Necessary Nutrients

Supplements that make a difference

Dr Mark Donohoe

Centre for Evidence-Based Complementary Medicine

www.cebcom.net

Overview

- Who am I (non existential version)
- Basics of the ANZ Nutritional Guidelines
- What are the nutrients our diet fails to provide?
- Which patients may benefit from supplements?
- Finding the people, finding the dose (simple guide)

Who am I

- Normal at one stage - Sydney Uni graduate 1980
- Environmental and nutritional medicine
- Minimal drug intervention in my practice
- Interest & publications in CFS, chemical injury
- Centre for Evidence-Based Complementary Medicine (CEBCoM) - www.cebcom.net
- Focus on Evidence-informed practice

All Kiwis get enough to eat, so what's the problem?

- Individual needs *can* get lost in the averages
  - Some groups at risk (dark skin, genes, poverty)
  - Elderly at risk (sunlight, exercise, appetite)
  - Kids at risk (high kilojoules, minimal nutrients)
  - Sick at risk (poor diet, high needs)
- Are we failing in *prevention* through nutrition

What Nutrients?

Vitamin D

Iodine

Omega 3 (EPA and DHA)

Vitamin K

(maybe Vitamin B12)

5 minutes of boring stuff

What do we know about the nutritional needs of Aussies and Kiwis?

Nutrient ReferenceValues for Australia and New Zealand

https://www.dropbox.com/sh/47m4yihqziljfnw/DEYuvmiqcm

Nutrient Reference Values

- Definitions adapted from Canadian Guidelines
- EAR • Estimated Average Requirement
- RDI • Recommended Dietary Intake
  - AI • Adequate Intake (used when an RDI cannot be determined)
- EER • Estimated Energy Requirement
- UL • Upper Level of Intake

Nutrient Reference Values

Estimated Average Requirement (EAR)

- A daily nutrient level estimated to meet the requirements of half the *healthy* individuals in a particular life stage and gender group.

Individuals

- Use to examine the probability that usual intake is inadequate

Groups

- Use to estimate the prevalence of inadequate intakes within a group

Nutrient Reference Values

Recommended Dietary Intake (RDI)

- The average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97–98 per cent) healthy individuals in a particular life stage and gender group.

Individuals

- Usual intake at or above this level has a low probability of inadequacy

Groups

- Do *not* use to assess intakes of groups

Nutrient Reference Values

Adequate Intake (AI)

- The average daily nutrient intake level based on approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate.
- **When RDI data are not available**

Individuals

- Usual intake at or above this level has a low probability of inadequacy
- *Mean* better than *median*

Groups

- Mean usual intake at or above this level implies low prevalence of inadequate intakes
- *Mean* better than *median*

Nutrient Reference Values

Estimated Energy Requirement (EER)

- The average dietary energy intake that is predicted to maintain energy balance in a healthy adult of defined age, gender, weight, height and level of physical activity, consistent with good health.
- In children and pregnant and lactating women, the EER is taken to include the needs associated with the deposition of tissues or the secretion of milk at rates consistent with good health.

Nutrient Reference Values

Upper Level of Intake (UL)

- The *highest* average daily nutrient intake level likely to pose *no adverse health effects* to almost all individuals in the general population.
- As intake increases above the UL, the potential risk of adverse effects increases.

Individuals

- Usual intake above this level may place an individual at risk of adverse effects from excessive nutrient intake

Groups

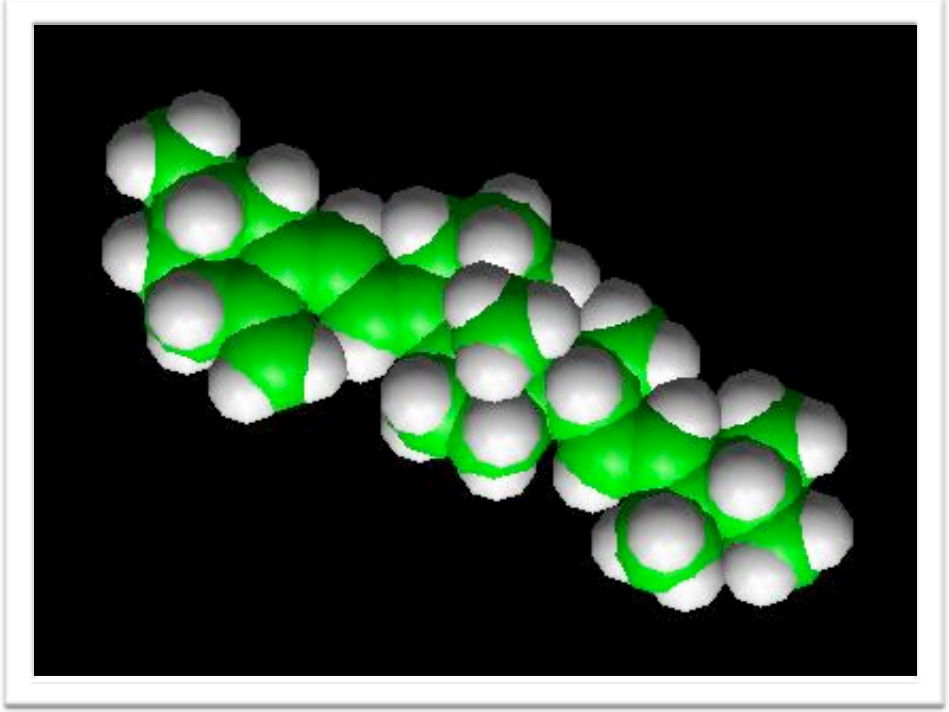
- Use to estimate the % of the population at potential risk of adverse effects from excessive nutrient intake

Limitations of Oz guidelines

- [The] Working Party agreed to retain the traditional concept of *adequate* physiological or metabolic function and/or avoidance of deficiency states as the prime reference point for establishing the EAR and RDIs *and to deal separately with the issue of chronic disease prevention*.
- ...assessing nutrient needs for chronic disease prevention ... was still problematical.

Problems with NRVs

- Apply to *healthy* population & individuals
  - Unhelpful for people you see in your Practice
- Prevents known deficiency disease
  - Doesn't address individual/disease requirements
  - Does not address prevention potential
- These are important when considering patients



Vitamin D

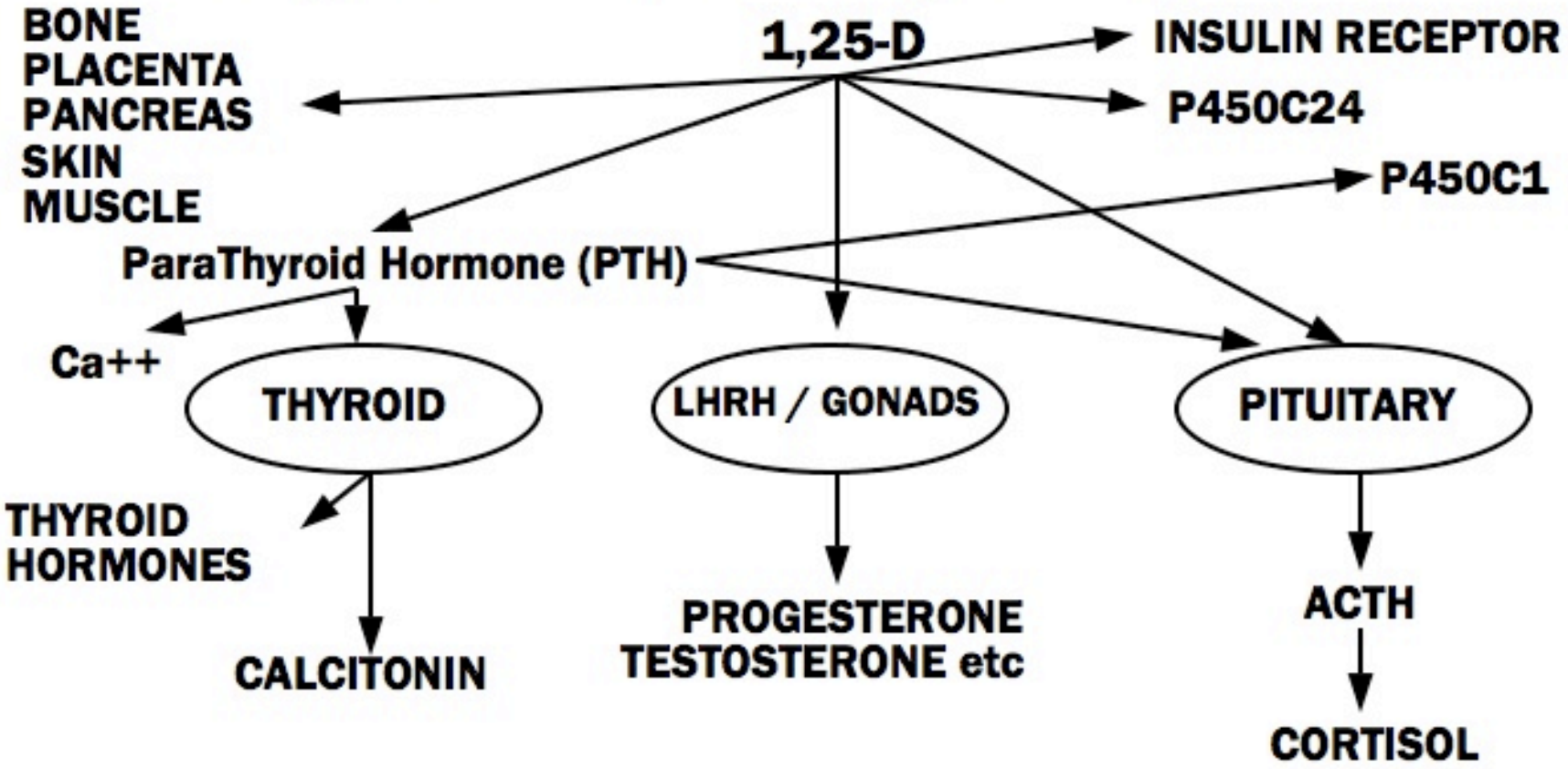
Basic Biochemistry

- Skin creation
  - Cholesterol to 7-dehydrocholesterol
  - 7-dhc + UVB => pre-Vit D_3 => Vitamin D_3
- Dietary Vitamin D_3 (usually <100IU/day)
- D_3 hydroxylated to 25(OH)D_3 in liver & stored
- 25(OH)D_3 converted in kidney to 1,25(OH)$_2D_3$
- *1 µg VitD = 40 IU Vitamin D (1 IU = 0.025µg)*

Mechanisms of Action

- More hormone than vitamin (photosynthesis)
- Regulates ~ 60 genes via vitamin D receptor
- Regulates calcium and phosphorous in blood
- Inhibits proliferative response, increases apoptosis
  - This may be the basis of cancer risk reduction
- Affects hormonal pathways • parathyroid, thyroid, sex hormones, insulin, pituitary and placenta

Hormonal Changes resulting from changes in 1,25-dihydroxyvitamin-D



1,25-dihydroxyvitamin D (1,25-D) regulates over 60 genes, whose actions include those associated with calcium homeostasis and immune responses as well as cellular growth, differentiation, and apoptosis (PMID 12055341, 11295155)

Vit D deficiency

WHY?	WHO?
Age (70% down by 80)	Office work, long hours
Sunscreen use	Nursing home patients
Pollution	Housebound esp elderly
Obesity	Patients with fractures
Clouds	Dark-skinned patients

Healthy Australians Adults

- *Brisbane, winter 2006, 126 people 42 yo average*
- 10.3% of adults deficient++ < 25nmol/L
- 31% insufficient in 25-50 nmol/L range
- 24.6% low in range 50-75 nmol/L
- 34.1% adequate with Vit D >75 nmol/L

=> 2 in 3 Australians sub-optimal

Tests to assess

- 25 hydroxy Vitamin D is best surrogate
- 1,25 di(OH)2 Vitamin D (in renal disease)
- Corrected calcium and urinary calcium
- PTH may help clear up confusing results
    - Sestamibi scan of parathyroid

Prevention Potential

- Joan Lappe study presented ICCMR 2008
- Population-based PC RCT 1179 females >55 yo
- > 80 nmol/L compared to < 50 nmol/L Vit D
  - Reduced fracture rates significant
  - Reduced cancer mortality 60-73% (Kaplan-Meier)
- Breast, *prostate*, colon & lymphoma main gains

Dietary & other sources

- Difficult to get adequate dietary Vit D (100 IU/day)
  - Fatty fish, liver, eggs, fortified milk
- Sunlight exposure is difficult politically
  - 2 hrs/wk sunlight exposure (T-shirt & shorts)
  - Sick people are NOT the same as healthy
- Take action and remeasure 25(OH)D3 at 3 months

Supplemental doses

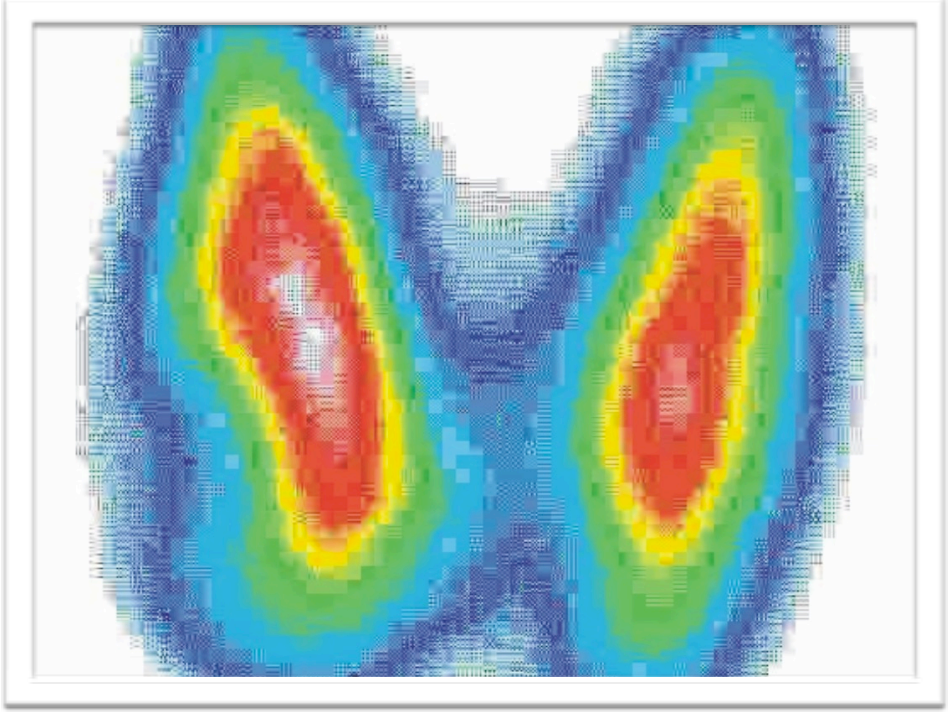
- Healthy adults and kids mainly indoors
  - 600 to 1,000 IU per day esp through winter
- Groups at risk
  - 2,000 IU per day
- Sick (renal, liver, skin and metabolic disorders)
  - 5,000 to 10,000 IU per day

Controversies & Gotchas

- Be aware of season in testing
  - Peak is early autumn, trough is early spring
- Time surgery for peaks, or supplement pre-op
- Sunlight is better than vitamin D *if possible*
- Seasonal variation of Vit D may be important
- There *will be downsides!* We are exploring hi dose

Practice Points

- Vitamin D deficiency is common and preventable
- Vitamin D is a photosynthesised hormone
- Deficiency causes much more than osteopenia
- Promote exercise in the sun where possible
- Disease induces deficiency, exacerbating disease
- Dosages of 2,000 to 5,000 IU/day for 3 months
- Simple, low cost can prevent many diseases



Iodine

The Basics

- Iodine deficiency causes goitre
- Dietary iodine concentrated in thyroid follicles
- I- bound to tyrosine under thyroperoxidase
- Mono- & di-iodo thyronine (MIT & DIT) in thyroglobulin (TG) to T_4, T_3 & reverse T_3
- Proteases release T_3 and T_4 from TG
- T_3 & T_4 bind to nuclear receptors in cell

What it does in the body

- Binds to thyroid hormone receptors in nucleus
- Sets the basal metabolic rate
- Regulate protein, fat & CHO metabolism
- Regulate protein synthesis rate
- Increase sensitivity to catecholamines (adrenaline)
- Thyronamines (T1a, T0a) *may* induce hibernation

Other factors of thyroid

- Genetics in nodular goitre and thyroiditis
  - Deiodinases and transporter genes
  - Oxidative damage leading to injury
- Toxic injury to thyroid
  - BP-A, PCB, halogenated compounds
- Iodine deficiency OR excess worsens these

Iodide Requirements

- RDI for healthy children, adults = 150 µg/day
- RDI pregnancy =220 µg/day, lactation = 270µg/day
- Upper level intake (UL) = 1,100 µg/day (adults)
- Typical dietary intake in Australia <100 µg/day
- Loss of past sources of iodine in milk and salt
- Good argument for supplementation

Evidence of deficiency

- MJA 2006 childhood survey, median 104 µg/L
  - 15-20% fall into mod-severe deficiency range
- My practice (chronic Δ) median is < 40 µg/L
- Fourfold rise in thyroid cancer
- Rise in thyroiditis (?commonest autoimmune Δ)

Tests to assess

- Examination shows goitre, sometimes nodules
- Spot morning urinary iodine is gold standard
  - >100 mcg/L is adequate and non-goiterogenic
- Basal temperature test is simple and low cost
- TSH is insensitive / useless in most cases
- FT3, FT4, thyroid antibodies, thyroid ultrasound

Prevention Potential

- Pregnancy • cretinism & developmental problems
- Childhood • intellectual impairment, learning
- All ages • Goitre and risk of thyroid cancer
- Exacerbation of underlying thyroiditis
- Fatigue and low metabolic rate / obesity

People most at risk

- Pregnancy and breastfeeding
- Early Childhood (years 1-3)
- Elderly, esp institutionalised
- Illness generally (impairs recovery)
- Thyroid disease

Dietary & other sources

- FSA • *Consideration of Mandatory Fortification with Iodine for Australia and NZ (April 08)*
  - Poor dietary iodine does not meet needs
  - Dairy, seafood, kelp and eggs are main source
  - Adding iodised salt for commercial bread
  - Use iodise salt as top-up source
  - Supplement in range 125 to 250 µg / day

Supplemental sources

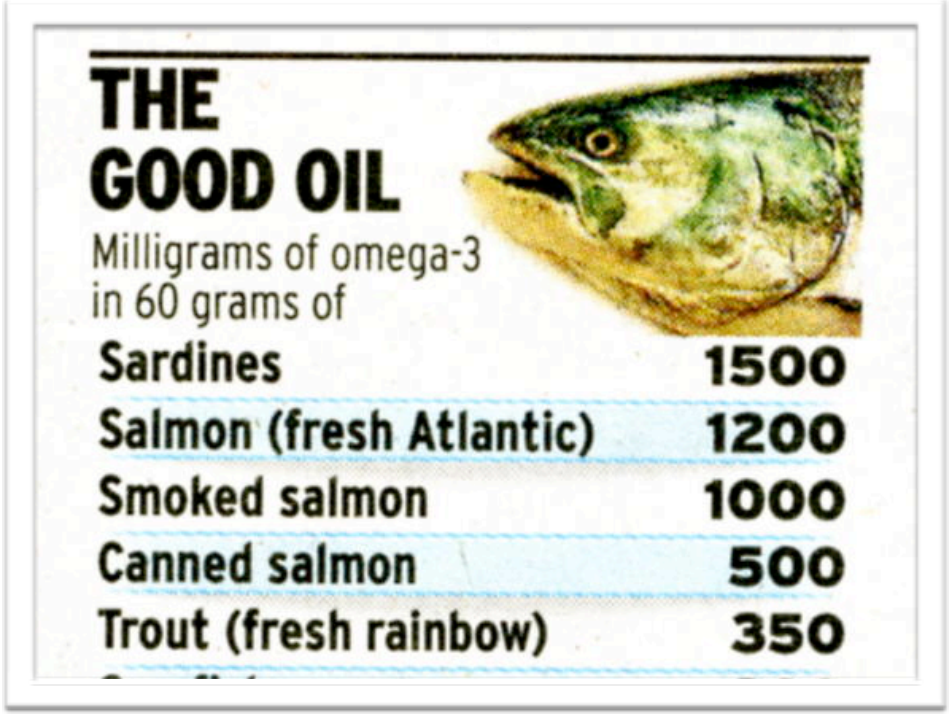
- Iodised salt @ 20-45mg/kg iodine = 3-9 g/day salt
  - Balance between salt restriction & I- need
  - Very slow clinical improvement
- Kelp with a guaranteed iodine content useful
- Lugol's iodine 1 drop/day 1 month, 2 drops/wk
- Daily supplement potassium iodide 125-250 µg

Controversies & Gotchas

- Do not rely on goitres to recognise deficiency
- There are limits to the urine testing
  - It is inaccurate, but may be best we can do
- Overdose of iodine is common, needs checking
- Care in Graves disease, can bring on a “crisis”

Practice Points

- Iodine deficiency is common and preventable
- Deficiency *may* be driving thyroiditis & cancer
- Deficiency worsens Hashimotos thyroiditis
- Iodine dose 250 - 1000 µg to increase low levels
- Iodine dose 100-200 µg to maintain w/o overdose



Omega-3 fatty acids

Omega-3 Basics

- Omega-6:Omega-3 ratio ideal is 1:4 to 4:1
- Typical Western diet now 10:1 to 30:1
- Both are precursors of eicosanoids
  - *prostoglandins, thromboxanes, prostocyclins*
- Omega-6 (esp arachidonic) pro-inflammatory
- Omega-3 (esp EPA) anti-inflammatory
- Inflammation control critical to doctors!

Why supplement omega-3

- Diet is grossly deficient in omega-3
- Restoration of normal eicosanoid balance
- Primary prevention of cardiovascular disease
- DHA in normal brain development
- EPA+DHA in resolution of inflammation
- Flaxseed and plant omegas of limited use

Evidence of deficiency

- No set RDI for omega-3 in the past
- Typical intake of EPA+DHA in adult = 90-160 mg
- Suggested dietary target = 610 mg (M) 430mg (F)
- Inadequate fish intake for most New Zealanders
- Abnormally large Omega-6:Omega-3 >10:1
- Chronic inflammation a major health issue

ASIDE - Inflammation

- Inflammatory responses are well organised for both initiation and resolution
- Inflammation turned on by omega-6 derivatives, mainly arachidonic acid metabolites
- Resolution of inflammation relies on a crossover to EPA+DHA metabolites - “Resolvins”
- Tissue protection maintained by “protectins”, especially “neuro-protectins”

Tests to assess

- Testing not needed for majority - aim is to restore dietary fatty acid balance using food / supplement
- Red cell essential fatty acid profile
- Presence of inflammation + diet low in omega-3

Prevention Potential

- Clinically, inflammation reduction is worthwhile across a broad range of illnesses and diseases
- CVD risk reduction appears strongest evidence
  - Reduce fibrin, TGs, BP + ox-LDL antibodies
- Arthritis inflammation control (High dose)
- Improve neural development in foetus/child
- Depression, ADHD, asthma via ? inflammation

Potential risks / overdose

- VERY low risk
- “Fishy burps”, overcome with new generation of hi-dose EPA or DHA supplements
- ?Bleeding, especially in surgery, aspirin, warfarin
- ?Suppression of inflammation / immune response
- ?Environmental sustainability

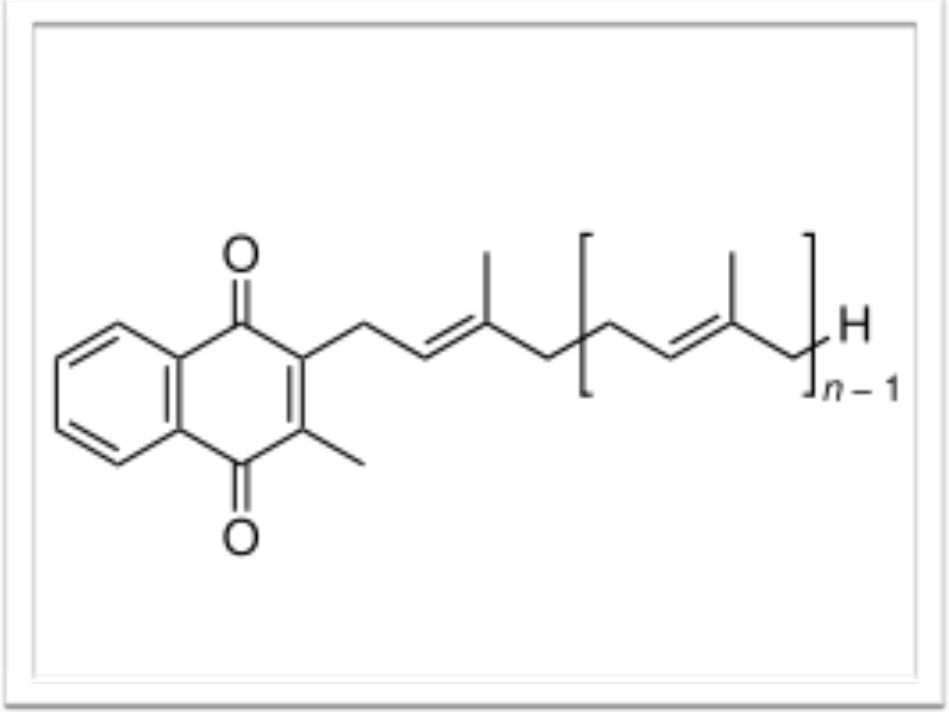
Dietary & other sources

- Fish and seafood at three meals / week *minimum*
  - *salmon, herring, mackerel, anchovies & sardines*
- Some value in plant **α**-linolenic acid (C18 ALA)
  - Flax, EPO, algae, walnuts, kiwifruit
- Venison/free-range/ grass-fed animals better ratio
  - Lamb, buffalo, kangaroo, lean beef

Supplemental sources

- Difficult to get adequate EPA + DHA from diet
- Oily fish run risks of mercury + dioxin toxicity
- ~ 500 mg EPA/day required for CVD prevention
- ~1,500 mg EPA/day for inflammation of arthritis
- ~500 mg DHA/day in pregnancy & lactation
- New specific omega ranges allow targeting

Briefly



Vitamin K

Thanks to

Hub Regtop, Ray Biffen of AgriCure and Trilogie

Poster at The 3rd International Congress on Complementary Medicine Research

The Basics

- Phylloquinone (K1) from plant source, menaquinone (K2) from meat, eggs & cheese
- Some contribution from gut flora (?importance)
- Original studies used IV vit K for clotting, and derived dosage from that flawed method
- Critical role in calcification of bones rather than arteries (ie reduce CVD)

What it does in the body

- Clotting system regulation
- Preferential bone calcification
  - Vitamin K carboxylates osteocalcin
    (the glue that binds hydroxyapetite to the bone)
  - Uncarboxylated calcitonin increases with age, associated with osteoporosis, Vit K treatable
- Liberates calcium from arteries, deposits in bone

Evidence of deficiency

- Bruising or clotting problems
- Osteoporosis in presence of aortic calcification
  - Cardiovascular calcification rising with age
  - Osteoporosis rising with age

Tests to assess

- Vitamin K deficiency is recognised by measuring the ratio of uncarboxylated osteocalcin/ carboxylated osteocalcin
- Calcium scoring for CVD
- Plain x-rays for aortic calcification
- Bone density (need Vit D, PTH status)

Prevention Potential

- Increasing Vit K2 (menaquinone-4) has potential to inhibit and reverse vascular calcification, reduce cardiac mortality, reduce osteoporosis
- Dosage and form of Vit K needs to be reviewed
  - 1-2 mg of K2, rather than current 60-120 µg K
- Potential for reduced fractures, reduced vascular disease, reduced heart disease from increased dose
- Put calcium where it belongs

Vitamin B12

Assessing genetic risks of individuals and controlling with supplements

Vitamin B12 and genetics

- The genome project has opened a can of worms for General Practitioners - rising expectations
- MTHFR C677T and MTHFR A1298C Mutations
- Increased homocysteine and CVD risk in males
- Methylation important in DNA expression
- Wide variety of health effects in carriers depending on other SNPs, environment & diet

Summary

Main Messages

- Nutritional deficiencies are common & important
- Some cause illness and disease directly
- They are straightforward to diagnose & treat
- Treatment with diet and supplements is cheap
- Optimising these nutrients now has evidence of potentially large benefits in prevention, especially cancer, CVD and inflammatory conditions

Main Messages

- Get Vitamin D levels above 80 nmol/L on average
  - Diet, sunlight + 1000-5000 IU supplement
  - Reduce cancer risk, improve bones, more
- Get urinary spot iodine to 100 mcg/L
  - Diet, salt, kelp + 100 - 250 mcg KI supplement
- Get omega 3 fats (EPA+DHA) above 600 mg/day
  - 3 fish meals a week, 3 fish oil caps minimum

Main Messages

- In people with osteoporosis and calcification of arteries, menaquinone-4 (K2) at 1-2 mg is worth considering
- In patients who seem treatment resistant or chronic and puzzling illness, look to genetics and environment for clues
- MTHFR single nucleotide polymorphisms SNPs) are common and important in chronic illness

We can but guide them...

QUESTIONS

Necessary Nutrients

Dr Mark Donohoe

Centre for Evidence-Based Complementary Medicine

doctormark@me.com

www.cebcom.net