

Chronic Fatigue

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See Supplemental materials at: <http://naimh.com/fatigue>

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<http://medherb.com>

Fatigue

- Fatigue is the second most common reason for a primary care medical visit, second only to pain.
- Involves changes in musculoskeletal, endocrine, nervous, digestive, and immune systems, cognitive function, judgment, reflexes, and psychology.
- About 50% of patients who seek medical help for fatigue have a diagnosable illness.
- The most common medical complaint of a diabetic at first diagnosis is fatigue.
- It is a ***therapeutic error*** to fail to make appropriate differential diagnosis as to the cause of fatigue, then stimulate the system while allowing an underlying pathology to progress.

Chronic fatigue syndrome

- Chronic fatigue lasting 6 months or more without known medical condition causing it.
- Is an artificially constructed diagnostic entity without an objective reality.
- May be due to many influences well-known in natural medicine
- Many cases are endocrine “burnout” and chronic maladaptation to stress

A model for stages of fatigue

- Stage I: Normal fatigue after normal daily activity. Recovery with nights sleep.
- Stage II: Excessive fatigue after abnormal activity (over-reaching in athletics, temporary sleep debt, etc). Physical, mental, immunological, and endocrine changes. Full recovery in days to weeks of restful activity. Normal.
- Stage III: As in stage II, distinguished only by delayed recovery time of weeks to months.
- Stage IV: Burnout. Same changes as in Stages II and III, but recovery in months to years, or not at all. Loss of response in HT axes. Endocrine gland atrophy. Signs and symptoms similar in II to IV, but assessed only by lack of response to therapeutic rest.

The maladaptation model of Selye

- Phase One. General alarm reaction (up to 48 hours). Multiple physiological changes.
- Phase Two: Beyond 48 hours. Hypertrophy of adrenals and thyroid; atrophy of gonads.
- Later Phase Two: Functions and organ appear near normal.
- Phase three: 1-3 months. Return of Stage I but now chronic. Atrophy of all endocrine glands. Recovery difficult or impossible.
- Chinese cancer researchers autopsied a number of patients who had been diagnosed with 'Kidney deficiency.' All had general atrophy of their endocrine glands.

Overtraining syndrome in athletics

- Normal training with *adequate rest and recovery* to adaptation. Normal recovery
- Overreaching. Delayed recovery.
- Non functional overreaching. Difficult recovery
- Overtraining syndrome. Recovery long term or not at all.

Medical conditions causing fatigue

- Anemia
- Iron deficiency
- Medication side effects
- Osteomalacia
- Persistent pain
- Sleep disorders
- Thyroid disorders
- Alcohol or drug abuse
- Addison's disease
- Disordered eating
- Mild traumatic brain injury
- Allergies
- Arthritis
- Autoimmune diseases
- Cancer
- Congestive heart failure
- Diabetes
- Chronic infection
- HIV disease
- Kidney disease
- Liver disease
- Malnutrition

Differentials for athletic burnout

- Anemia
- Epstein–Barr virus (acute)
- Other infectious diseases
- Lyme disease
- Endocrinological diseases (diabetes, thyroid, adrenal gland)
- Major disorders of eating behavior
- Allergies
- Biological abnormalities (increased erythrocyte sedimentation rate, C-reactive protein, creatinine, or liver enzymes, decreased ferritin, I)
- Injury (musculoskeletal system)
- Cardiological symptoms
- Adult-onset asthma

Meeusen R, et al. Prevention, diagnosis, and treatment of the overtraining syndrome. *Med Sci Sports Exerc.* 2013 Jan;45(1):186-205.

Anemia

- Common condition
- Common cause of fatigue in women
- May or may not be caused by iron deficiency
- Iron supplementation may worsen some forms of anemia
- Screen all patients complaining of fatigue
- Obtain differential diagnosis of anemia type/cause
- Other risk factors, heavy menses, other blood loss, celiac disease, malabsorption syndrome, vegetarian or vegan diet, disordered eating.

Common lifestyle factors causing fatigue

- Sleep debt
- Disordered digestion, including food intolerance
- Suboptimal protein in the diet
- Insufficient food/protein early in the day
- Deficiencies of magnesium, B-vitamins, zinc.
- Vitamin D deficiency/osteomalacia
- Iron deficiency in women
- Essential fatty acid deficiency
- Lack of moderate exercise most days
- Over exercise relative to nutrition.

Common pathological syndromes

- Systemic inflammation
- Food intolerance
- Insulin resistance
- Disordered eating
- PTSD
- MTBI

Epstein Barr Virus

- More than 90% of adults shown signs of previous infection.
- Active infection causes *infectious mononucleosis*, which may be accompanied by profound fatigue.
- Was at one time thought to be a major cause of chronic fatigue, and CFS was at one time called Chronic Viral Fatigue Syndrome.
- Levels in patients with CFS overlap significantly with normal controls. Koo D Chronic fatigue syndrome. A critical appraisal of the role of Epstein-Barr virus. West J Med. 1989 May;150(5):590-6.
- “Antiviral” botanicals have little effect as monotherapy on CFS or generalized fatigue.

Osteomalacia

- The adult form of Ricketts (vitamin D deficiency)
- In children, the growing bones are malformed and respiratory immunity is impaired.
- In adults, there is generalized fatigue and malaise, symptoms of bone pain, and muscle atrophy and weakness.
- Wintertime averages of serum 25(OH)D in North America and Europe are below the threshold where osteomalacia begins to appear. (16 ng/mL)
- Muscle weakness occurs progressively as 25(OH)D levels fall below 30 ng/mL

Some pharmaceuticals given for CF

- Zolpidem (Ambien) – sedative hypnotic short acting – FDA recently lowered dosing for women by 50% due to induction of daytime drowsiness while driving.
- Temazepam (Restoril) – benzodiazepine. All benzodiazepines are addictive within 4 weeks of use. Withdrawal more severe than alcohol.
- Sleep medications create addictive dependence with rebound insomnia and anxiety in many people.
- Corticosteroids. Dose to “give the adrenals rest” then wean after 1-2 years.

Sleep medications and mortality

- An estimated 6%-10% of US adults took a hypnotic drug for poor sleep in 2010 (=up to 30,000,000)
- Subjects (mean age 54 years) were 10 529 patients who received hypnotic prescriptions and 23 676 matched controls , followed for an average of 2.5 years
- Mortality risk was elevated for zolpidem, temazepam,eszopiclone, zaleplon, other benzodiazepines,barbiturates and sedative antihistamines.
- Hypnotic use in the upper third was associated with a significant elevation of incident cancer
- Receiving hypnotic prescriptions was associated with greater than threefold increased hazards of death even when prescribed <18 pills/year

Kripke DF et al.Hypnotics' association with mortality or cancer: a matched cohort study. BMJ Open. 2012 Feb 27;2(1)

Krebs cycle substrates and function

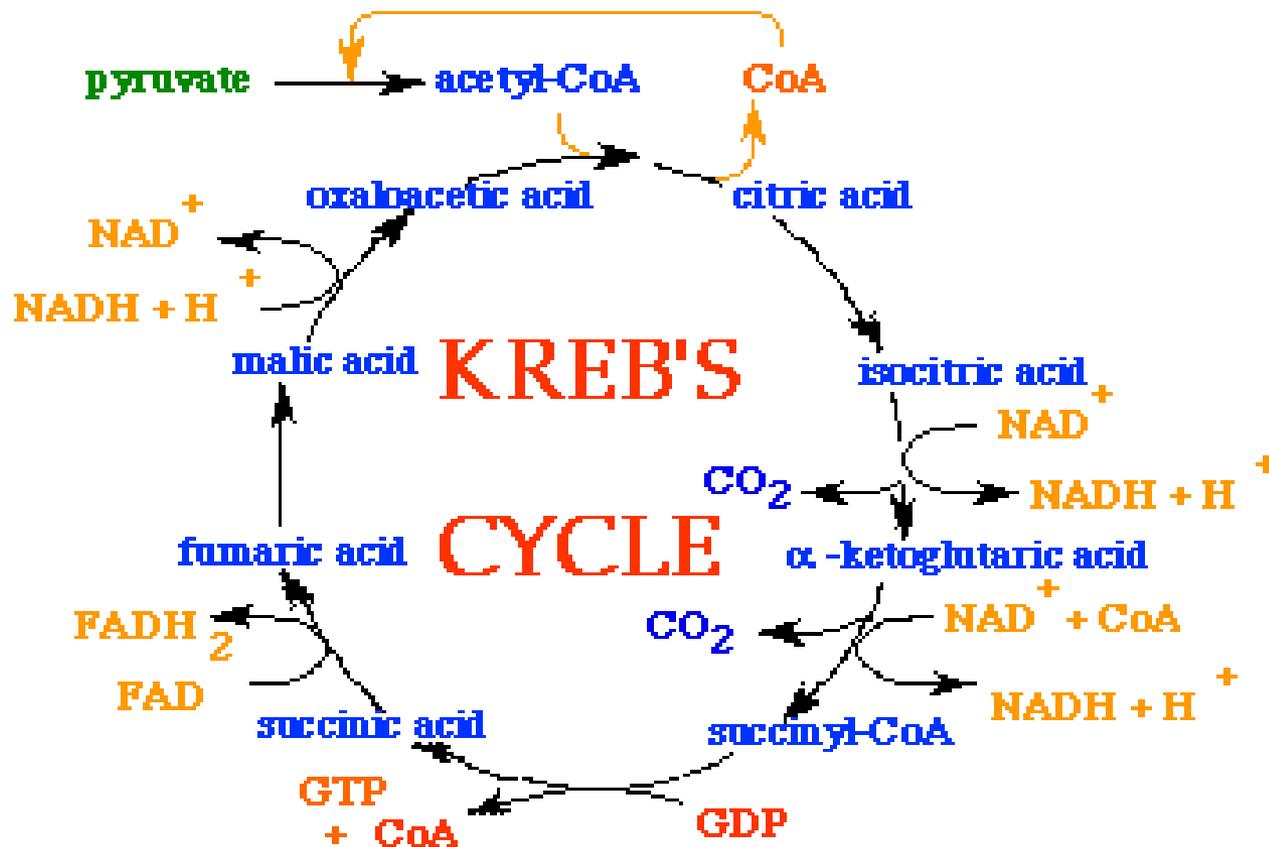
Adrenal vs mitochondrial function

- A common error to equate fatigue with “adrenal exhaustion”
- Standards for adrenal tests in middle age are controversial.
- It is difficult to change adrenal test results with natural interventions.
- Reduction of fatigue with natural methods frequently shows no or only minor change in adrenal test results.
- For cerebral or muscle fatigue, ATP production via mitochondrial function is critical.
- See BURNOUT section later in this presentation.

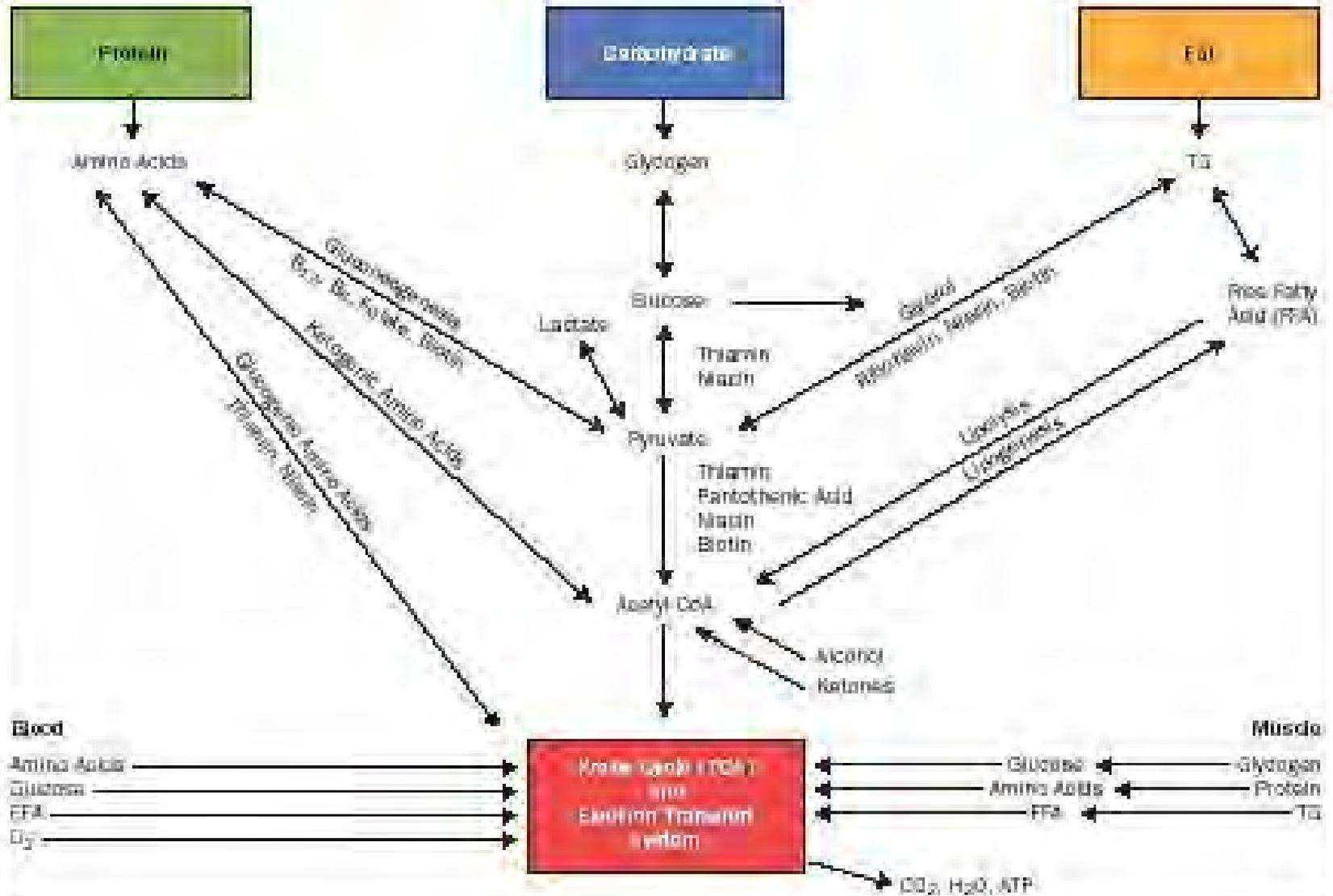
Krebs cycle

- Acetyl-CoA from glucose, fatty acids, amino acids, ketones plus oxygen
- Combines with oxaloacetate to form high energy citric acid.
- Citric acid degrades back to oxaloacetate, releasing energy from fuels.
- Energy is transferred to ADP molecules to add a high energy bond for a third P atom = ATP
- Water, and CO₂ are released
- Occurs only in ***mitochondria*** of the cells

Krebs cycle intermediates



INTERRELATIONSHIPS AMONG CARBOHYDRATE, PROTEIN, AND FAT IN HUMAN METABOLISM

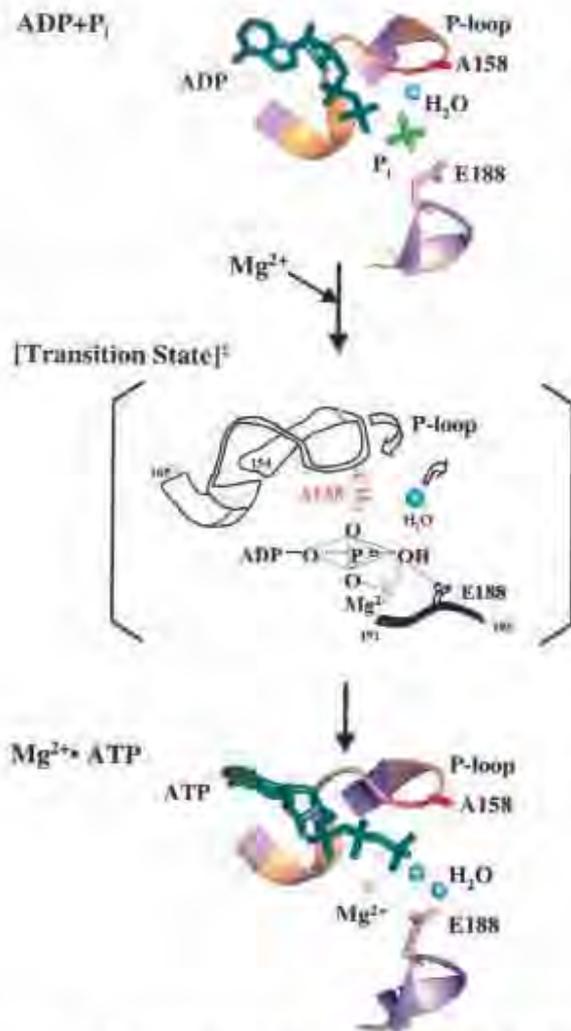


B vitamins

- Take as a complex
- Take as part of a multi-vitamin
- Do not need mega-dosing, may take pill with RDA 3x per day, or supplements with higher doses 2-3 times per week.
- May be the main reason the people feel better with more energy shortly after starting to take taking a multi-vitamin.

Magnesium and energy

- Most common mineral deficiency in U.S.
- Suboptimal in >80% of population, including many with otherwise good diets.
- Declining in the food supply with increase in “empty calorie” foods; also due to farming practices.
- Is excreted in supernormal amounts in conditions of insulin resistance > 60% of population.
- Symptoms: low energy, muscle cramping or stiffness, inflammation.



Magnesium stabilizes the third high-energy bond in ATP. Research in chronic fatigue and Fibromyalgia shows that fatigue scores and magnesium status have inverse relationship.

FIG. 4. Diagram illustrating the pivotal role that Mg^{2+} may play in transition state formation in the ATP synthase-catalyzed reaction. See text for description. Please note that to emphasize the importance of Mg^{2+} in formation of the transition state, we have depicted its entry following that of ADP and P_i . However, the order in which Mg^{2+} enters the reaction remains to be elucidated.

Magnesium supplementation

- Dietary intake should be 500-600 mg per day.
- Therapeutic dose 600 up to 1200 mg/day for six weeks
- Better absorbed with small frequent doses.
- Not when kidney clearance is impaired.
- Some people do not respond well to pills, but liquid ionic forms work rapidly.
- Causes loose stool due to local factors in the gut as the intestine secretes fluid to dilute concentrated magnesium from a supplement.
- Take smaller frequent doses to avoid loose stool

Apple cider vinegar magnesium elixir

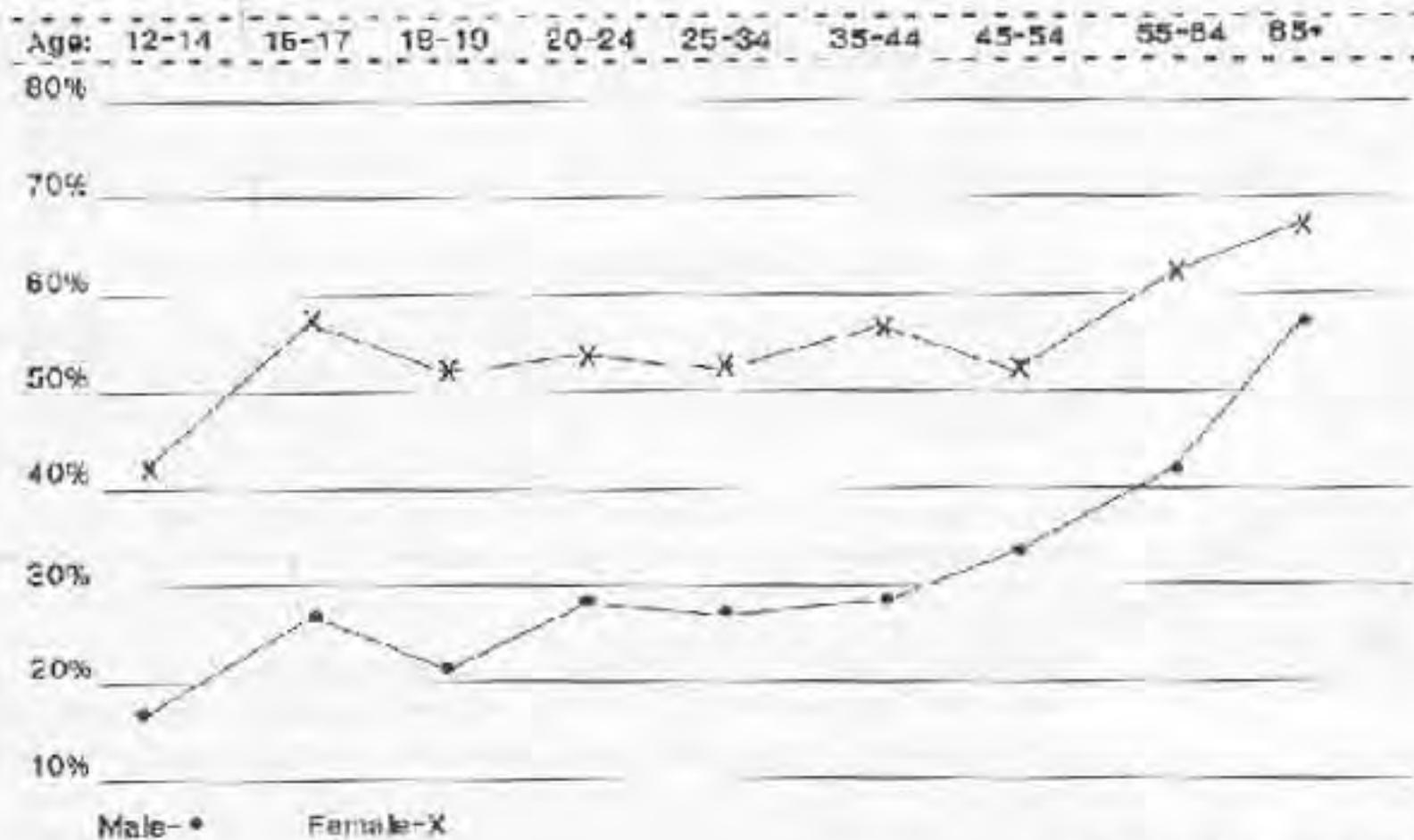
- 1 ounce of milk of magnesium
- 4 to 4.5 ounces of apple cider vinegar.
- Add vinegar and stir. Wait 5 minutes. If not clear, then add a little more vinegar.
- Some residue will remain from vinegar, but liquid should be clear. Tastes very bad.
- Contains about 42mg of ionic free Mg per tsp.
- Add 1-3 Tbs per liter to drinking water to make “heavy” magnesium water.
- Drink throughout day.

Protein and fatigue

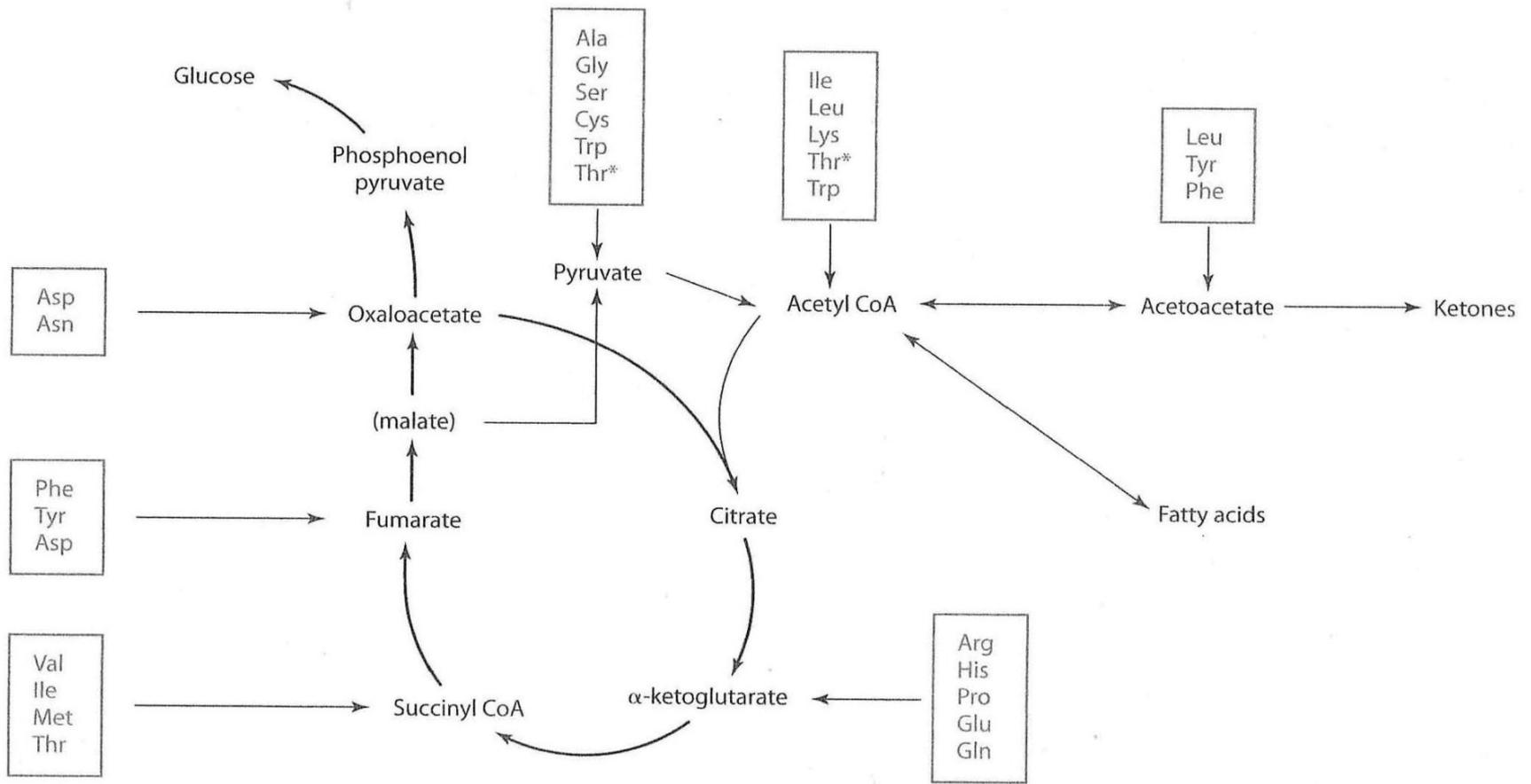
- Increasing protein in the diet reliably improves fatigue
- Meat is traditional tonic food in TCM and Ayurveda.
- About 50% do not get the RDA at some phase of life. 60% of women.
- The RDA of protein is inadequate for optimal subjective and objective health measures in active adults and elders. Wolfe RR Protein Summit: consensus areas and future research *American Journal of Clinical Nutrition*, Vol. 87, No. 5, 1582S-1583S, May 2008

Americans Below the RDA for Protein

(Percent by Sex and Age)



(Data from NCHS 1979a: 57)



*Physiological contribution unclear

Figure 6.27 The fate of amino acid carbon skeletons. Ketogenic: Lys and Leu; partially ketogenic and glucogenic: Phe, Ile, Thr, Trp, Tyr; glucogenic: Ala, Gly, Cys, Ser, Asp, Asn, Glu, Gln, Arg, Met, Val, His, Pro.

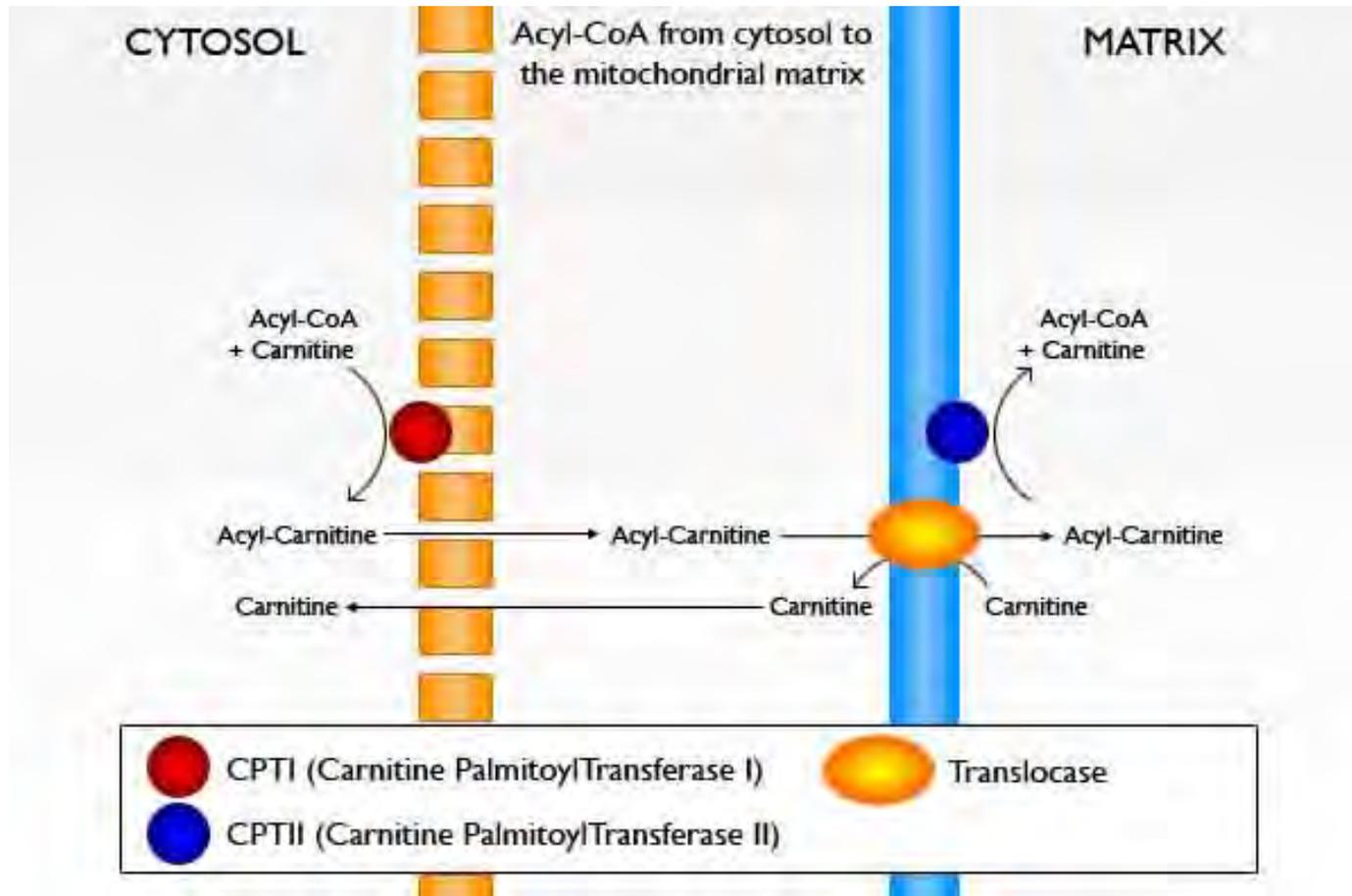
Protein in the diet

- Consuming 25-35 grams protein in the context of a low carbohydrate breakfast improves energy and reduces carbohydrate cravings throughout the day.
- In the fatigued patient, .75 grams protein per pound of body weight. (1.6 g/kg).
- Cooked easy-to-digest forms. Soups, stews, roasts, etc.

Food sources and amounts of protein in *ounce of*:

Meat, fish, poultry	5-8 grams
Milk (1 cup)	9 grams
Cottage cheese	5 grams
Hard cheese	7 grams
Ice cream (1 cup)	6 grams
Egg (1 whole)	6 grams
Dried dense beans ½ cup cooked	7 grams
Peanut butter (1 tablespoon)	4 grams
Vegetables (1/2 cup)	1-3 grams
Fruits (1/2 cup)	1-2 grams
Wheat bread (per slice)	2-3 grams
Rice (½ cup cooked)	2 grams

Carnitine and energy



Left: the cell cytoplasm

Right: interior of the mitochondrion

Carnitine deficiency and diet

- Hypocartinemia in 52% of vegans
- Hypocartinemia in 18% of lacto-vegetarians
- Hypocartinemia in 3% of omnivores

Krajcovicová-Kudlácková M, et al. Correlation of carnitine levels to methionine and lysine intake. *Physiol Res.* 2000;49(3):399-402.

Carnitine content of food

Product	Quantity	Carnitine
Beef steak	100 g	95 mg
Ground beef	100 g	94 mg
Pork	100 g	27.7 mg
Bacon	100 g	23.3 mg
Tempeh	100 g	19.5 mg
Cod fish	100 g	5.6 mg
Chicken breast	100 g	3.9 mg
American cheese	100 g	3.7 mg
Ice cream	100 ml	3.7 mg
Whole milk	100 ml	3.3 mg
Avocado	one medium	2 mg
Cottage cheese	100 g	1.1 mg
Whole-wheat bread	100 g	0.36 mg

Red meat nutrients and fatigue

- Amino acids
- B-vitamins
- Iron
- Zinc
- Carnitine
- Potassium (high K/Na ration in wild or grass-fed meat)
- EFA in wild or grass-fed meat

Energy nutrients in 16 oz lamb

- Protein 76 grams
- Niacin 27 mg
- Iron 7 mg
- Zn 15 g
- Magnesium 100 mg
- Potassium 1043 mg
- Sodium 263 mg
- Carnitine 868 mg

Heme iron

- Contained in the hemoglobin of the blood
- About 40% is assimilated
- Compare to about 2% of iron in plant food is assimilated
- Traditional 'meat tonics' for anemia, paleness, "blood deficiency."

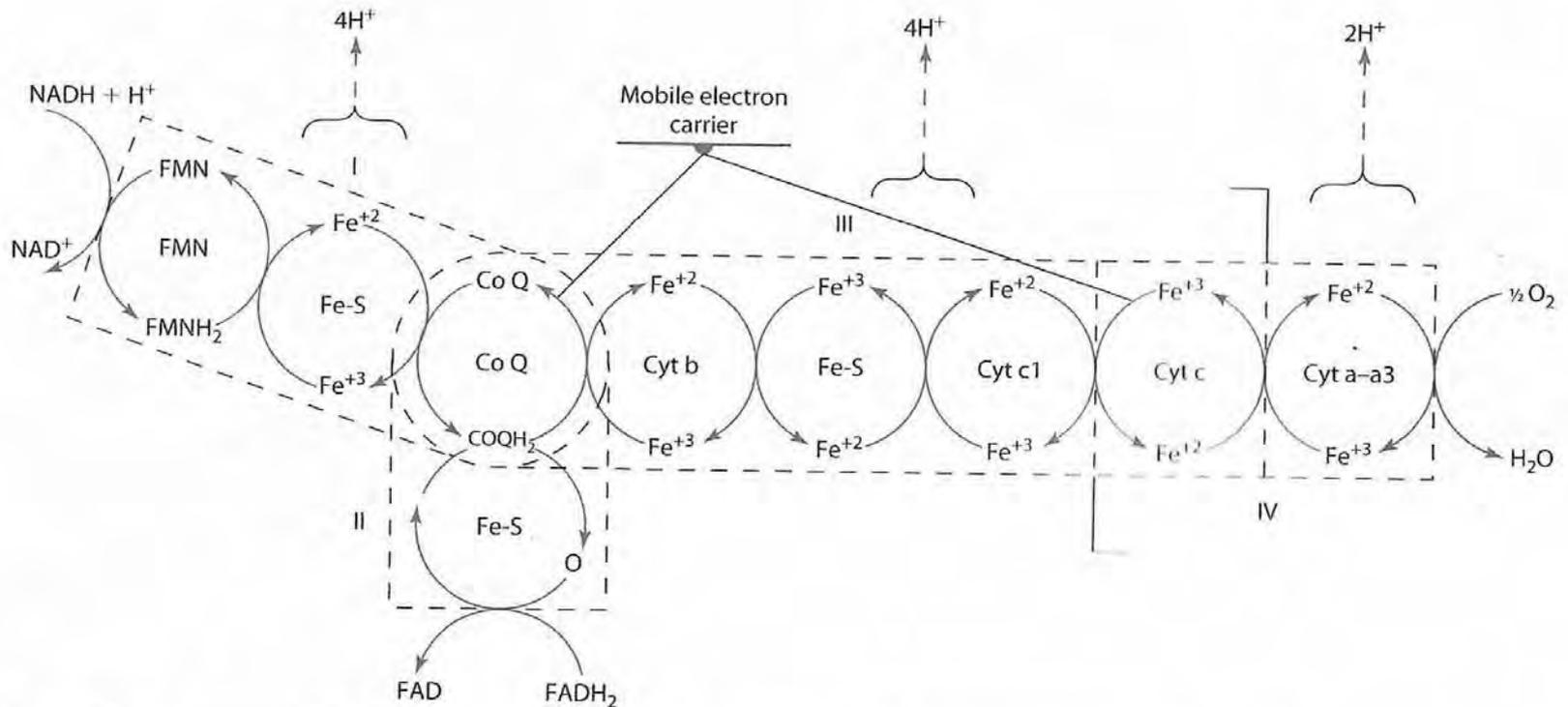


Figure 3.26 The sequential arrangement of the components of the electron transport chain, showing its division into four complexes, I, II, III, and IV. Coenzyme Q (ubiquinone) is shared by Complexes I, II, and III. Cyt c is shared by Complexes III and IV.

Iron is involved in electron transport in the production of ATP in the mitochondrial matrix

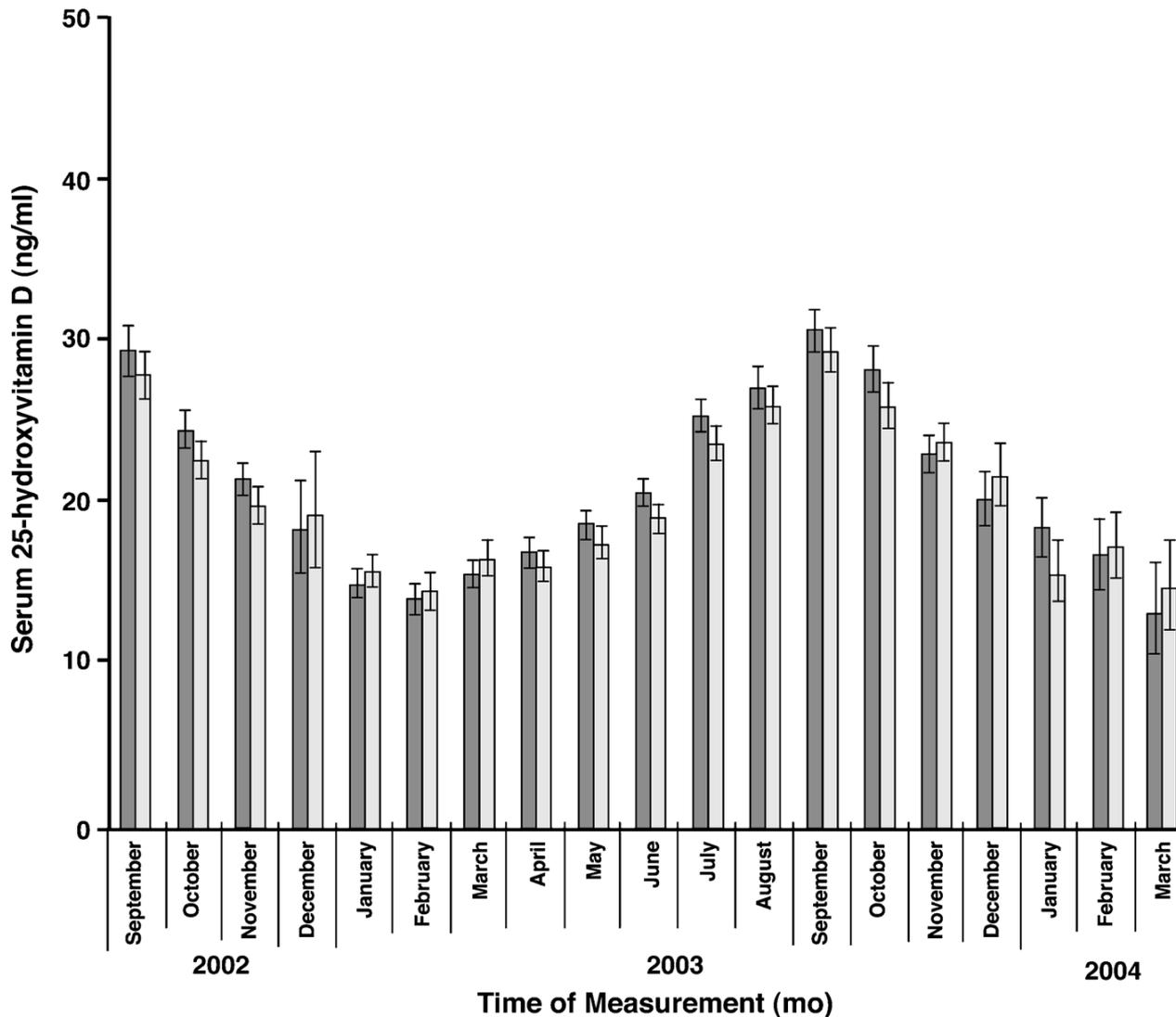
Iron supplementation

- Because iron is pro-oxidant, it should not be supplemented unless a deficiency is detected.
- Do not treat anemia with iron until a differential diagnosis has been performed
- Iron deficiency in a male is a red flag symptom.
- Caution with iron storage disorders

Vitamin D

Cholecalciferol

- Rule out osteomalacia in all CF/fibromyalgia patients
- Some meet diagnostic criteria with 25(OH)D3 levels at 16 or below.
- 50% meet diagnostic criteria with 25(OH)D3 levels at 7 or below.
- Symptoms: ***muscle weakness, muscle pain, bone pain, fatigue, mental depression, frequent respiratory infection***
- Supplement until serum 25(OH)D3 levels are ≥ 50 ng/mL. 60-80ng/mL may be optimal.
- May require doses $>10,000$ IU/day for rise to optimal levels within 30 days. (10,000 IU proposed upper safe limit for regular consumption)



Geometric average monthly variations in serum 25-hydroxyvitamin D [25(OH)D] concentrations in men (dark shade, n = 3723) and women (light shade, n = 3712) in a 1958 British (England, Scotland, and Wales) cohort at age 45 yr. (Redrawn from figure in: Hyppo[™] nen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. *Am J Clin Nutr.* 2007;85(3):860–868.

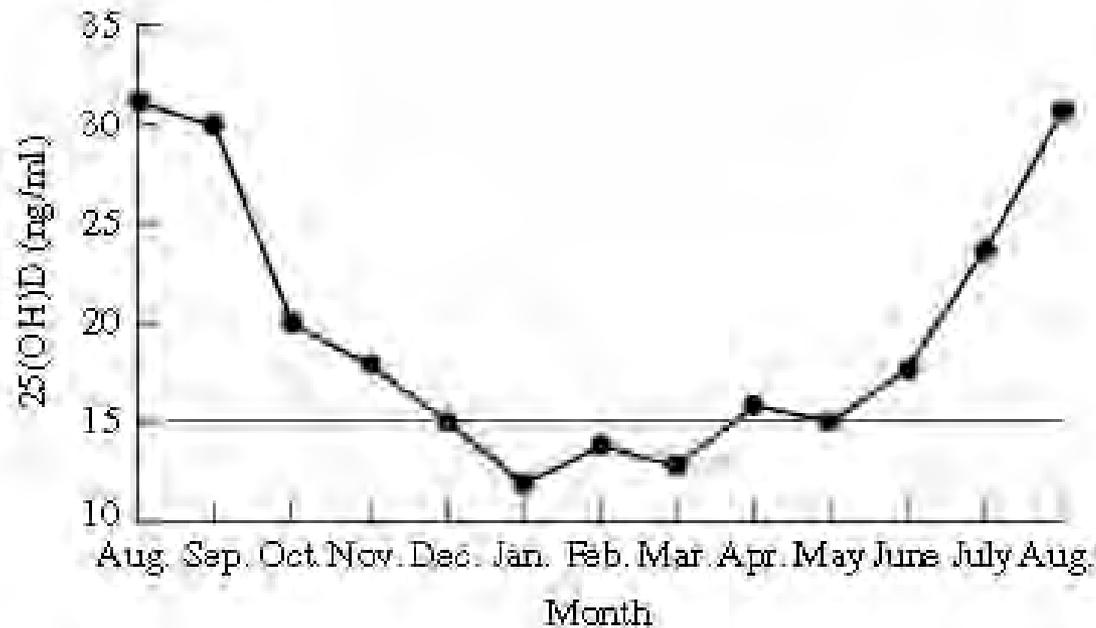


Fig. 3. Seasonal variation of 25(OH)D levels in a population-based sample of inhabitants of a small southern German town, aged 50-80 years. (Reproduced/amended with kind permission of Springer Science and Business Media, Scharla, S.H., 1998.)

Serum 25(OH)D3

- Below 16 ng/mL. Ricketts/Osteomalacia is possible.
- Below 20. Current standard for deficiency
- Below 32. Bone health is impaired. Current standard for “insufficiency.”
- Below 40. All D3 is immediately converted to 25(OH)D3; D3 undetectable in blood. Deficiency sign.
- Below 50. Mother conserves all her 25(OH)D3 and puts none into breast milk. Deficiency sign
- Below 60. Cancer incidence and other diseases increase in a linear fashion.

Note: if in nmol to convert to ng/ML divide by 2.5

September levels -- primary care practice

- Below 30 ng/mL 89% insufficiency
- Below 20 ng/mL 45% deficiency
- Below 12 ng/mL 10% severe deficiency

Fatigue and muscle weakness reported increasingly in patients with deficiency

Merlo C, et al. Prevalence and symptoms of vitamin D deficiency in general practices. Praxis (Bern 1994). (article in German) 2012 Oct 31;101(22):1417-22.

Vitamin D and muscle fibers

- Vitamin D promotes protein synthesis in muscles.
- Type I *Slow-twitch* fibers: low force/power/speed production and high endurance
- Type IIA *Fast-twitch*: Intermediate force/endurance
- Type IIB *Fast-twitch*: high force/power/speed production and low endurance.
- Vitamin D is essential to the development of Type II fibers. Individuals with deficiency have *decreased* Type II muscle mass, and supplementation in deficient individuals increases muscle mass without exercise.

Vitamin D and mitochondrial function

- Mitochondrial function depressed in a group of patients with severe vitamin D deficiency
- D levels raised with supplementation from below 10 ng/mL to above 40 ng/mL.
- ATP production (oxidative phosphorylation) increases by 20%, in linear fashion proportional to increase in D status.
- All patients reported a reduction in fatigue.

Sinha A, et al. Improving the vitamin D status of vitamin D deficient adults is associated with improved mitochondrial oxidative function in skeletal muscle. *J Clin Endocrinol Metab.* 2013 Mar;98(3):E509-13

Vitamin D and fatigue

- Fatigue and other quality of life indicators were measured in women.
- Three groups:
 - 25(OH)D <20 Highest fatigue score
 - 25(OH)D = 20-30 Lower fatigue score
 - 25(OH)D > 30 Lowest fatigue score
- Fatigue and other measures of vitality improved as 25(OH)D status improved across all 3 groups.

Ecemis GC, Atmaca A. Quality of life is impaired not only in vitamin D deficient but also in vitamin D insufficient premenopausal women. J Endocrinol Invest. 2013 Mar 19.

Fatigue of autoimmune diseases

- Patients with systemic lupus and D deficiency report lessened fatigue when levels are raised through supplementation.

Ruiz-Irastorza G, et al. Changes in vitamin D levels in patients with systemic lupus erythematosus: Effects on fatigue, disease activity, and damage. *Arthritis Care Res (Hoboken)*. 2010 Aug;62(8):1160-5.

- Patients with myasthenia gravis with D deficiency report lessened fatigue when levels are raised with supplementation.

Askmark H, et al. Vitamin D deficiency in patients with myasthenia gravis and improvement of fatigue after supplementation of vitamin D3: a pilot study. *Eur J Neurol*. 2012 Dec;19(12):1554-60.

Supplementation protocol

- Full body sunbathing for 20 minutes in light-skinned person will produce about 20,000 IU of D3
- Bathing to sunburn level will produce up to 50,000 IU
- 2000 IU/ day is insufficient to raise levels above 32 ng/mL in many people. Especially those with fat mass.
- 4000-7000 IU/day in wintertime is necessary to prevent “vitamin D winter” effect. One family physician reduced hospitalization of her patients by 70% by giving this dose to most patients.

- 4000 IU/day is current conservative upper safe limit. 10,000 IU/day is current proposed USL by vitamin D experts.
- One protocol for an infant with Ricketts is to give a single dose of 300,000 IU.
- There is some indication that doses above 50,000 IU may briefly disturb bone metabolism.
- For the severely deficient, doses of 50,000 IU per day may be given for a short period (1-2 weeks).
- For the generally deficient or insufficient, a single dose of 50,000 IU/week will raise levels to normal in most patients.

Safe serum levels

- The official normal in labs is either from 32-80 ng/mL or 32-100 ng/mL depending on the lab
- A group of patient had their levels experimentally raised to an average of 150 ng/mL with a range up to 220 ng/mL and only 4 patients over 200 ng/mL showed calcium metabolism disturbance.
- Patients with granulomatous diseases (sarcoid, tuberculosis, some cancers, etc) may develop calcium toxicity at normal levels in the serum.
- Optimal level is probably between 50 and 80 ng/mL, or 80-100 in serious chronic disease.

Sleep and Sleep debt

Sleep debt and fatigue

- Average hours of sleep per night in US in 1900: 9.0
- Average hours of sleep per night in US in 1963: 8.5
- Average hours of sleep per night in US in 2002: 5.9 on Sunday through Thursday, and 8.0 on Weekends.
- Average of 6.9 to 7.2 for week.
- Symptoms of sleep debt: fatigue, cognitive decline, cortisol cycle disturbances, insulin resistance, immunodeficiency.
- Recovery dose: 10-12 hours bedrest with 9.5+ hours sleep for 3 nights.

Endocrine effects of short-term sleep debt

- Thyroid hormone levels rise within 4 days.
- Time of growth hormone secretion during sleep is reduced.
- Afternoon cortisol become elevated.
- Cortisol suppression of ACTH is blunted
- Multiple effects on measures of insulin resistance

Sleep debt and insulin resistance

- Glucose clearance reduced by 40% within 4 days.
- Impaired glucose tolerance in previously normal subjects within 4 days.
- Increased incidence of obesity with chronic debt
- Abdominal pattern of obesity with long term debt
- Increased tendency of blood to clot with long term debt.
- Elevated triglycerides long term correlation

Cardiovascular effects

- Elevated hypertension long term correlation.
- Heart attack risk increased 200-300% in men who get less than 5 hours of sleep 2 nights per week.
- Heart attack risk increased 82% in women sleeping less than 5 hours per night
- Heart attack risk increased 30% in women sleeping less than 6 hours per night.

Effects on brain functioning

- Night-time problem solving activity is reduced
- Ability to incorporate new information in problem solving is reduced.
- Ability to modify unsuccessful problem solving strategies is completely curtailed in some studies.
- Consider implications for self-care and judgment in lifestyle.

See: Dreamland: Adventures in the Strange Science of Sleep. David K Randall

Differentiate bed rest and sleep

- 8 hours of bedrest (with lights off) will yield an average of 7.5 hours sleep period, range 7.0 to 7.9 in healthy volunteers. Actual sleep average is 7.1, range 6.5 to 7.4 hours.
- Patients commonly mis-report bed rest as sleep. Patients commonly over-report both bed rest and sleep.
- Consider using smart phone or other sleep monitors.
- Prescribe bed rest rather than sleep.

Patient self-reporting of sleep

- 669 young adults in 2002-2003
- Average reported sleep was 6.8 hours.
- Actual sleep averaged 6.0 hours
- People sleeping 5.0 reported on average 6.3 hours
- People sleeping 7.0 reported on average 7.3 hours
- Self-reporting systematically over reports sleep

Lauderdale DS Self-reported and measured sleep duration: how similar are they? *Epidemiology*. 2008 Nov;19(6):838-45

Sleep Debt

- Average spontaneous sleep is about 8.5 hours per night on 7th day of complete rest.
- Range is 8.0 to 10.2 hours
- Average amount of actual bedrest required to get the above total sleep time is 11.4 hours
- Range is 10.1 to 12.2 hours.
- In some individuals endocrine changes typical of sleep debt occur with 8 hours of sleep.

52 year-old male with insulin resistance recovering from jet lag

Day	Bed rest	Fasting glucose
1	10	103
2	10.5	105
3	11	81
4	9.5	86
5	9.5	94
6	8.5	92
7	8.0	88
8	8.0	102
9	9.0	99
10	10.0	91
11	9.5	92
12	9.5	98
13	9.0	86
14	9.5	91

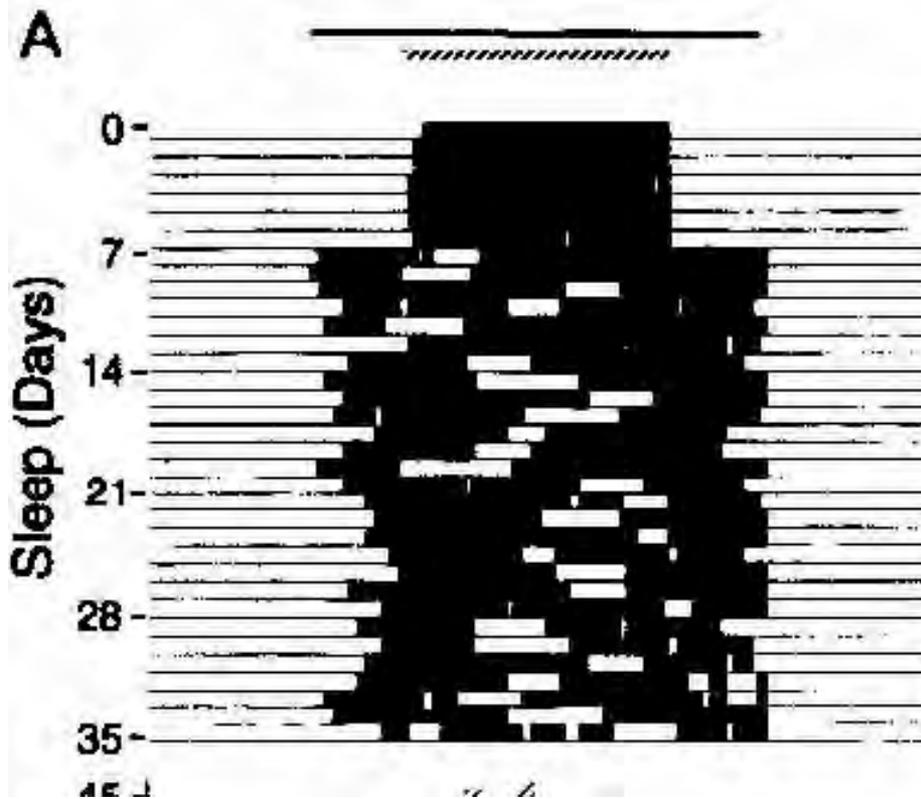
Note: "Prediabetic" serum glucose >100 mg/dl

Bed rest vs actual sleep

- Time to fall asleep
- Waking time during night
- Time dozing in morning
- Note: “Second Sleep” phenomenon occurs when bed rest and time between first falling asleep and awakening is sufficiently long. A normal pattern for humans, hunter-gatherers, farmers, and people in northern latitudes sleeping with the circadian rhythm.
- Note possible physiological and psychological benefits of the “restful wakefulness” period between sleep.

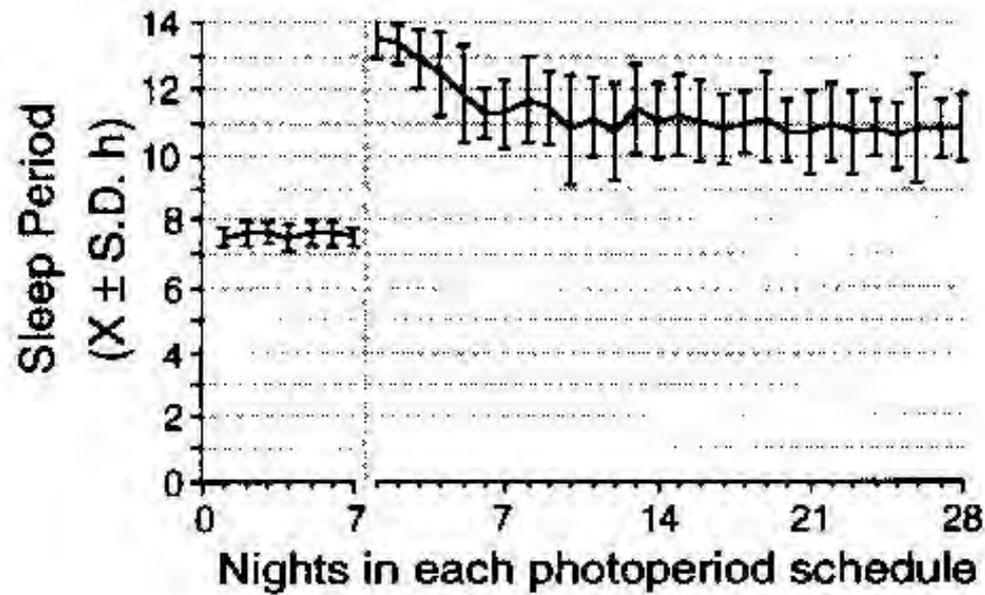
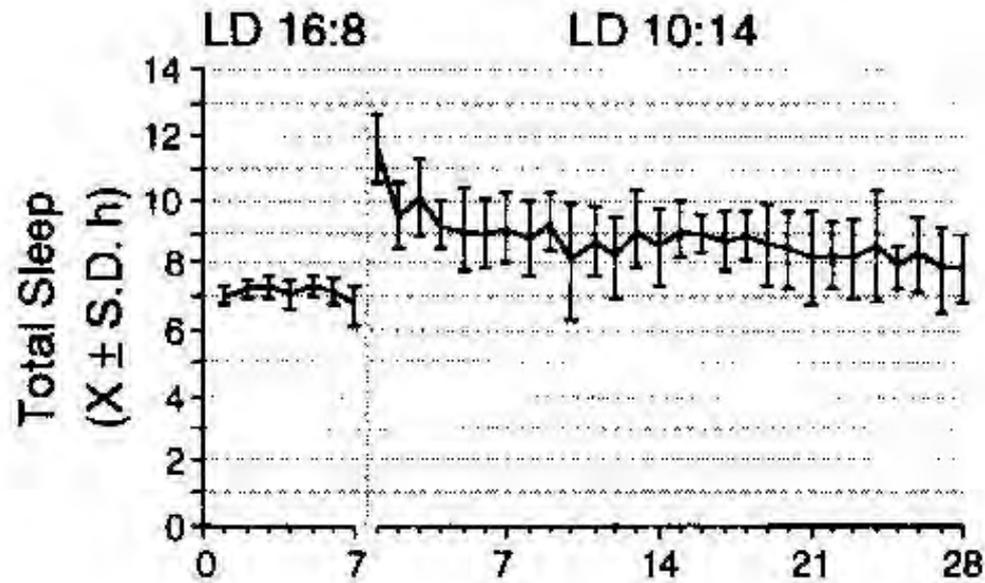
The Art of rolling over

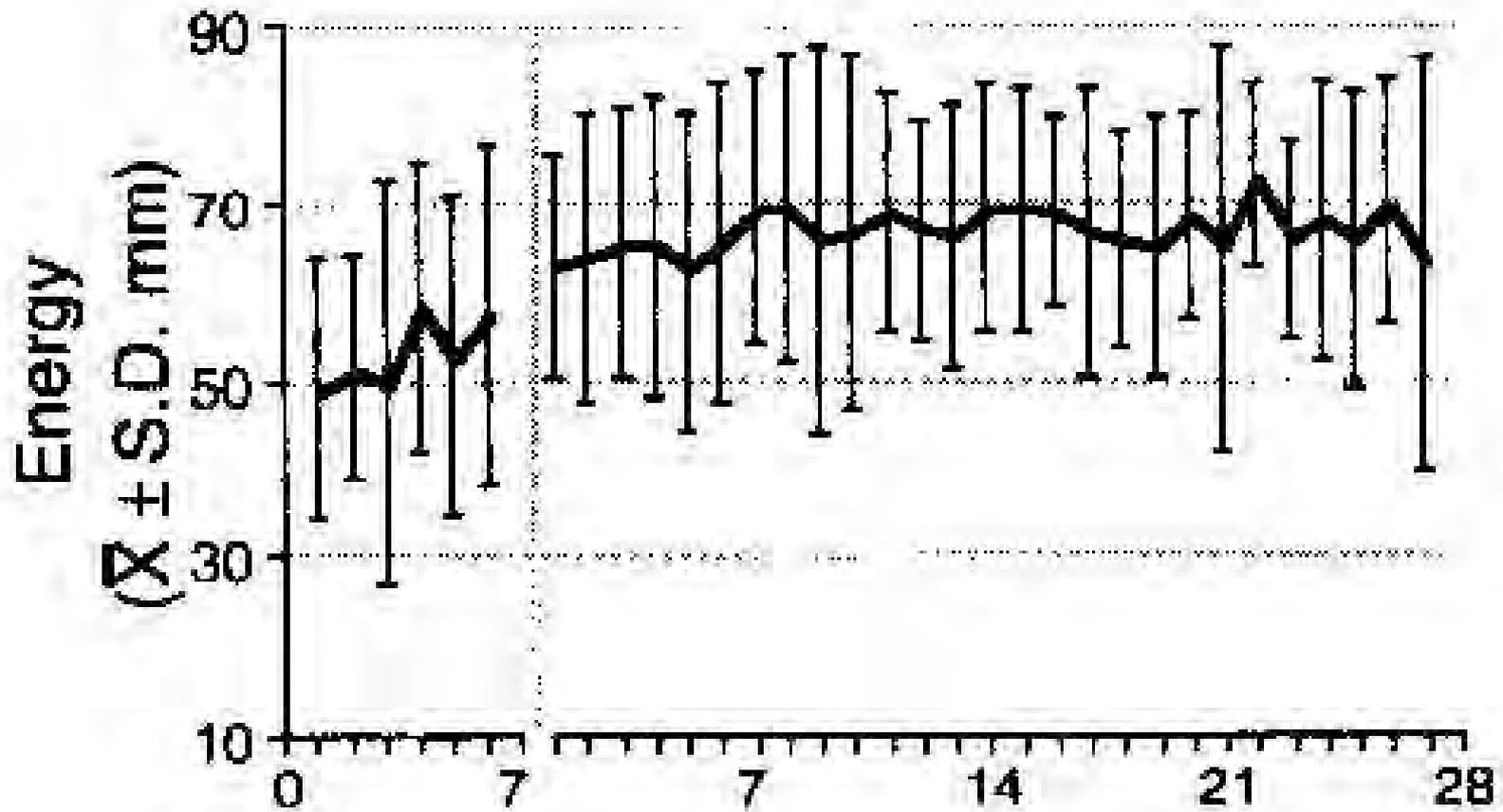
- On first awakening, a short surge of stress hormones is secreted.
- Individuals may mistake this for a sign that they are now rested.
- The surge may be more exaggerated in a state of sleep debt rather than less.
- If the individual remains resting in bed, the surge passes in about ten minutes.
- Many individuals can then get about 2 hours more restorative sleep after rolling over.

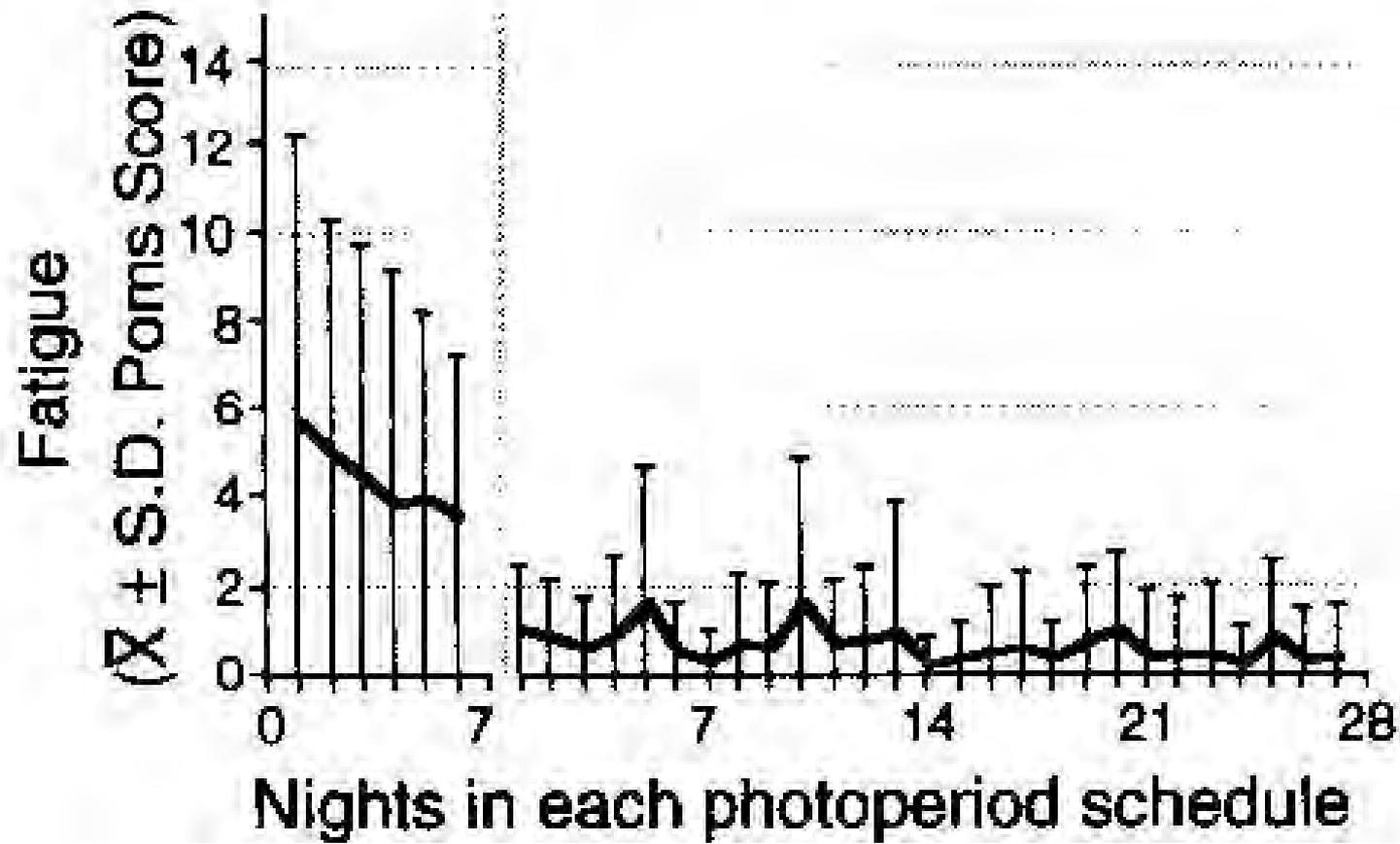


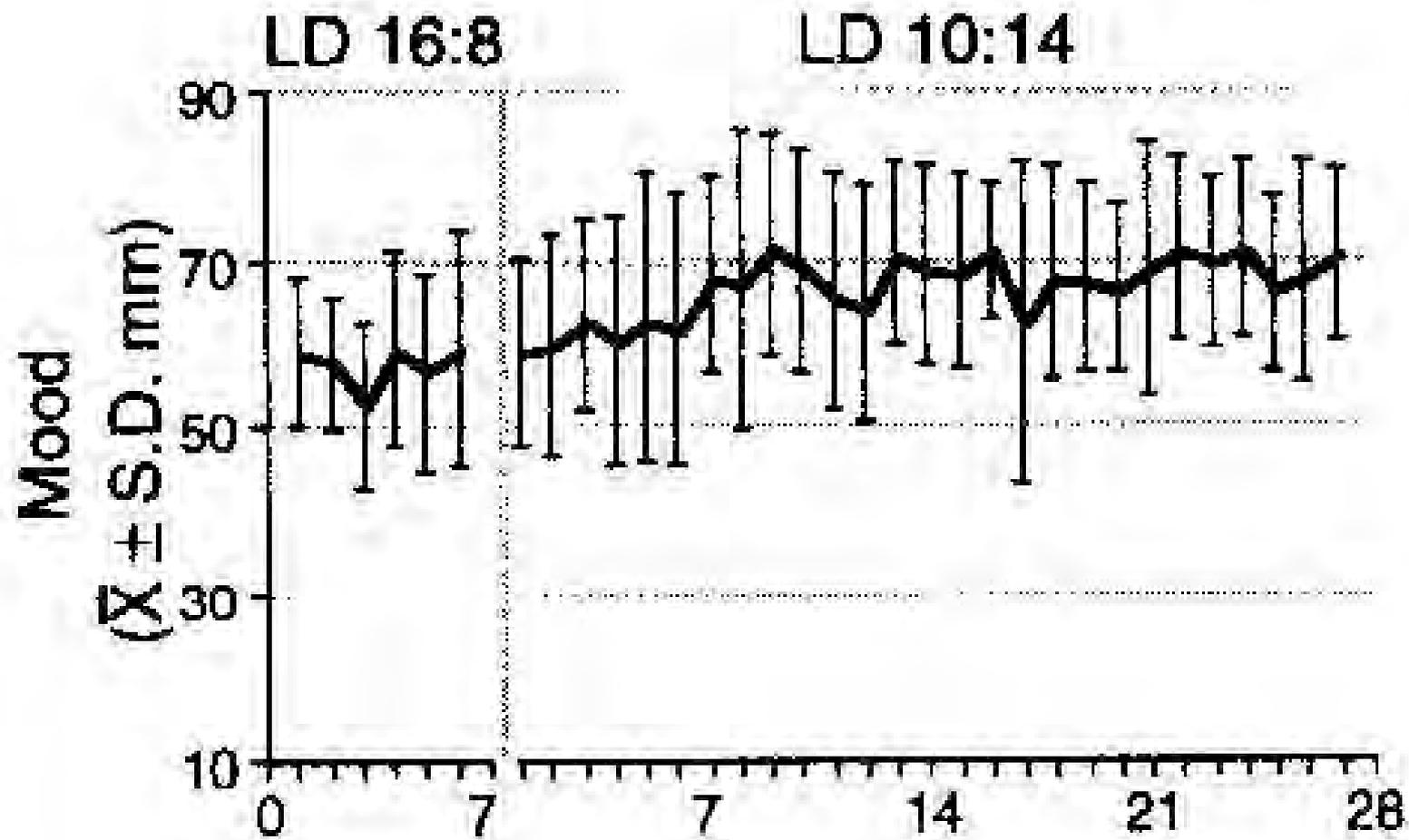
8 hrs bedrest for 7 days
 compared to 14 hours bedrest
 for 28 days. Dark lines represent
 sleep, light show wakefulness

Wehr TA, et al. Conservation of photoperiod-responsive mechanisms in humans.
 Am J Physiol. 1993 Oct;265(4 Pt 2):R846-57.









Hours of high hormonal levels

Hormone	Short sleep	Long Sleep	% increase
Prolactin	9.9	12.9	30%
GH	2.7	4.3	59%
Melatonin	10.3	11.9	15%

from Wehr op.cit.

Interventions with bed rest

- May be therapeutic
- May be diagnostic of level of fatigue/burnout
- Circadian rhythm bed rest prescription
- Sleeping in nature prescription (camping without lights)
- 10-12 hour bed rest prescription
- Weekend bed rest
- Longer period of bed rest.

Case study

- A patient went to an elder MD-homeopath (originally licensed in 1920s).
- Highly stressed businessman with chronic sleep debt.
- CC: fatigue, muscle weakness, and depression
- Prescription: 2 weeks complete bed rest
- Result: no improvement at 2 weeks
- Patient then identified a dairy allergy and did a withdrawal
- Patient lost 20 lbs in 30 days, and was restored to vitality.

Factors supporting circadian rhythm

- Timing of daily activity
- Body temperature cycle
- Light stimulus/dark cycle
- General autonomic tone and flexibility
- Body position: standing, sitting, lying
- Constitutional considerations: deficient yin with heat; vata aggravation
- Daily cycle of supporting herbal medicines

See “Routine for Establishing Healthy Sleep” handout in Sleep Debt article in files

Nervine tonics for daytime use

- Tincture of *Scutellaria*
- Tincture of milky oats (*Avena*)
- *Turnera*
- *Ophiopogon*
- *Withania*
- *Asparagus racemosus*
- Consider other demulcent Yin tonics in the dry patient

Select sleep herb energetics

- Address dryness in the dry patient
- Bitter cooling sedatives: Verbena spp. Leonurus, Chamomilla, Scutellaria infusion
- Warming aromatic sedatives: Melissa, Nepeta, Lavandula, Ferula assa-foetida

Autonomic “switching” herbs

- Paeonia spp
- Pulsatilla spp
- Verbena spp.
- May be taken in small doses with efforts to relax, such as meditation, progressive relaxation, etc to support switch from sympathetic to parasympathetic dominance when coming home in the evening.

Heavier bedtime sedatives

- *Scutellaria* infusion (do not boil)
- *Passiflora incarnata*
- *Valeriana*
- *Humulus*
- *Piscidia, Eschscholtzia*
- Consider anodynes and/or antispasmodics in any sleep formula, but especially if pain contributes to insomnia
- Use “pulsed” dosing. Small dose 90 minute pre-sleep, moderate dose 45 minutes pre-, and large dose at bedtime, with dose at bedside for middle of night.
- Use in conjunction with sleep routines.

Case Study

- **Patient:** 47 yo female, 5'4", 145 lbs
- **Chief complaint:** Severe insomnia; four hours of rest less sleep per night, three years duration.
- **Other complaints: Depression, “problems with**
- **let ting go,”** bladder in continence increasing for last two years, night sweats for one year. Excess uterine bleeding causing anemia, scheduled for hysterectomy and bladder “tacking.” Post Traumatic Stress Disorder from spousal abuse (previous marriage, twenty years prior).

Treatment plan

- High protein breakfast and increase protein at lunch.
- High quality multi vitamin and essential fatty acids.
- Herbal formula: Equal parts of milky oats tincture, scullcap, passiflora, and lemon balm.
- White Chestnut flower essence (worried thoughtpatterns); Olive flower essence (exhaustion), two drops each in tincture bottle.
- Follow bedtime routine from handout.

First follow-up, seven days later

Compliance: Slight increase in breakfast and protein; multi vitamin and fish oil capsules; followed sleep routine and took sleep formula as instructed.

Results: First two nights fell asleep promptly, woke once during night, slept eight hours. Next five nights, same results with only one dropperful of the tincture instead of two.

Second follow up, six weeks since initial visit

- **Compliance:** Increasing daily protein intake, and eating breakfast most days. Taking the multivitamin and fish oils.
- **Results:** Recovered from surgery well, 30 days prior to visit. Returned to work at four weeks instead of the scheduled six weeks. Sleeping well, except when not taking her tincture dose. Night sweats have completely disappeared. Weaning from Paxil prescription. Psychologically beginning to deal with dysfunctional family background issues.

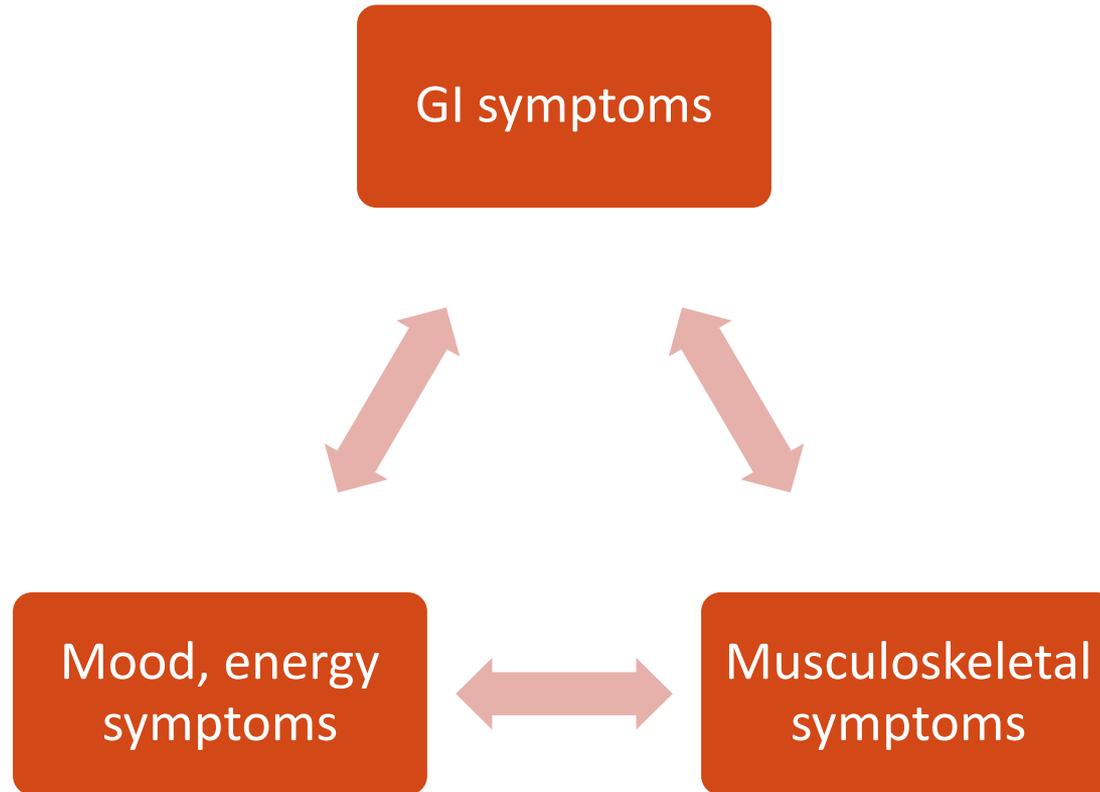
- **Third visit:** 17 weeks after initial visit
- **Compliance:** Same. Only requires sleep tincture three nights per week.
- **Results:** Vitality is visibly higher. Still sleeping eight hours per night, has reduced Paxil prescription by half. Celiac disease has recently been diagnosed, and she has begun a gluten withdrawal. She is also making arrangements to return to school to further her education in a medical field, and is interested in lifestyle changes to reduce her cardiovascular risk.

Other factors causing fatigue

Factors which may cause fatigue despite nutrition and sleep

- Malnutrition/malabsorption/undereating
- Food Intolerance
- Insulin resistance
- PTSD
- MTBI
- Each causes an unremitting load on the adrenals; cortisol elevated in earlier stage, depleted later.
- Best therapeutic strategy for factors which cannot be changed is ***optimal nutrition*** and ***rest therapy***

The Food Intolerance Triangle



Presence of symptom triangle and improvement on withdrawal and rechallenge of one or more intolerances confirmed in sequence of more than 200 cases

Evening-to-morning bloating pattern before dairy removal



Resolved chronic headaches, chronic yeast infections, constant nausea, and chronic fatigue

Abdominal swelling before and after elimination of dairy and gluten



Migraine headaches completely absent after withdrawal

Withdrawal and rechallenge

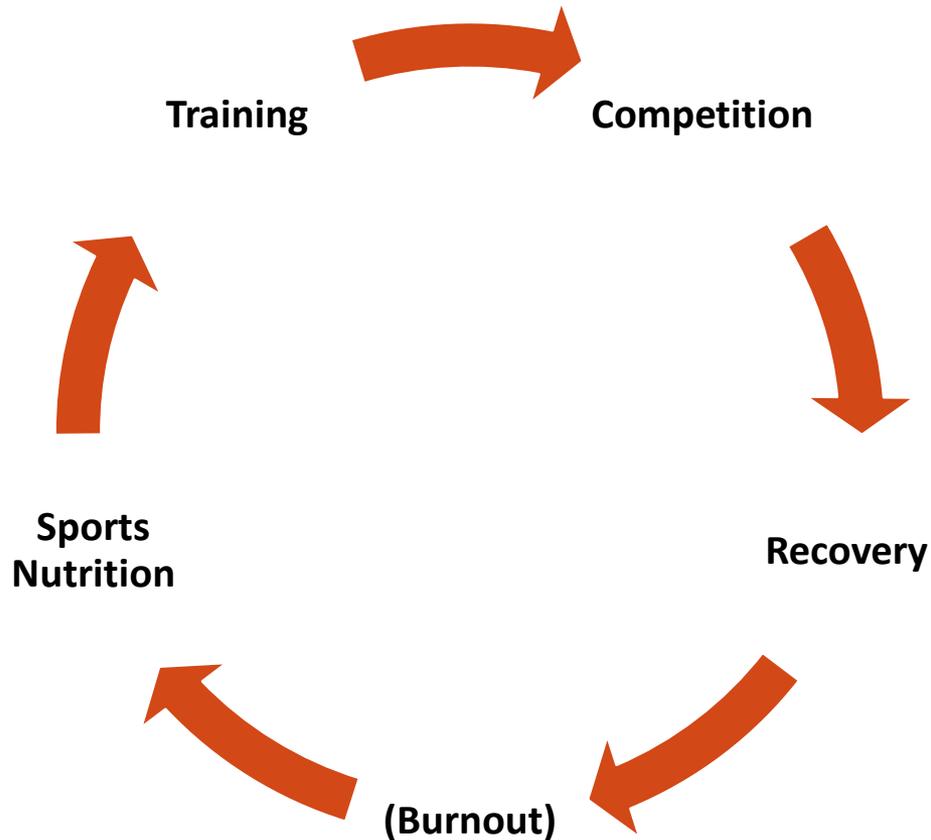
- Must have initial global symptom list
- Withdrawal must be complete
- Reassess symptoms at 3 weeks
- Continue then reassess at 6 weeks.
- Rechallenge with daily consumption of food for 4-7 days.
- Reassess global symptoms, including energy and mood.

Adjunct herbs in food intolerance recovery

- *Mentha/Matricaria*: May benefit gut inflammation/leaky gut syndrome
- *Althea, Calendula, Plantago.* ,may help with inflammation and tissue healing
- *Arctium* decoction or powder in conjunction with probiotics
- Administer herbs in food amounts and on empty stomach
- Consider tea, powder, powder in honey, powder in applesauce

Exercise and fatigue

The Athletic Cycle



Recovery and Nutrition are as Important for Performance as Training

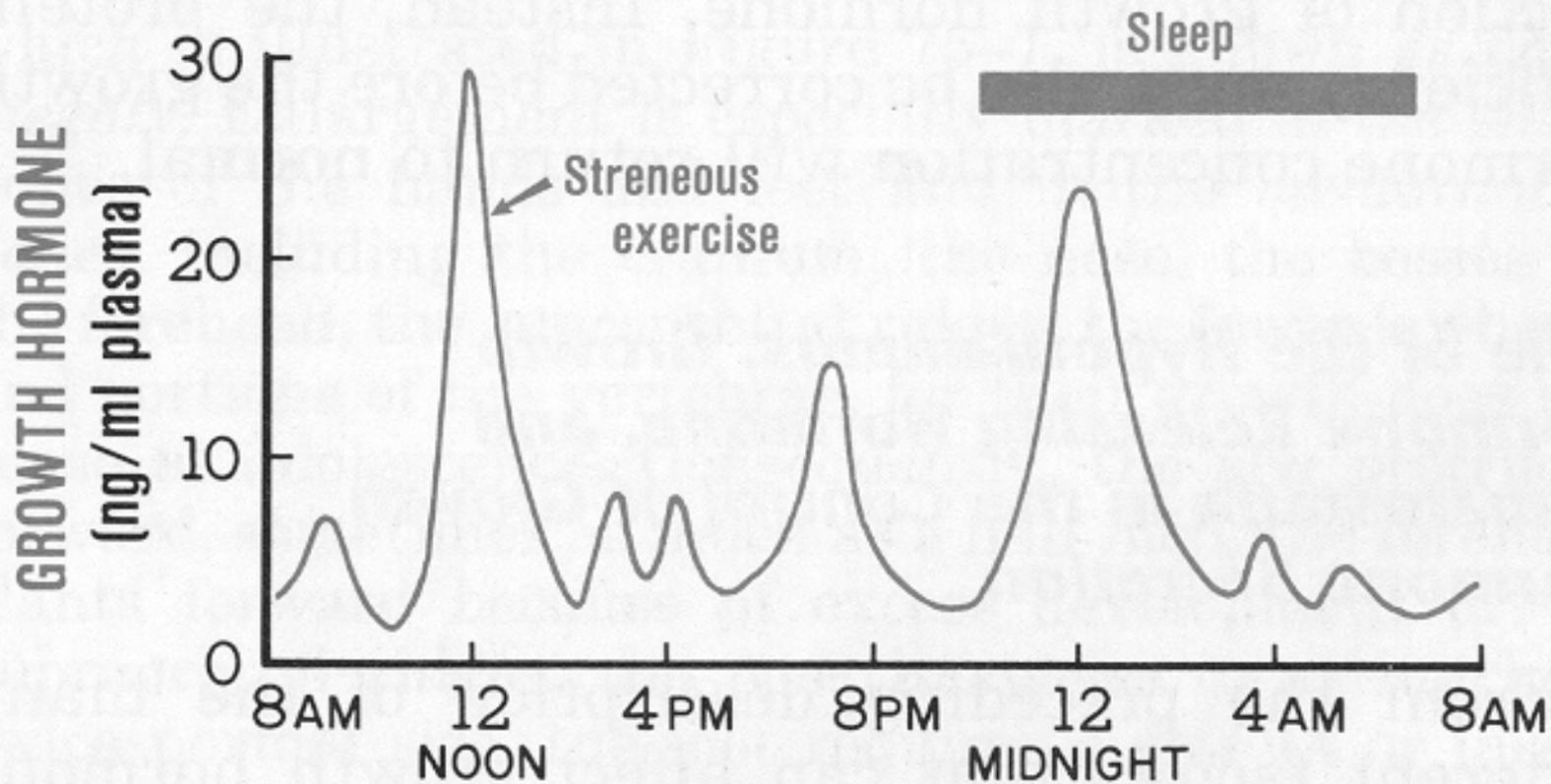


Figure 75–5. Typical variations in growth hormone secretion throughout the day, illustrating the especially powerful effect on secretion caused by strenuous exercise, and illustrating also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

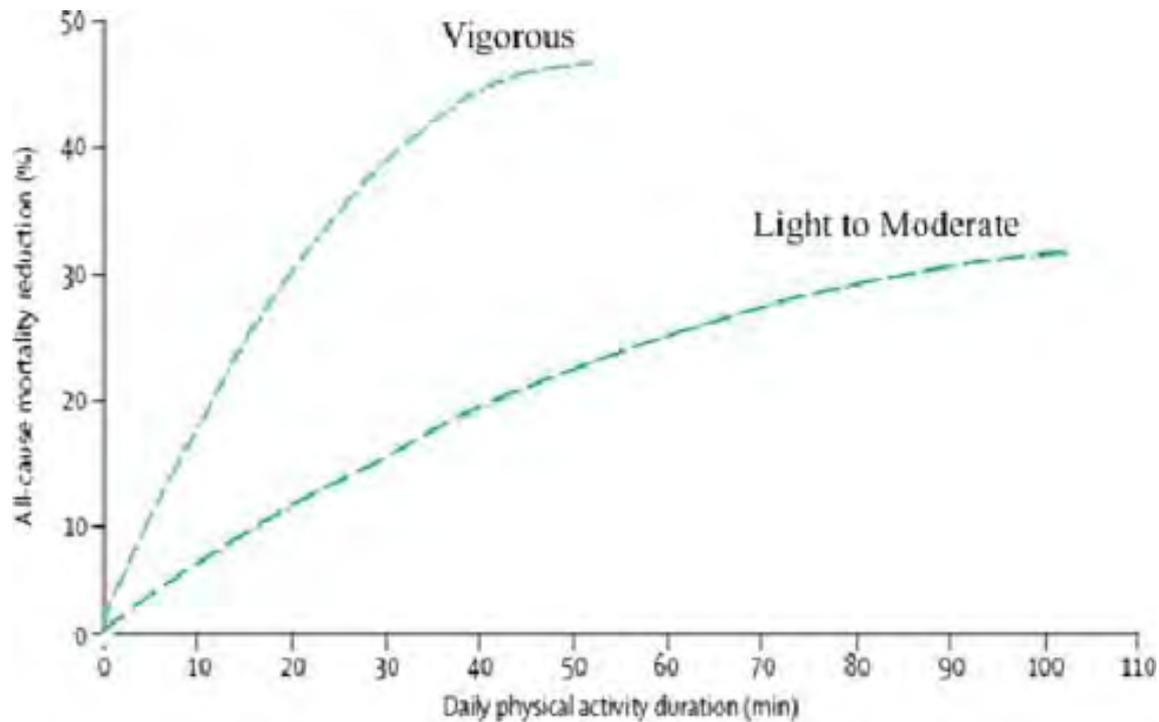
The Athlete/exercizer is not necessarily healthy

- The athlete trying to maximize performance courts burnout of the vital reserve.
- Maximum performance or excessive training may cause physical or metabolic injury
- *Nutritional advice should be given in conjunction with assessment of motivation in exercise and education about healthy exercise and burnout.*
- Tonic herbs to stimulate performance may facilitate burnout.
- Nutrition and tonic herbs may assist with recovery or help treat burnout.
- Nutrition may assist with harm reduction in the extreme athlete.

Optimal exercise for Health

The right amount of nourishment and exercise, not too much, not too little, is the safest way to health'.

Hippocrates

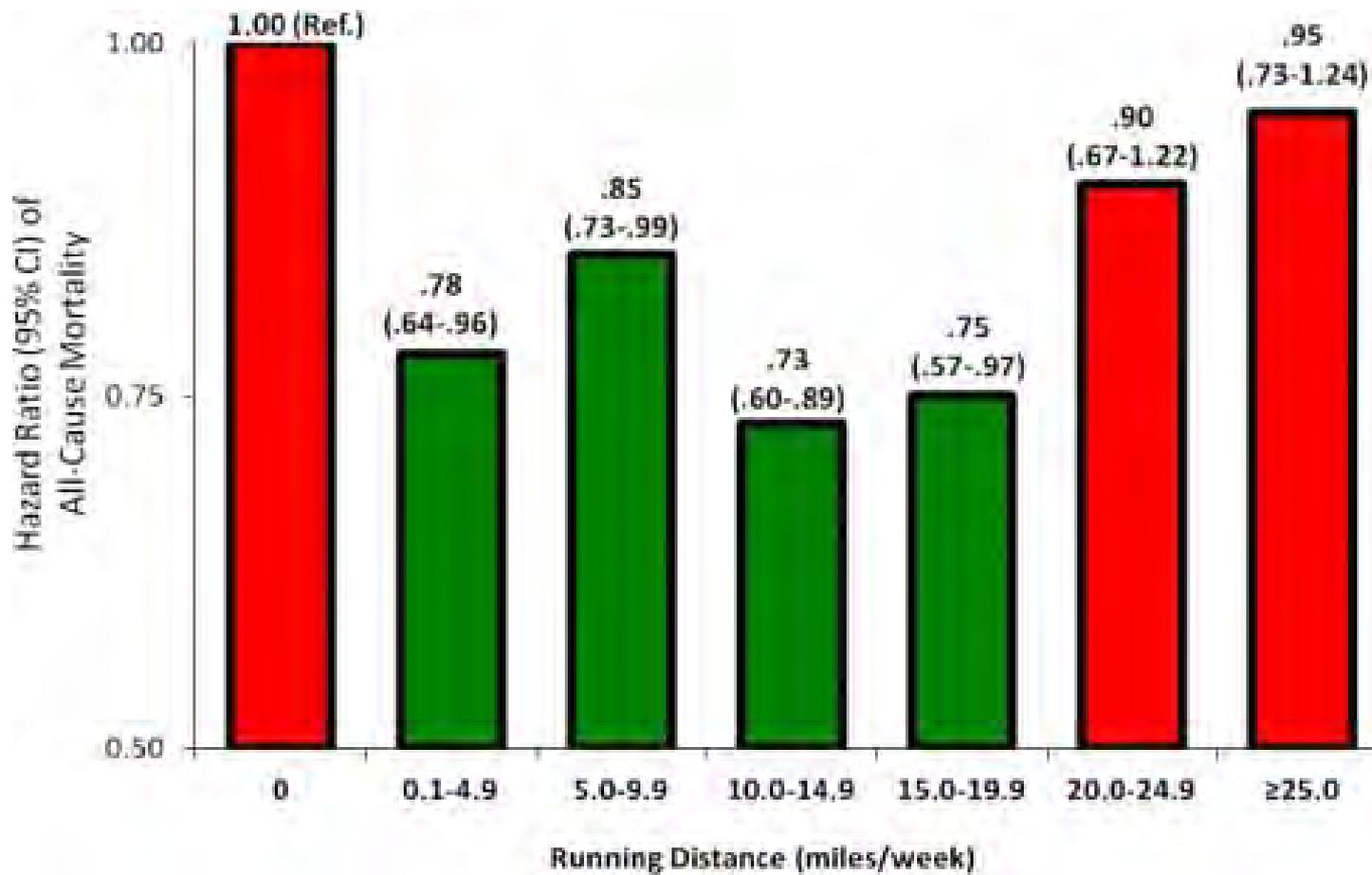


Duration of daily exercise and reduction in long-term all-cause mortality.

“Vigorous” was the equivalent of jogging 13 minutes per mile.

“Moderate” was equivalent of walking a 24 minute mile on flat ground

Wen CP, Wai JP, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011;378:1244–53.



Lee DC, Pate RR, Lavie CJ. Running and all-cause mortality risk—is more better? In: Medicine ACoS, ed. Medicine & Science in Sports & Exercise. American College of Sports Medicine San Francisco, CA: 2012:S699.

52,600 individuals for three decades; 15,000 runners

- Runners as a group had 19% lower all-cause mortality
- Runners in the moderate range had 25% lower all-cause mortality
- Running at more than 20 miles per week had no significant advantage over sedentary controls
- Optimal longevity attained by 5 mi/wk; only slightly better at 10-15.
- Optimal pace at 10 minutes per mile, an easy jog.
- Optimal frequency 2-5 days per week.
- ***No mortality benefit*** for exercise at 8 miles per hour or above or for exercise 6-7 days per week.

Optimal exercise for immunity

- As cortisol increases toward 30 minutes, immunity is enhanced.
- After 30 minutes, benefit begins to decline
- At sixty minutes, it is back to baseline
- Over 60 minutes immunity is depressed.

See: Why Zebras Don't Get Ulcers by Robert Sapolsky

Copenhagen City Heart Study

Odds ratio of developing Metabolic Syndrome over ten years, in a group of more than 10,000 individuals:

- 0.71 for those who engaged in moderate or high leisure time activity.
- 0.51 for those who engaged in fast walking
- 0.60 for those engaged in jogging.
- 1.22 for those who walked at a leisurely pace

Laursen et al. Intensity versus duration of physical activity: implications for the metabolic syndrome. A prospective cohort study. *BMJ Open*. 2012 Oct 8;2(5).

Copenhagen City Heart Study

Followed 20,000 Danes since 1976

- Joggers had 44% lower death rate, lived 6 years longer
- Optimal benefits at slow to moderate pace
- Optimal benefits at 1-2.5 hours per week total

Schnohr P. Assessing prognosis: a glimpse of the future. Jogging healthy or hazard?
In: Cardiology ESo, ed. EuroPrevent 2012. Dublin, Ireland: European Heart Journal, 2012.

Reasons for over exercise

- Poor coaching. Ignorance of training cycle.
- Body Image problems. May be a form of bulimia
- Calories in/out fallacy
- Failure to reduce intensity with age.

Calories in/out

- A sedentary person who begins moderate exercise will experience a reduction in appetite and 1-2% of body weight loss.
- A person who already exercises moderately will experience appetite aggravation proportional to increased activity, and body weight plateaus.
- Young people who do burst type exercise may lose some fat and gain muscle due to GH effects.
- This effect is lost in middle age and beyond.

Activity prescription in fatigued patient

- If does not exercise, increase to brisk but comfortable walking most days for 20-40 minutes
- Multiple sessions better than one.
- If exercising more than 40 minutes more than 2 days per week, and if not balanced by recovery days, reduce exercise to no more than 30 minutes.
- If in any state of athletic burnout, coaching or counseling to get proper recovery. Brisk walking exercise only, with full days off, until recovered

Standard training/recovery regimen

- Monday rest/cross-train
- Tuesday race-intensity intervals*
- Wednesday short, slow distance
- Thursday “tempo” run at sub-maximal*
- Friday rest
- Saturday slow, long distance
- Sunday slow very short distance
- No training to exhaustion
- Terminate slow work on recovery days when tired.

Sports Nutrition for training, recovery, or prevention of injury

- Nutritional requirements are increased
- Increased protein to minimum 1.6 mg/kg for healthy exercise, or 1 gram per lb for competitive athlete
- Minerals and trace elements: Zn, Si, Cu
- Blood building nutrients: Fe, folic acid
- Connective tissue strengthening nutrients: C, flavonoids
- Vitamin D
- Antioxidant nutrition/flavonoids

Burnout

- Signs: Insomnia, irritability, fatigue, declining performance, persistent soreness, frequent colds or infections, dryness with heat may be present
- Present in 30-50% of high school and college athletes
- Lab work: Elevated cortisol, depressed testosterone
- Well-coached individuals know baseline hormone levels and are alert for presenting signs.
- Poor nutrition with macro or micronutrients may promote. Good nutrition may delay or prevent.
- Other stressors in lifestyle may promote

Endorphin addict

- Usually no coaching
- No sports nutrition, or emphasis on sports drinks and health food store fad supplementation
- May abuse performance enhancing drugs
- Poor attention to or impatience with recovery
- Poor surveillance for signs of burnout, usually exhibits signs of burnout.
- Tonic herbs for performance may cause ***substantial metabolic injury***
- Nutrition may assist with ***harm reduction***

Disordered body image

- Obsessive exercise with attention to body image
- No attention to recovery periods or burnout
- No sports nutrition, deficient diet
- Extremely destructive to health
- In a dietician practice in Boulder, CO, 1/3 of patients with anorexia nervosa were engaged in triathlete training programs
- May be an aspect of bulimia, with exercise to 'purge' calories from binges.
- Performance-enhancing herbs may cause ***substantial metabolic injury***.
- Nutrition may contribute to ***harm reduction***

Athletes in middle age

- Reduced capacity for recovery
- Decreased growth hormone in response to exercise
- Decreased androgens
- Increased adrenal dysfunction
- Increased potential for injury
- Increased incidence of overweight
- Should be discouraged from intense performance competition, shift emphasis to training for cardiovascular and metabolic fitness and health
- Performance enhancing herbs may contribute to ***substantial metabolic injury***
- Attention to nutrition may help prevent injury

Protocols for middle age and beyond

- RUN-WALK-RUN protocols.
- Walk before you get tired; early and often in a run
- Suggested ratios (Galloway)

Pace	Run	Walk
8min/mi	4 min	30 seconds
8.5	3	30
9	2	30
10	1.5	30
12	1	30
14	1	1 min
16	30 sec	45 sec

See: *Running Until You Are 100*. Jeff Galloway

Performance enhanced with light training

- 56 year old male member of SAR team.
- Baseline performance assessed with uphill hiking time 2 miles with 1000 ft gain in elevation and a 30 lb pack.
- Engaged in standard training for a 5K race (mixed intervals, tempo run, light exercise, and rest days) was experiencing knee and back problems.
- Routine changed to 5 days/wk low aerobic walking bout of 70-90 minutes on flat ground for 28 days.
- Performance time at uphill hiking decreased from 63:15 minutes to 44:10.

Burnout

The maladaptation model of Selye

- Phase One. General alarm reaction (up to 48 hours). Multiple physiological changes.
- Phase Two: Beyond 48 hours. Hypertrophy of adrenals and thyroid; atrophy of gonads.
- Later Phase Two: Functions and organ appear near normal.
- Phase three: 1-3 months. Return of Stage I but now chronic. Atrophy of all endocrine glands. Recovery difficult or impossible.
- Chinese cancer researchers autopsied a number of patients who had been diagnosed with 'Kidney deficiency.' All had general atrophy of their endocrine glands.

Overtraining syndrome in athletics

- Normal training with adequate rest and recovery to adaptation. Normal recovery
- Overreaching. Delayed recovery.
- Non functional overreaching. Difficult recovery
- Overtraining syndrome. Recovery long term or not at all.

Adrenal hormones in the stages

	Cortisol	DHEA
I	n	n
II	+	n
III	+	-
IV	-	-

Endocrine effects in stages of burnout

- Stage I Normal
- Stage II Elevated Response to stress. Adrenal and thyroid
- Stage III Elevated adrenal and thyroid responses with reduction of reproductive glands
- Later Stage III. May appear near normal.
- Stage IV. Atrophy of broad endocrine function, adrenal, thyroid, gonadal.
- It is impresice to call this “adrenal burnout” or “adrenal dysfunction”

Descending cycle in fatigue #1

- Low energy produces low appetite and poor digestion
- Emphasize easy to digest foods
- Have proteins in easy to digest forms – soups or stews
- Includes herbs or spices to promote digestion
- *Atractylodes*
- *Zingiber*
- *Astragalus*
- *Inula*
- Many more

Descending cycle in fatigue #2

- Low energy gives low ability/motivation to make difficult changes
- Promote sleep recovery/bedrest as the initial primary strategy
- Appropriate use of milder tonic herbs *in support of* positive changes. Test low doses for intermittent periods, not as an ongoing strategy.
- *Withania, Panax quinquefolius, Ophiopogon, Asparagus racemosus (Shatavari), others.*

Stimulants

- Many patients take stimulants or sedatives for fatigue
- May be food, non-prescription, prescription, or illegal.
- Some injure the endocrine system (ephedra, amphetamines, cocaine)
- Other do not injure the endocrine system directly, but enable the patient to overreach into exhaustion.
- Caffeine is the most common.
- Adaptogens and tonic herbs may also do this if substantial changes to the stressor are not engaged in.

Caffeine

- Does not affect adrenals, cortisol, or adrenalin secretion in the amount consumed as food.
- Caffeine acts by blocking adenosine receptors.
- Adenosine is an ***inhibitory*** chemical.
- The pharmacological effect is stimulation, by blocking the inhibition of adenosine.
- The body adapts within about 10 days to produce more adenosine receptors until equilibrium is reached.
- The caffeine user now requires caffeine to prevent excessive adenosine effects.
- The fatigue of caffeine withdrawal is not an endocrine or adrenal state, but excess adenosine effect, which is brief and transitory (about 10 days)

Tonic herbs

- Apply according to traditional indications and contraindications in support of restorative lifestyle changes
- May also be used in a manner similar to stimulants

Signs of *chi* and yang deficiency

Signs in common

- Pale complexion
- fatigue
- low spirits
- spontaneous
- sweating
- low voice
- weak digestion
- enlarged tongue

Chi def. signs

- short of breath
- pronounced fatigue
- loose stool
- dribbling of urine
- weak pulse

Yang def. signs

- aversion to cold
- cold hands and feet
- plentiful urine
- clear urine
- loose stool with undigested food
- dark colored tongue
- slow pulse

Some *Chi* tonics

- *Panax ginseng*
- *Astragalus spp.*
- *Codonopsis*
- *Eleutherococcus*
- *Ganoderma*
- *Panax quinquefolium*
- *Glycyrrhiza*

Some *Yang* tonics

- *Cordyceps*
- *Schisandra*
- *Withania*
- *Glycyrrhiza*
(honey-fried)

Signs of Blood and *yin* deficiency

Signs in common

- emaciation
- dizziness
- spots before the eyes
- heart palpitations
- insomnia
- little tongue coat
- thin, thready pulse

Blood def. signs

- pale complexion
- pale lips
- pale tongue
- numbness of limbs

Yin def. signs

- flushed face
- hot hands and feet
- dry mouth and throat
- night sweats
- premature ejaculation
- dry, red tongue
- fast pulse

Some *Blood* tonics

- *Rehmannia*
- *Angelica sinensis*
- *Astragalus*
- *Paeonia*
- *Polygonum multiflorum*
- *Lycium*

Some *Yin* tonics

- *Panax quinquefolius*
- *Asparagus (Shatavari)*
- *Polygonum multiflorum*
- *Lycium*
- *Ophiopogon*

“Kidney” tonics

- Chinese herbalists have recognized Seyles stage of maladaptation, and call it “Kidney” deficiency = endocrine atrophy, of adrenal and gonadal function.
- “Kidney” tonification is undertaken in the context of rest, chi gong exercises, breathing, and general conservation of energy.
- There is a general debate among practitioners about whether recovery is possible once the “jing” of the kidneys has been depleted. Most practitioners say it is not possible except with chi gong. Panax ginseng is reported to help restore “source chi” when taken in the above context.