract: Evidence for pain relief; But contain chemicals that are similar to conventional nonsteroidal anti-inflammatory compounds (NSAIDs); don't use with warfarin
- Cat's Claw - May increase the risk of bleeding if taken with blood-thinning drugs (e.g. Warfarin, Heparin)
- Stinging Nettle - May increase the effects of tranquilisers and sedative drugs. May decrease the effect of certain cardiac and diabetic drugs
- Thunder God Vine- Used for over 2000 years in Chinese medicine, 5 open trials- total of 248 patients with lupus with improved fever, rash, fatigue, lymphadenopathy, and laboratory abnormalities. Some serious side effects: GI upset, infertility

Echinacea

- Echinacea is popularly believed to be an immunostimulator, stimulating the body's immune system and warding off infections
- A controlled double-blind study in the NEJM found that echinacea extracts had "no clinically significant effects" on rates or duration of infection after viral exposure



Echinacea

- In one investigation by an independent consumer testing laboratory, five of eleven selected retail echinacea products failed quality testing
- Reported adverse effects: allergy, TTP, leucopenia, abdominal pain, nausea, dysuria, arthralgia, myalgia
- Should not be taken by persons with progressive systemic and auto-immune disorders; should not be used with immunosuppressants or hepatotoxic drugs



DHEA

Although not a nutrient or a dietary supplement, this steroid hormone can be purchased over-the-counter

- Naturally occurring adrenal steroid that is secreted mainly as DHEA sulfate
- Works as a substrate for androgens and estrogens
- Also has immunomodulatory effects
- Large multi-center RCT with n=381
- 86/147 in the prasterone group (200 mg) vs 65/146 in placebo group had either stabilization or improvement in their disease
- Lipid profile improved significantly and complement levels decreased
- Acne and hirsutism were the most frequent side effects

Arthritis and Rheum46:2924, 2002

Probiotics



Probiotics are dietary supplements of live bacteria or yeasts thought to be healthy for the host organism. According to the currently adopted definition by FAO/WHO, probiotics are:

'Live microorganisms which when administered in adequate amounts confer a health benefit on the host'

Probiotics

- Intended to assist the body's naturally occurring gut flora; claims to strengthen the immune system
- Issues: Costly, lack of hard evidence
- Recent data supported by the LRI showing benefit in lupus prone mice (FASEB Journal. 2008;22:1b477)

Nutrition and lupus

- Cardiovascular health:
 - diets low in saturated fat, omega-6-fatty acids, and cholesterol
- Benefits of omega-3-fatty acids
- Vitamins

Nutrition studies

• Beneficial effects of protein and caloric restriction?

- Severe caloric restriction delays the onset of glomerulonephritis in rats and mice (NZB/W)
- Protein restriction especially of phenylalanine and tryptophan have a beneficial effect on lupus in rats

In general- not recommended: no evidence in humans; exception would be in the setting of kidney dysfunction

Nutrition studies

- Diets rich in saturated fats and omega-6 fatty acids, and L-canavarine (alfalfa) have a deleterious effect on lupus in mice
- Little to no human studies to date have confirmed these findings
- One of the few human studies in which SLE patients reduced their omega-6 polyunsaturated fatty acid intake found that after one year, the number of patients with active SLE dropped from 11 to 3. Problems of interpretation:
 - Spontaneous improvement, placebo effects, and lack of a control group

Foods high in omega-6- fatty acids

- Sunflower, poppyseed, corn, wheatgerm, walnut, cottonseed, peanut, and sesame oil
- Mayonnaise
- Liquid margarine
- Brazil nuts
- Pine nuts
- Pumpkin kernels

Fish oil and Omega-3-fatty acids in lupus

- Majority of mice studies show that fish oils retard the development of lupus in mice
- Human studies show modest results
 - In 1 RCT, 8/17 lupus patients given 6-8 grams of fish oil per day improved compared with 2/17 given placebo
 - In 2 other uncontrolled studies patients given large doses of fish oil did not show any improvements in DNA, immune complexes, or renal parameters
 - In a double blind study of 26 lupus patients who were followed for 2 years, there was no improvement in renal parameters or DNA antibodies. However, lipids did improve in the treated group.
 - In a small uncontrolled study of 9 patients with lupus, 30 grams of flax seed oil conferred some beneficial effects on renal parameters and atherogenesis
 - Recent small randomized study (3 gm) of 60 patients found small but significant improvements in disease activity

Omega-3 fatty acids

- Fatty fish such as salmon, tuna, halibut
- Canola Oil, flaxseed oil, hemp oil, soybean oil
- Walnuts, flaxseeds, pumpkin seeds
- Soy and tofu
- Green leafy vegetables
- Some eggs are enhanced with omega-3s

Flax seed

- Two studies, one with mice and the other with human subjects, suggest that flaxseed may be beneficial in SLE
- Eight humans with SLE were given 30 grams of flaxseed mixed in with their cereal or juice, and were reported to have improved renal function
- Flaxseed contains natural antagonist of platelet activating factor, high in omega-3 fatty acid, alpha-linoleic acid
- Possible allergic reactions

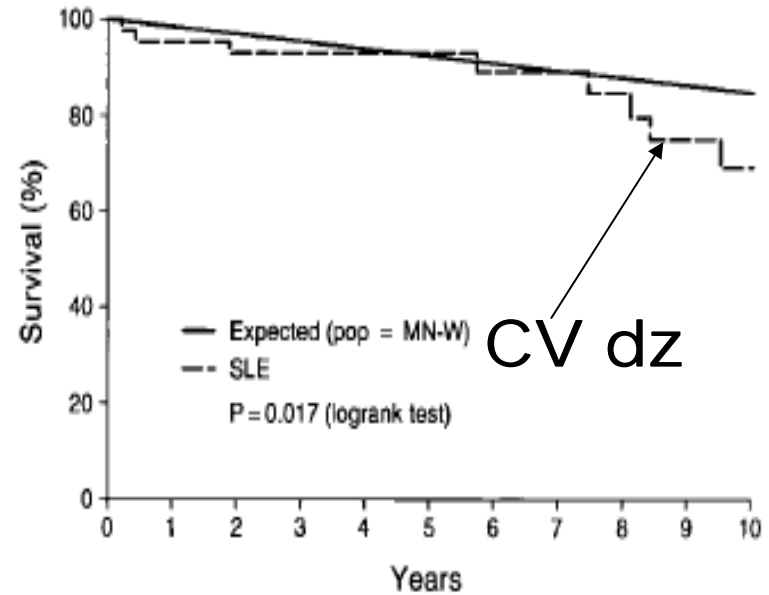
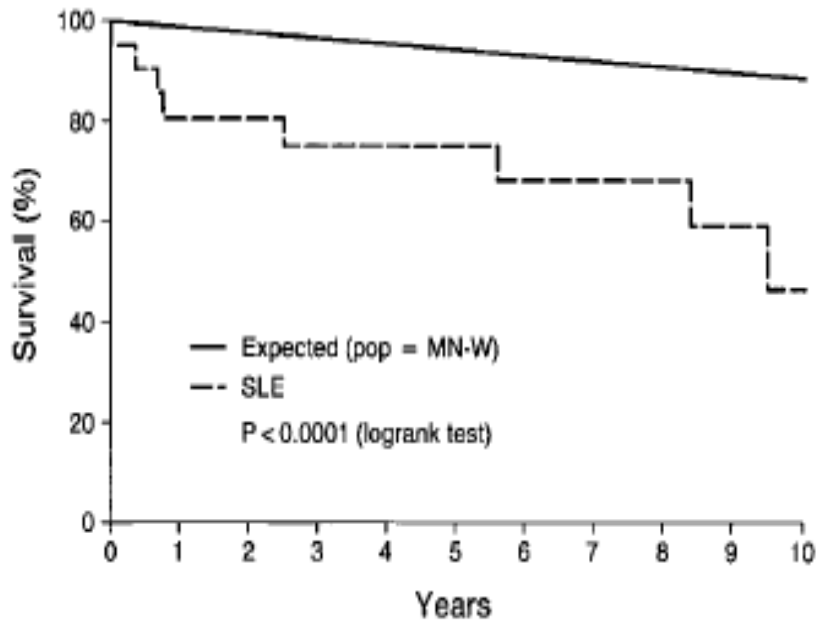
Atherosclerotic disease in SLE

- Clinical CAD is very common in lupus cohorts: 6-10%
- Women with SLE have a 5-6-fold increased risk of cardiovascular disease compared to the general population
- Women aged 35-44 years have a 50-fold increased risk!!
- SLE patients are more likely to have certain classic risk factors: HTN, diabetes, obesity
- 'SLE factors'

Overall survival in lupus has improved

1950-1979

1980-1992



Bimodal mortality pattern

- Early mortality in lupus is due to active SLE or associated complications such as infection
- Late death (>5 years after diagnosis) are frequently associated with atherosclerotic complications

What can lupus patients do to decrease their risk of heart disease?

Ways to improve risk factors without medications

- Reduced intake of saturated fat and cholesterol
- Increased physical activity
- Weight control
- Stop smoking

Vitamins

- There have not been adequate scientific studies proving that specific vitamins are helpful in treating lupus. However, it is important to have a good, balanced diet to maintain health

Vitamin E

- Vitamin E has been advocated for lupus patients since the 1940s
- Several positive studies have been reported
- A closer look at the literature shows several negative studies as well

- A recent meta-analysis of literature showed that high dose vitamin E over 400IU per day was associated with a higher mortality and higher incidence of heart attacks and strokes

MORE IS NOT NECESSARILY BETTER!

Vitamin A

- Vitamin A has been reported to have beneficial effects in SLE
- 3 patients with skin lesions were given vitamin A in high doses. In 1 week all lesions cleared up.
- Other researchers have reported an improvement in immune function parameters with vitamin A supplementation
- Caution advised to patients using vitamin A from animal sources as these are fat soluble and can accumulate and cause toxicity

Selenium

- Selenium supplementation has been reported to be beneficial in lupus mice
- No human studies
- Caution advised as excess selenium can cause diarrhea, vomiting, hair loss, skin lesions, and nervous system dysfunction

Supplements to avoid

Those containing:

- protein (high meat diet)
- omega-6 polyunsaturated fatty acids
- zinc (also found in Brazil nuts and oysters, some supplemented cereals)

Vitamin D

- Vitamin D and osteoporosis
 - Osteoporosis is common in SLE
 - recent observational study of 163 women with SLE
 - median age of 47
 - 55% post-menopausal, 52% taking steroids, 85% h/o steroids
 - 23% osteoporotic, 56% osteopenic
 - Vitamin D is important for bone health; vitamin D deficiency is extremely common
 - Recommend MVI with calcium and vitamin D in SLE to prevent and treat osteoporosis

Almehed et al. Rheum 46:1185, 2007 "Prevalence and risk factors of osteoporosis in female SLE patients"

Vitamin D and lupus

- Vitamin D and autoimmunity
 - Vitamin D has potent anti-inflammatory properties, suppressing immune cells that take part in the autoimmune reaction
 - Vitamin D and Lupus
 - Supplementation of lupus mice with Vitamin D improves disease
 - Some studies have found a higher prevalence of vitamin D deficiency in SLE

Rheumatology (Oxford). 2008 Vitamin D deficiency in systemic lupus erythematosus: prevalence, predictors and clinical consequences.; Ruiz-Irastorza et al. ; ARD 2007 Vitamin D and autoimmunity: new aetiological and therapeutic considerations, Arnsen et al.

Nutrition studies

- Recent study of 92 SLE patients
 - 75% and 15% presented with vitamin D insufficiency and deficiency, respectively.
 - Female sex ($P = 0.001$), treatment with HCQ ($P = 0.014$) and treatment with calcium and vitamin D ($P = 0.049$) predicted higher levels of 25(OH)D.
 - Photosensitivity [odds ratio (OR) 3.5] and photoprotection (OR 5.7) predicted vitamin D insufficiency and deficiency, respectively.
 - Patients with vitamin D deficiency had a higher degree of fatigue as quantified by a 0-10 VAS (mean 5.32 vs 4.03, $P = 0.08$).
 - No relation was seen between vitamin D insufficiency or deficiency and disease duration, SLEDAI or SLICC-ACR indexes.
- ACE study of vitamin D supplementation in SLE

Some points to remember

- There are no magic cures for lupus. Do not be conned into spending money on a product that claims to be a 'cure-all'. If in doubt consult your doctor.
- Do your homework- ?safety, ?efficacy
- Natural Isn't Necessarily Safer
- Herbal supplements are virtually unregulated
- Little data regarding herbal treatments and lupus
 - please be careful when taking alternative medicines
 - avoid any herbal treatments that claim to 'stimulate the immune system'

General recommendations on nutrition

- Healthy well-balanced diet is advisable for general health, cardiovascular health, and possibly lupus specifically.
 - Data for omega-3-fatty acids
- **WHAT YOU CAN DO-**
lifestyle modification to decrease risk of CV disease
- Basic MVI with daily recommended amounts of vitamins is reasonable
 - Exception to this is that vitamin D may require extra supplementation

Resources for more information

- Arthritis foundation: www.arthritis.org
- National Center for Complementary and alternative medicine: www.nccam.nih.gov
- Johns Hopkins review of alternative therapies for arthritis
- <http://www.uklupus.co.uk/medcont.html>

**POSSIBLE HARMFUL DIETARY SUBSTANCES RELATED TO
LUPUS ERYTHEMATOSUS**

Possible

Harmful Substances	Suggested Maximum Daily Intakes^a
Excess Energy	2400-2600 calories (men)/ 1600 calories (women) ^b
Excess Protein	63 g (men)/50 g (women)
High Fat (especially saturated & polyunsaturated omega-6 fatty acids)	30% of calories/65 g (total fat) 10% of kcalories/20 g (saturated fat)
Zinc	15 mg (men)/12 mg (women)
Iron	10 mg (men)/15 mg (women)
L-canavanine (alfalfa tablets)	NA

^a Based on the

1989 Recommended Dietary Allowances (RDA) for adults 25-50 yrs; 1997 Dietary Reference Intakes (DRI); Reference Daily Intakes (RDI) and Daily Reference Values (DRV).

^b Note: These values represent the average daily caloric intake of Americans (the majority of which are overweight) and are below the RDA values for men (2900 kcalories) and women (2200 kcalories).

**POSSIBLE BENEFICIAL DIETARY SUBSTANCES RELATED TO
LUPUS ERYTHEMATOSUS**

<u>Beneficial Substances</u>	<u>Daily Intakes^a</u>	<u>Possible</u>
Vitamin E ^b	30 IU/9 mg alpha-TE/(400-1500 IU/130-500mg)	
Vitamin A (beta-carotene)	5000 IU/1000 ug RE	
Selenium	70 ug	
Fish Oils ^c (omega-3 fatty acids)	(1.5 - 3 g of EPA/DHA)	
Evening Primrose Oil	(5 g)	
Flaxseed	(30 g)	
Plant Herb ^d (Tripterygium wilfordii)	(10 mg – side-effects?)	
DHEA ^e (dehydroepiandrosterone)	(200 mg - side-effects?)	
Food Allergy Elimination Diets	NA	
Calcium (if taking corticosteroids)	1000 mg	
Plus Vitamin D	400 IU/10 ug	

^a Based on the Reference Daily Intakes (RDI). Amounts in () represent tentative research data (refer to review).

^b High dosages of vitamin E act as an anticoagulant.

^c Most fish oil capsules contain about 300 mg of omega-3 fatty acids, so about 2-3 tablets/meal will yield 1.8 - 2.7 g.

^d Previously reported side-effects include, but are not limited to, gastrointestinal upset, infertility, suppression of lymphocyte proliferation, and possible cardiac toxicity and birth defects.

^e Caution: People should not take DHEA unless under the care of their physician who approves such a regimen. The benefits of DHEA reported in people with lupus occurred at high, and questionable, intakes of 200 mg/day. DHEA is an androgenic with male hormonal influences, and dosages as low as 50 mg/day have been reported to cause minor side-effects such as acne, facial hair growth, menstrual changes, and improved mood. There are also animal studies in which DHEA appears to cause liver cancer in rats.