
A Detailed Study of Vitamins & Minerals

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Learning Outcomes

- 1. Name the key food sources of the given micronutrients**
- 2. Discuss the absorption and metabolism of dietary and supplemental sources of these micronutrients**
- 3. List the major nutrient-nutrient interactions these micronutrients**
- 4. Describe the metabolic functions and therapeutic uses of these micronutrients**
- 5. Outline the signs and symptoms of these micronutrients deficiency, excess and toxicity**
- 6. List the major nutrient-drug incompatibilities these micronutrients**
- 7. Outline the recommended daily allowance and therapeutic doses for these micronutrients**
- 8. Discuss the preferred forms for optimal uptake of these micronutrients**
- 9. Outline the factors which affect individual requirements for these micronutrients**

Vitamin B9 – Folic Acid

Forms:

- Folate is a name given to a family of compounds called *pteroglutamates*
- Other names used are: **folic acid, folacin**
- Its primary active form in the body-**THF (tetrahydrofolate)** serves as part of an enzyme complex, active in numerous metabolic reactions
- Folic acid is the synthetic form found in supplements and fortified foods. It is not naturally occurring



(Bender 2002;Liska et al 2004)



Food Sources of B9

- Folate is especially abundant in foods of plant origin, mainly legumes, vegetables and some fruit
- The vitamin name suggests *foliage*, and indeed, leafy green vegetables are the richest source
- Other rich sources:

- Legumes
- Citrus fruit
- Liver



Reference Nutrient Intakes

- Because bioavailability of folate ranges from 50% upwards in foods and 100% in supplements, taken on an empty stomach, **Dietary Folate Equivalent (DFE)** have been developed.
 - **DFE = 1 μ g food folate + (1.7 x μ g synthetic folate)**
 - Synthetic folate is 1.7 x more available than dietary folate
 - Thus a person consuming 100 μ g from foods and 100 μ g from supplements receives 270mcg of DFE
 - Recommendations for adult people vary from **200 μ g (UK)** to **400 μ g (US)**

Recommended Dietary Allowances

(mcg/d)

Age	Irish Recommendations (1983, revised 1999)
0-12 months	(UK) 0.2 – 0.4
1-3 years	100
4-6 years	200
7-10 years	200
Males 11-14 years	300
Males 15-17	300
Females 11-14	300
Females 15-17	300

(FSAI 1999)

Recommended Dietary Allowances

(mcg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	300
Males 65+	300
Females 18-64	300
Females 65+	300
Pregnancy	500
Lactation	400

Reference Nutrient Intakes

(mcg/day)

Age	UK recommendation	US recommendation
0-6 months	50	65
7-12 months	50	80
1-3 years	70	150
4-6 years	100	200
7-10 years	150	200
Males 11-14 years	200	300
Males 15-50+ years	400	400
Females 11-14 years	200	300
Females 15-50+ years	400	400
Pregnancy	+ 200	600
Lactation	+ 100	500

Food Sources of B9 (Folic Acid)

Food per 100g	mcg
Lentils	479
Kidney Beans	394
Soybeans	375
Beef Liver	290
Romaine Lettuce	136
Broccoli	63
Asparagus	52
Orange	17
Beef steak	12

Dosage of B9 (Folic Acid)

- RDAs – see table
- Supplemental Range: 1000-5000mcg
- 400mcg recommended during preconception and first trimester of pregnancy



Age	Vitamin B9
Infant	100mcg
Child (1-3 yrs)	200mcg
4 – 18 yrs	200mcg
Adult (EU)	200mcg
Pregnancy	400 - 800mcg

Folic Acid - Absorption and Availability

- **Heat and oxidation** during cooking and storage can **destroy up to 50%** of the folate in foods
- Folic acid is quite stable in the presence of light
- It is absorbed in the small intestine
- The bioavailability of food folate is approximately 80% of that from supplements, higher than previously thought
read more: <http://ajcn.nutrition.org/content/85/2/465.full.pdf+html>



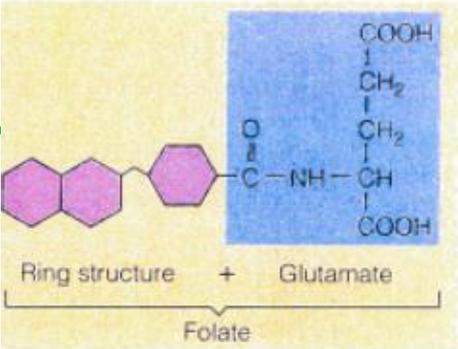
(Mahan and Escott –Stump 2008; Winkels et al 2007)



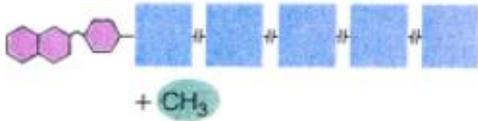
Folic Acid - Metabolism

- After absorption a **methyl group** ($-\text{CH}_3$) is added to folate and in this form it is delivered to body cells.
- In order for the folate to function in the body the methyl group must be removed by an enzyme that requires vitamin B12.
- Without that help folate becomes trapped inside cells in its methyl form (**5-methyl THF**), unavailable to perform its functions: DNA synthesis and cell growth – a metabolic situation called **the folate trap**.

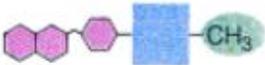
Folate's Absorption and Activation



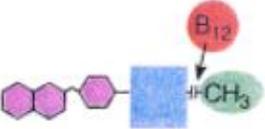
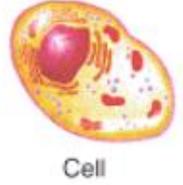
In foods, folate naturally occurs as polyglutamate. (Folate occurs as mono-glutamate in fortified foods and supplements.)



In the intestine, digestion breaks glutamates off . . . and adds a methyl group. Folate is absorbed and delivered to cells.



In the cells, folate is trapped in its inactive form.



To activate folate, vitamin B₁₂ removes and keeps the methyl group, which activates vitamin B₁₂.



Both the folate coenzyme and the vitamin B₁₂ coenzyme are now active and available for DNA synthesis.



5-methyl THF;
inactive

THF; active

(Rolfes et al 2006)

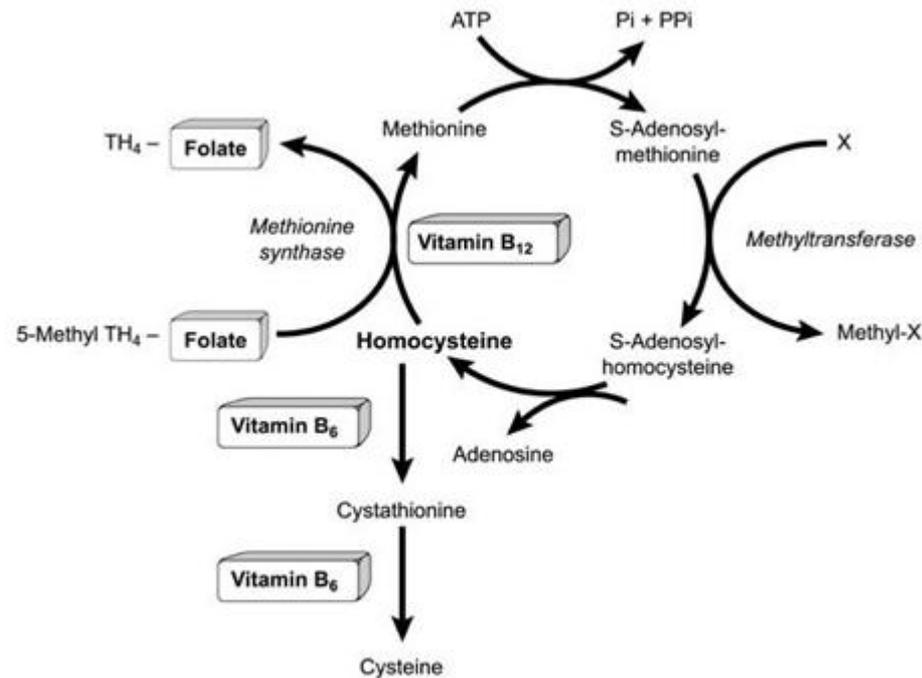
Folic Acid - Metabolic Functions

- **Tetrahydrofolate (THF)** plays a role in many reactions metabolising amino acids and nucleotides.
 - It functions in the **synthesis and repair of the DNA**
 - It is required for the **conversion of amino acids**
 - It provides methyl groups for the **synthesis of methionine from homocysteine** (this conversion also needs vit B12)
 - Deprivation of vitamin B12 can produce a secondary folate deficiency by interrupting the regeneration of THF from 5-methyl THF

(Liska et al 2004; Mahan and Escott-Stump 2008)

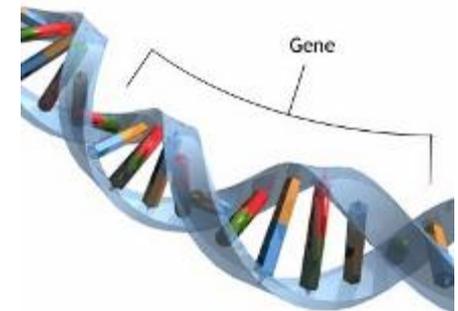
Metabolic Functions

The Role of Folate in the Homocysteine Cycle



Metabolic Functions

- In their role in the synthesis and repair of DNA, both folate and B12 are crucial in **maintaining gene stability**
 - Lower levels of folate are associated with development of tumours
- Folate is essential for the **formation of red and white blood cells** in bone marrow and for their maturation
- It is crucial in the **formation of haem**



(Mahan and Escott-Stump 2008)

Folate in Pregnancy

- During the 1980s it was discovered that **spina bifida** and other **neural tube defects** were associated with **low intakes of folate** and that increased intake in pregnancy may be associated with reduced risk.
- It is now established that **supplements of folic acid taken periconceptually** (before conception) prevent neural tube defects.
- It is recommended that intakes be increased by 400µg **before conception** :
 - Closure of the neural tube occurs by day 28 of pregnancy, which is before the woman knows she is pregnant

Folate in Pregnancy

- A typical Western diet does not supply this amount, that is why supplements are recommended to all women.

- However, excellent levels of folate is contained in:
 - Spinach 1 cup = 260 μ g
 - Boiled red kidney beans 1 cup = 230 μ g
 - Boiled lentils 1 cup = 360 μ g
 - Broccoli 1 cup = 95 μ g
 - Asparagus 1 cup = 260 μ g

- **If you are not confident the patient is going to change her diet significantly you should recommend a supplement to women who may be about to conceive.**

Folate - Specific Therapeutics

- **Homocysteinaemia:** taking folic acid orally at 800-1000 $\mu\text{g}/\text{day}$ lowers homocysteine levels by about 20% to 30%.
- In people with **asymptomatic atherosclerosis**, lowering homocysteine levels with folic acid, reduces the progression of atherosclerosis and improves arterial blood flow.
- Consumption of at least 300 mcg per day of **dietary folate** seems to be associated with a 20% **lower risk of stroke** and a 13% **lower risk of cardiovascular disease**, when compared with consumption of less than 136 mcg of folate per day.
 - Is this effect caused by folate alone, or by the plant foods that contain folate, in which it acts in synergy with other nutrients?

Folate - Specific Therapeutics

- Consuming **dietary folate** seems to decrease the risk of **breast cancer**, especially in women who also consume high amounts of vitamin B12, or B6
- **Depression:** taking folic acid orally (200-500 mcg daily) with conventional antidepressants might improve treatment response; however, folic acid is not effective as a replacement for conventional antidepressant therapy
- **Pancreatic Cancer:** consuming greater than 280 mcg per day of **dietary folate** is associated with a decreased risk of **pancreatic cancer**
- **Vitiligo:** taking folic acid orally seems to improve symptoms of vitiligo; however very high doses (5mg) a day were used, only under medical supervision

Folate Deficiency

- Folate deficiency **impairs cell division and protein synthesis** - critical metabolic processes in the body
- In folate deficiency, the fast dividing cells of the body are affected first: red blood cells and GI tract cells resulting in:
 - **Anaemia (megaloblastic anaemia)**
 - **Gastrointestinal (GI) tract deterioration**
 - GI deterioration can be triggered by alcohol abuse, which increases folate loss from the body, leading to further GI tract weakening and folate loss (vicious circle)

Folate Deficiency

- **Homocysteinaemia** (increased homocysteine levels in the blood)
 - Due to inability of 'trapped' folate to regenerate methionine from homocysteine
 - This increases the risk of cardiovascular disease and is very common among apparently healthy people suggesting that subclinical deficiency might be common
- Other symptoms include:
 - **Weakness, depression, dermatologic lesions, poor growth**

Factors That Might Affect Individual Requirements

- Deficiency can develop in infants fed goat's milk, which is very low in folic acid
- Deficiency may also result from:
 - **Impaired absorption** (alcoholism)
 - **Unusually high metabolic need**, when cell multiplication speeds up:
 - Pregnancy
 - Cancer
 - Skin-destroying diseases (chickenpox, measles)
 - Burns
 - Blood loss

(Rolfes et al 2006)

Factors That Might Affect Individual Requirements

- Of all the vitamins, folate appears to be most vulnerable to interactions with drugs, which can lead to secondary deficiency
- Increased risk of deficiency in patients taking:
 - **Anticancer drugs**
 - **Aspirin**
 - **Antacids**
 - **Oral contraceptives**



Folic Acid - Toxicity

- Naturally occurring folate **from foods alone** appears to cause **no harm**
- Folic acid supplements in excess of 350µg/day may impair zinc absorption
- Folic acid supplements mask the megaloblastic anaemia of vitamin B12 deficiency and may hasten the development of the irreversible nerve damage
- Recent studies suggest that long-term intake in **supplemental form increased the risk of growth of already present colon cancers. Folic acid supplements may negatively interfere with normal metabolic processes – you will have more information on genetic variances responsible for this in your level 2 lectures.**
- **Tolerable Upper Intake Level for Adults: 1000 µg/day**



Folic Acid - Drug Interactions

- **Anticonvulsant drugs** - (phenytoin, fosphenytoin, phenobarbital, primidone): supplemental folic acid can interfere with anticonvulsant drugs and increase seizure frequency
- Folic acid can also have a direct convulsant activity

(Lewis et al 1995; Froscher et al 1995)



Vitamin C

Forms:

- **Vitamin C (ascorbic acid)** is a vitamin for only a limited number of species: humans and other primates, guinea pigs , bats, some birds and most fish
- The vitamin C deficiency **scurvy** has been known for many centuries and was described by Hippocrates in 1500BC
- The Crusaders are said to have lost more men through scurvy than were killed in battles
- Recognition that scurvy was due to a dietary deficiency came from James Lind in 1757, who demonstrated that orange and lemon juice is protective
- Both **ascorbic acid** and **dehydroascorbic acid** have vitamin activity

(Bender 2002)





Food Sources of Vitamin C

Vitamin C is abundant in fruits and vegetables such as :

- Blackcurrants & redcurrants
- Citrus fruits
- Guava
- Parsley
- Pineapple
- Rosehips
- Strawberries, raspberries, blackberries
- Peppers
- Kale, rocket watercress, bok choy, spinach



Very significant losses occur as vegetables wilt, or when they are cut (as a result of the release of ascorbate oxidase from the plant tissue)

Reference Nutrient Intakes

- Vitamin C illustrates well how different criteria of adequacy and different interpretations of experimental evidence can lead to different estimates of requirements and to reference intakes ranging from 30-80mg/day.
- The requirement to **prevent scurvy** - **10mg/day**
- The requirement for **optimum wound healing** - **20mg/day**
- Allowing for individual variations in metabolism gives the reference intake for adults of 30mg/day - which was the **British recommendation** until 1991; then it was changed to **40mg**.
- **The Dutch and US recommendations at 80 and 60mg** respectively are based on different criteria to the British recommendations (they estimate the total body content of vitamin C and then measure the rate at which it is metabolised).

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
0-12 months	(UK) 25
1-3 years	45
4-6 years	45
7-10 years	45
Males 11-14 years	50
Males 15-17	60
Females 11-14	60
Females 15-17	60

Recommended Dietary Allowances

(mcg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	60
Males 65+	60
Females 18-64	60
Females 65+	60
Pregnancy	80
Lactation	80

Reference Nutrient Intakes (mg/day)

Age	UK recommendation	US recommendation
0-6 months	25	40
7-12 months	25	50
1-3 years	30	15
4-6 years	30	25
7-10 years	30	25
Males 11-14 years	35	45
Males 15-50+ years	40	90
Females 11-14 years	35	45
Females 15-50+ years	40	75
Pregnancy	+ 10	85
Lactation	+ 30	120

(Geissler and Powers 2005)

Vitamin C in Selected Foods

Food per 100g	Mg
Kale (raw)	120
Kiwi	108
Papaya	61
Strawberries	58
Oranges	45
Spinach (raw)	28

Dosage of Vitamin C

- RDAs – see table
- Supplemental Range: 250 – 10,000mg
- No high doses in third trimester of pregnancy. The baby becomes accustomed to high doses that are unsustainable when it is born.

Age	Vitamin C
Infants	40mg
1-3 yrs	50mg
Adults (EU)	80mg



Vitamin C-Availability and Absorption



- Significant losses occur in cooking :
 - Through leaching into water
 - Through atmospheric oxidation which continues when foods are left to stand before serving
- Refrigeration and quick freezing can help retain the vitamin :
 - Most frozen foods are processed so close to the source of supply that their ascorbic acid content is often higher than that of fresh foods that have been shipped and spent a long time in storage.

(Mahan and Escott –Stump 2008)

Vitamin C - Availability and Absorption

- Both ascorbic acid and dehydroascorbic acid are absorbed in the mouth and in the small intestine
- Some 80-95% of dietary ascorbate is absorbed at intakes up to 100mg/day
- The absorption of larger amounts is lower
- **Unabsorbed ascorbate** from very high doses is a substrate for intestinal bacterial metabolism **causing gastrointestinal discomfort and diarrhoea**

(Mahan and Escott –Stump 2008)

Vitamin C - Availability and Absorption

- Both vitamins are transported into cells by glucose transport and **high blood glucose levels** (e.g. in diabetics) can **inhibit vitamin C uptake significantly**.
- It has been suggested that hyperglycaemia (high blood sugar) induces cellular vitamin C deficiency which may lead to oxidative stress in cells and contribute to an increased risk of atherosclerosis.
- There is no specific storage organ for vit C; leukocytes, adrenals, and pituitary gland show the highest concentrations.

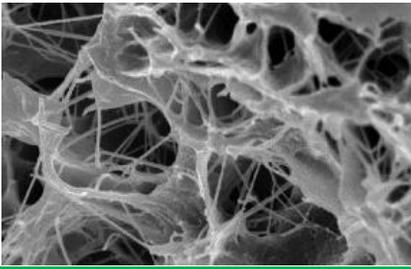
Vitamin C - Metabolic Functions

- **As an antioxidant:** vitamin C loses electrons easily, which allows it to perform as an antioxidant, defending against free radicals and thus against tissue damage
 - In the intestines, vitamin C **enhances iron absorption** by protecting iron from oxidation (it keeps it in Fe²⁺ form, not allowing it to become Fe³⁺ , which is not bioavailable)
 - A dose of 25mg of vitamin C taken **together with a meal** increases iron absorption by 65%
 - Optimum iron absorption may require more than 100mg/day

(Rolfes et al 2006; Bender 2002)

Vitamin C - Metabolic Functions

- **As a prooxidant:** high levels of supplementation with vitamin C can create a pro-oxidant stress in the body
- Vitamin C has antioxidant activity when it reduces oxidizing substances such as hydrogen peroxide, however, it can also reduce metal ions which leads to the generation of free radicals through the fenton reaction:
- $2 \text{Fe}^{3+} + \text{Ascorbate} \rightarrow 2 \text{Fe}^{2+} + \text{Dehydroascorbate}$
- $2 \text{Fe}^{2+} + 2 \text{H}_2\text{O}_2 \rightarrow 2 \text{Fe}^{3+} + 2 \text{OH}\cdot + 2 \text{OH}^- \rightarrow \text{free radicals}$
- The metal ion in this reaction can be reduced, oxidized, and then re-reduced, in a process that can generate reactive oxygen species (free radicals)



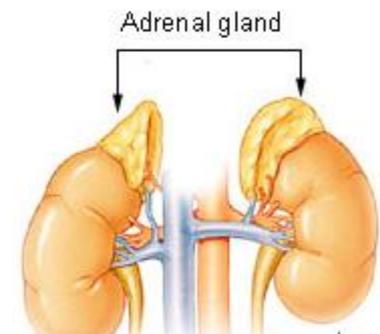
Vitamin C - Metabolic Functions

- **As a cofactor in collagen formation:** vitamin C helps to form the fibrous structural protein of connective tissues known as collagen:
 - Collagen serves a matrix on which bones and teeth are formed
 - When a person is wounded, collagen glues the separated tissues together
 - Collagen helps the arteries expand and contract

(Rolfes et al 2006; Bender 2002)

Vitamin C - Metabolic Functions

- **As a cofactor for other reactions:**
 - **Hydroxylation of carnitine** (a compound that transports long-chain fatty acids into the mitochondria for energy production)
 - **Conversion of tryptophan and tyrosine** to the neurotransmitters **serotonin and norepinephrine**
 - **Synthesis of thyroxin** (thyroid hormone)
 - **Synthesis of adrenal steroid hormones**



(Rolfes et al 2006)

Vitamin C - Metabolic Functions

As a cofactor for other reactions:

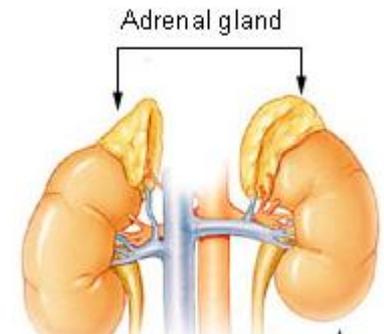
- **Inhibition of nitrosamine formation**

- The additives nitrates and nitrites in cured meats are suspected to be responsible for increased colon cancer risk resulting from eating cured meats
- Nitrates and nitrites can be converted into carcinogens **nitrosamines**
- Vitamin C can prevent formation of nitrosamines from nitrates and nitrites



Vitamin C - Metabolic Functions

- **In stress:** the adrenal gland contains more vitamin C than any other organ:
 - During stress the adrenals release vitamin C with other hormones into the blood
 - The exact role of vitamin C in stress is unknown, but it is known that stress raises vitamin C needs
 - Burns, infections, toxic metal intakes, chronic use of medications and cigarette smoking are among the stresses that increase vitamin C need



(Rolfes et al 2006)



Vitamin C -Metabolic Functions

- **As a cure for the common cold:** newspaper headlines touting vitamin C as a cure for colds have appeared frequently over the years, but research supporting such claims has been conflicting and controversial.
- A review of all the research in this area reveals a modest benefit:
 - A difference in duration of less than 1 day per cold in favour of those taking daily dose of at least 1g/day
 - Interestingly, those who received the placebo, but thought they were receiving vitamin C had fewer colds than the group who received vitamin C but thought they were receiving placebo –***the healing power of faith?***

(Douglas et al 2007)

Vitamin C - Specific Therapeutics

- **Age-related macular degeneration (AMD):** taking vitamin C 500 mg orally, in combination with elemental zinc 80 mg, vitamin E 400 IU, and beta-carotene 15 mg/day - seems to provide a reduction in visual loss and some reduction of progression of AMD in patients with advanced AMD.
- **Albuminuria (protein in urine):** taking vitamin C (1250mg) plus vitamin E (680IU) can reduce the excretion of protein by about 19%, when given for 4 weeks, in patients with type 2 diabetes. This might also reduce the risk of end-stage renal disease in patients with type 2 diabetes.
 - Excretion of protein in diabetes type 2 is a sign of vascular kidney damage triggered off by diabetes.

(AREDSRG 2001; Gaede et al 2001)

Vitamin C - Specific Therapeutics

- **Atherosclerosis and peripheral arterial disease:** taking vitamin C (250mg) orally seems to decrease the risk of atherosclerosis; patients with atherosclerosis appear to have lower levels of vitamin C and higher levels of C-reactive protein, a marker of inflammation.
- **Cancer:** dietary vitamin C might decrease the risk of developing mouth cancer and other cancers; some evidence suggests that a diet low in vitamin C might increase the risk of mortality due to all cancers.
- **Gallbladder disease:** there is some evidence that vitamin C supplementation and increased vitamin C serum levels decreases the risk of developing gallbladder disease in women; however, it doesn't seem to have this effect in men.

(Langlois et al 2001; Khaw et al 2001; Simon et al 2000)

Vitamin C - Specific Therapeutics

- **Helicobacter pylori (H pylori):** taking vitamin C orally (1g) seems to decrease gastritis associated with antacid therapy in patients with H. pylori infection; after H. pylori is eradicated, vitamin C appears to decrease the incidence of precancerous changes in stomach tissue.
- **Osteoarthritis:** consuming vitamin C from **dietary sources** seems to reduce the risk of cartilage loss and disease progression in people with osteoarthritis.
- **Sunburn:** taking vitamin C orally (2g) in combination with vitamin E (1000IU) seems to reduce redness of ultraviolet (UV) radiation-induced sunburn; guard against toxicity at these levels!

Vitamin C - Deficiency

- The two most notable signs of vitamin C deficiency reflect its role maintaining the integrity of blood vessels:
 - The **gums bleed easily** around the teeth
 - Capillaries under the skin break spontaneously producing **pinpoint haemorrhages**
- When the intake falls to about 1/5 of its optimal store size (ca. 1 month on a vitamin C depleted diet), **scurvy** symptoms begin to appear :
 - Further haemorrhaging from inadequate collagen synthesis
 - Muscle degeneration
 - Rough, brown scaly skin; wounds do not heal
 - Bone rebuilding falters-fractures develop
 - Teeth become loose

resolved in 5 days
of vitamin C
intake(100mg/day)

Factors That Might Affect Individual Requirements

- Insufficiency can occur in people with low fruit and vegetable intake on the following medications:
 - Aspirin
 - Barbiturates
 - Oral contraceptives
- Smokers have lower levels of serum vitamin C, and the reference nutrient intake for this group is 80mg/day, however many practitioners recommend upwards of 1000mg/day in divided doses.
- 25mg of vitamin C is lost with every cigarette smoked.



Factors That Might Affect Individual Requirements

Suspect insufficiency, when patients present with:

- Fatigue accompanied with petechiae (smaller bleeding lesions under the skin)
- Gingivitis
- Poor wound healing
- History of recurrent infections and colds
- Thickening of the skin on the buttocks and lower extremities





Vitamin C - Toxicity

- At high levels 3000mg day, toxic effects are reported :
 - Nausea
 - Abdominal cramps
 - Diarrhoea
- People with kidney disease and those with tendency toward gout are prone to forming kidney stones if they take large doses of vitamin C long-term
- Long-term high-dose vitamin C supplements can adversely affect people with iron overload (exacerbating cellular damage through iron-induced free radicals)-in this case vitamin C will act as a **prooxidant**
- **Tolerable Upper Intake Level for Adults: 2000 mg/day**



Vitamin C - Drug Interactions

- **Cancer Drugs:** the use of high-dose vitamin C as an adjunctive therapy, in combination with other antioxidants to treat cancer, is controversial.
- Some experts think these supplements might increase the sensitivity of tumour cells to radiation and reduce toxicity in normal cells.
- Other experts worry that antioxidants might protect cancer cells from the effects of radiation.
- Preliminary evidence suggests that vitamin C might reduce the effectiveness of some chemotherapy drugs, including doxorubicin, cisplatin, vincristine, methotrexate, and imatinib.

(Prasad et al 2002; Heaney et al 2008)



Vitamin C -Drug Interactions

- **Oestrogens:** increases in plasma oestrogen levels of up to 55% occur under some circumstances when vitamin C is taken with oral contraceptives or hormone replacement therapy, including topical products .
- **Niacin/Statin:** a combination of niacin and simvastatin (Zocor) effectively raises HDL cholesterol ("good cholesterol") levels in people with coronary disease and low HDL levels; a combination of antioxidants (vitamin C, vitamin E, beta-carotene, and selenium) seems to blunt this rise in HDL.
- **Warfarin:** massive doses of vitamin C can counteract the effect of anti-clotting medications.
- **Diabetes tests:** large amounts of vitamin C obscure the results of tests used to detect diabetes giving **false positive** or **false negative** results.

(Vihtamaki et al 2002; Brown et al 2001; Rolfest et al 2006)

Biotin



Forms and Sources:

Biotin was originally discovered as:

- Part of the complex called **bios** which promoted the growth of yeast, and separately as **vitamin H**, the curative factor in ‘egg white injury’ –the disease caused by consuming high amounts of uncooked egg whites
- Biotin is widely distributed in many foods like liver, soybean, egg yolk, peanuts, walnuts, bean sprouts, kidneys, milk.
- It is also synthesized by intestinal flora (however it is not know to what extent it is available to the host)

(Osiecki 2004; Bender 2002)

-
- The Food Safety Authority of Ireland's Working Group also has not established a RDA for biotin. (FSAI 1999)

Reference Nutrient Intakes

The Food Standards Authority in the UK stated:

- Biotin is widely distributed in natural foodstuffs but at very low levels compared to other water-soluble vitamins.
- Liver contains approximately 1 mg/kg biotin
- Fruits and most other meats contain approximately 0.01 mg/kg biotin.
- Biotin, usually either in the form of crystalline D-biotin or brewer's yeast, is included in many dietary supplements, infant milk formulas and baby foods.
- The maximum dose in supplements sold in the UK is 2 mg. Several medicines containing biotin, which are available only from pharmacies, are licensed for the prevention and treatment of nutrient deficiency, supplementation of special diets and malabsorption. The maximum daily dose of biotin in licensed medicines is 0.50 mg.
- Due to insufficient data, COMA was unable to set Dietary Reference Values for biotin, but considered that intakes between 0.010 and 0.20 mg/day are both safe and adequate (COMA, 1991).

Dosage of Biotin

- RDAs – see table
- Supplemental Range: 0.5-15mg
- Synergistic nutrients
B2, B3, B5, B6, B9,
B12, Mg, Mn, Cr

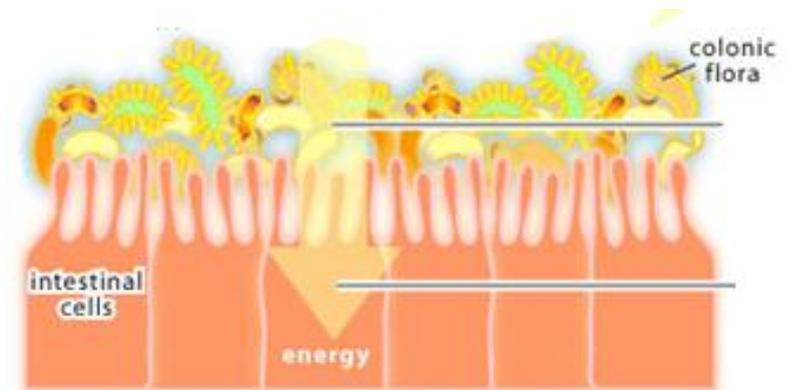
Age	Biotin
0-0.5 yrs	10mcg
1-3 yrs	15mcg
4-6 yrs	20mcg
7-10 yrs	25mcg
11-14 yrs	30mcg
15-18 yrs	30-300mcg
Adult (EU)	50mcg

Biotin - Availability and Absorption

- Most biotin in foods is protein bound, which is then metabolised in the intestines to yield free biotin
- Free biotin is absorbed in the small intestine
- It is not known to what extent biotin bound in foods is biologically available to humans
- **Absorption is impaired by chronic alcohol intake and raw egg whites** containing *avidin* (a glycoprotein that may irreversibly bind biotin)
 - Avidin is denatured by cooking

Biotin- Availability and Absorption

- Smaller amounts of biotin can also be absorbed from the colon, which facilitates the use of biotin produced by colon microflora
- Colon absorption may be enhanced by the effects of a vegetarian diet on gut flora



(Liska et al 2004)

Biotin - Metabolic Functions

- Biotin is involved in reactions crucial for **energy metabolism and fatty acid synthesis**
 - Biotin deficiency has been observed to lead to accumulation of odd-numbered fatty acids
- Biotin is also involved in the **promotion of healthy hair and nails**, a benefit that may come from its ability to positively affect the metabolism of oils in the integumentary system
- It is also involved in **creating the active form of folate**

(Liska et al 2004)

Biotin - Specific Therapeutics

- **Cradle cap:** in infants, cradle cap appears to be a common manifestation of biotin insufficiency
 - This may be due to biotin influence on fatty acid biosynthesis
 - However supplementation does not seem to improve symptoms
- **Seborrhoeic dermatitis** (adult version of cradle cap) is characterised by biotin deficiency, however there are no studies on the efficacy of supplementation in this condition

(Brenner et al 1988; Keipert et al 1976; Inaloz et al 2002)

Biotin - Specific Therapeutics

- **Brittle nails:** preliminary evidence shows that biotin might increase the thickness of fingernails and toenails in people with brittle nails
- **Diabetes:** preliminary evidence shows that a combination of biotin (2mg) and chromium (600mcg) might lower blood glucose and **haemoglobin A1c** levels in type 2 diabetes patients for whom oral diabetic drugs are not effective; however, biotin alone doesn't seem to have any effects
 - **Haemoglobin A1c** is a marker of long-term blood sugar levels
 - Average supplemental range of biotin is from 300-600µg/d
 - No toxicity has been reported in patients taking up to 10mg/day

(Hochman et al 1993; Geohas et a 2004; Baez-Saldana et al 2004; Liska et al 2004)

Biotin - Deficiency

- Biotin is widely distributed in foods and deficiency is unknown, except among people who are:
 - Maintained on total parenteral nutrition
 - Consuming very large amounts of uncooked egg whites (ca. 10 a day)
 - Deficiency symptoms:
 - Scaly and seborrhoeic dermatitis
 - Dry scaly rash around openings of eyes, mouth, nose, anus
 - Hair loss
 - Nausea
 - Depression
 - Anorexia
 - Burning /tingling sensations
 - Dry greyish skin
 - Extreme fatigue
 - Glossitis or smooth pale tongue
- cured with supplements of 60-200µg/day**

Minerals

PART 1.

Minerals

Introduction

- Minerals represent about 4-5% of body weight (2.8-3.5kg in adult men and women respectively) and out of this:

- 50% - **calcium (Ca)**
 - 25% - **phosphorus (P)**
 - 25% - other **macrominerals** and **microminerals**
- } **99% of Ca and 70% of phosphate are found in bones**

Mg (magnesium), Na (sodium), K(potassium), Cl (chlorine), S (sulphur)

Fe (iron), Zn(zinc), I (iodine), Se (selenium), Mn (manganese), F (fluoride), Mo (molybdenum), Cu (copper), Cr (chromium), Co (cobalt), B (boron)

- Ultratrace elements** -negligible amount of weight

(As) arsen, (Al) aluminium, (Sn) tin, (Ni) nickel, (V) vanadium, (Si) silicon

Minerals

Introduction

- Macrominerals exist in the body and food mainly in the **ionic state**
 - **Na (sodium), K (Potassium), Ca (Calcium)** - as positive ions (cations)- e.g. Na^+ , K^+ , Ca^{2+}
 - **Cl, S, P**- as negative ions (anions) –e.g. chlorine as chloride; sulphur and sulphate, phosphorus as phosphates
- Minerals also exist as **components of organic compounds** :
 - Phosphoproteins, phospholipids, metalloenzymes, metalloproteins (e.g. haemoglobin)

Minerals

Introduction

- Minerals are **absorbed in their ionic** state (exception-haem iron)
 - Therefore minerals that are :
 - Bound to organic molecules (**chelated**)
 - Bound to inorganic complexes
- } **are not bioavailable;**
 except for some
 minerals that are better
 absorbed bound to
 amino acids (e.g.
 selenomethionine)
- Unabsorbed minerals are excreted in the faeces
 - Absorbed minerals are:
 - **Transported into the blood**
 - Or **kept in the intestinal cells** bound to protein, and when the cell dies, they are sloughed off into the intestinal lumen for excretion (probably a mechanism for protecting from toxicity)

Minerals

Introduction

- **Bioavailability:** absorption of a mineral after its digestion from food and before its use in tissues and cells
- Several factors can affect bioavailability:
 - **Body mineral status** (e.g. in Fe deficiency, Fe absorption increases dramatically)
 - **Substances present in food** like phytates, vitamin C, etc
 - **Other minerals present in food** (e.g. Zn absorption is reduced by iron supplements)
 - **Disease states:** e.g. fat malabsorption can cause formation of soaps from Mg and Ca with fatty acids and render those minerals unabsorbable
 - **High concentration of one mineral** in the intestines (e.g. excess Ca binds to phosphates and precipitates)

Minerals

Bioavailability:

Examples of Mineral-Mineral Interactions

- In general in mineral deficiency states, more mineral transport proteins appear in the intestinal tract - which may allow for greater absorption of toxic elements
 - Essential mineral deficiency can thus increase a person's vulnerability to toxic element exposure
- Excess intake of Zn antagonizes intestinal Cu absorption to the point that copper deficiency may result despite adequate copper intake!
- Cu deficiency exacerbates iron deficiency anaemia

(Lord and Bralley 2008)

Minerals

- **Minerals with high bioavailability from foods:**

Sodium(Na), potassium (K), chloride (Cl), iodide (I) fluoride (F)

- **Minerals with medium bioavailability from foods:**

Calcium (Ca), magnesium (Mg)

- Minerals with low bioavailability from foods:

Iron (Fe), chromium (Cr), manganese (Mn)

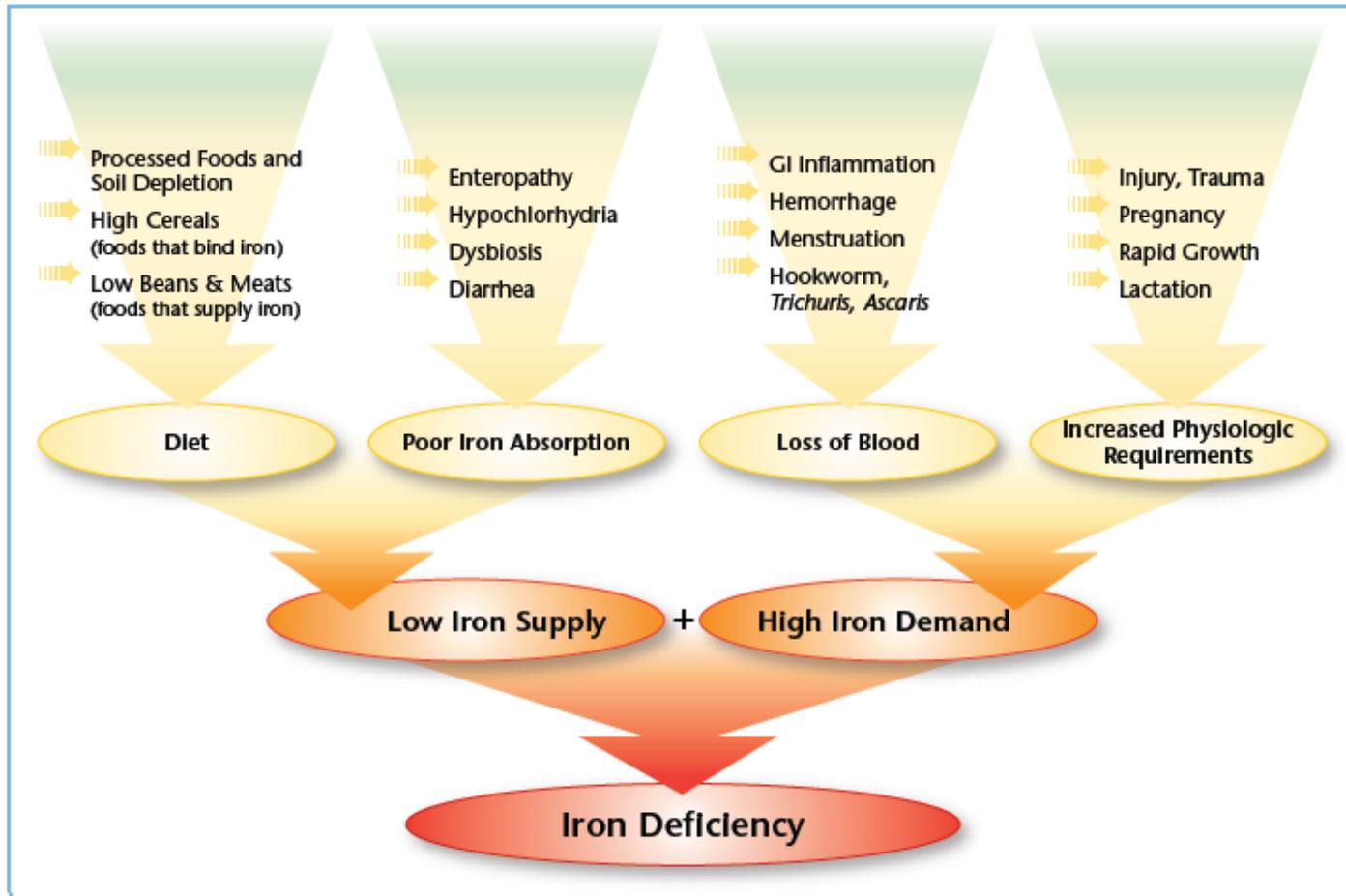
(Mahan and Escott-Stump 2008)

Minerals

Mineral deficiencies or excesses are involved in the pathogenesis of many health conditions e.g. heart disease, hypertension, cancer

- Certain groups demonstrate relatively high incidence of elemental deficiencies:
 - Pregnant women
 - Children and adolescents
 - The elderly
 - Those with certain diseases (e.g. those who are immuno compromised)
- Causes of deficiency: factors that **decrease supply** and **increase demand**

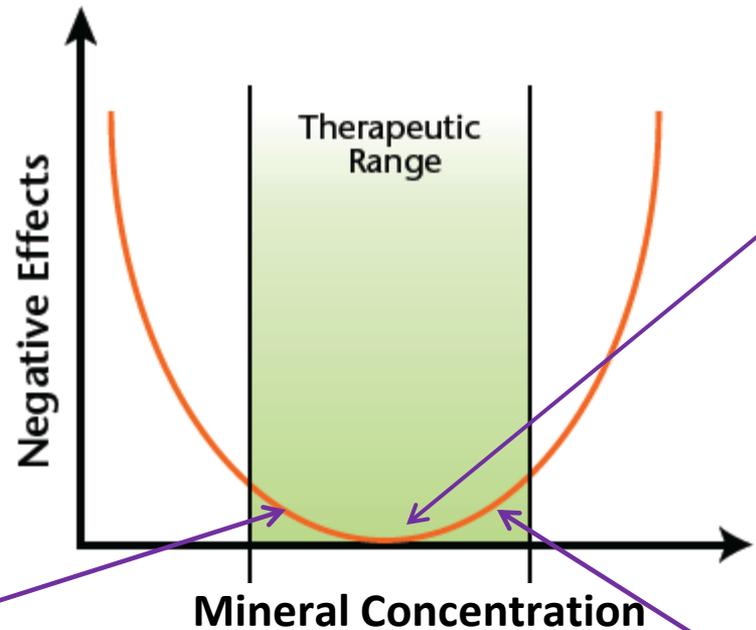
Causes of Iron-Deficiency



Minerals

- **Government objective:** to derive safe and effective levels of intake to prevent frank deficiency and possible toxicity
- **Practitioner objective:** to assess the patient, taking into account all the individual factors that might cause deficiency/excess. To provide optimum mineral supply through manipulating diet and if that is not sufficient-introducing supplementation

Minerals



practitioner's objective is to estimate the ideal level of patient's nutrient intake

lower level of intake (mainly through faulty diet; increased needs) increases the risk of negative effects

higher level of intake (mainly through supplementation) increases the risk of negative effects

(Lord and Bralley 2008)

Calcium

Forms:

- Calcium (Ca) is the most abundant mineral in the body
- Ca was among the first substances known to be essential in the diet
- It makes up about 1.5%-2% of the body weight; 39% of body minerals
- The majority of it is contained in the skeleton (as hydroxyapatite-complex of calcium and phosphate)

(Strain and Cashman 2002; Sharp 2005)



Food Sources of Calcium

Milk and dairy products are the most concentrated food sources of calcium

All foods of vegetable origin contain Ca, though not as concentrated, but often more bioavailable:

- Dark green leafy and cruciferouces vegetables
- Kale, collards, broccoli, chinese cabbage, Brussel sprouts
- Almonds, sesame seeds
- Soybeans; calcium set tofu
- Dried figs
- Calcium fortifeid orange juice
- Small bones of sardines and salmon-another animal source



Reference Nutrient Intakes

- The maintenance of bone calcium reserves is the major determinant of calcium needs
- Therefore the needs vary throughout life considerably, with greater needs during growth, pregnancy and lactation
- There is considerable disagreement over human calcium requirements, which is reflected in the wide variation in estimates of daily requirements
 - UK recommendation for adults above 24years -700mg/day
 - US recommendation for adults above 24years -1000-1200mg/day
- **Different recommendations stem from applying different methods to establish Ca needs**

Recommended Dietary Allowances

(mg/d)



Age	Irish Recommendations (1983, revised 1999)
0-12 months	(UK) 525
1-3 years	800
4-6 years	800
7-10 years	800
Males 11-14 years	1200
Males 15-17	1200
Females 11-14	1200
Females 15-17	1200

(FSAI 1999)

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	800
Males 65+	800
Females 18-64	800
Females 65+	800
Pregnancy	1200
Lactation	1200

Reference Nutrient Intakes (mg/day)

Age	UK recommendation	US recommendation
0-6 months	525	210
7-12 months	525	270
1-3 years	350	500
4-6 years	450	800
7-10 years	550	800
Males 11-18years	1000	1300
Males 19- 50+ years	700	1000 (1200 after 50)
Females 11-18 years	800	1300
Females 19-50+ years	700	1000 (1200 after 50)
Pregnancy	no increment	1000
Lactation	+ 550	1000

(Geissler and Powers 2005; FSA 2007)

Dosage of Calcium

RDA's – see table

Supplemental Range:
1000-2500mg



Age	Calcium
0.5-1yrs	540-600mg
1-10yrs	800-1200mg
11-24yrs	1000-1500mg
Men (EU)	800mg
Women	800-1000mg
Pregnancy	1200mg
Lactation	1200mg
Post Menopausal Women	1200-1500mg

Daily Reference Intakes

- **It is difficult to establish optimum dietary intakes as calcium balance depends on numerous lifestyle factors:**
 - **High protein, salt, caffeine intake**
 - **Low sun exposure or vitamin D intake**
 - **Low physical activity**

} **calcium wasting factors
(see slides further on)**
- There is a wide variation of calcium intakes around the world
- Higher intakes, when accompanied by calcium-wasting lifestyle factors are not necessarily linked to lower rates of calcium deficiency diseases (e.g. of bone fractures)
- In Western societies, where Ca wasting factors are very common, **higher recommendations are justified!**

% Calcium Absorption

Food	Calcium in 100g	Calcium in 150kcal	Absorbable calcium from 150kcal	% of absorption
Chinese Cabbage	77mg	721 mg	382mg	53%
Kale	135mg	405 mg	202 mg	50%
Full fat milk	113mg	283 mg	90.5 mg	32%
Cabbage	40mg	240mg	153.6 mg	64%
Broccoli	47mg	220 mg	116 mg	52.6%
Brussels sprouts	42mg	142 mg	90mg	63%
Cauliflower	22 mg	132 mg	89mg	68%

Ca from cruciferous vegetables is absorbed 2x as efficiently as Ca from dairy

Calcium - Availability and Absorption

- Ca is absorbed by all parts of the small intestine, but the most rapid absorption after a meal occurs in the more acidic duodenum
- Only about 30% of ingested Ca is absorbed, very few individuals may absorb only 10% and some (rarely) as much as 60%
- Ca is absorbed by an **active** and **passive mechanism**
- The **active absorption** of Ca is controlled by **1.25-dihydroxyvitamin D**
 - Vitamin D stimulates the production of calcium-binding proteins (calbindins)
 - It is important when Ca intakes are below recommended levels
- The **passive absorption** occurs without the help of vit D
 - When a lot of Ca at once is consumed, e.g. from dairy foods

Calcium- Availability and Absorption

- Numerous factors affect Ca bioavailability:
 - The **greater the need and/or the smaller the dietary supply**-the more efficient the absorption
 - e.g. pregnancy, lactation, during resistance exercise (resistance exercise leads to higher bone density)
 - **Low vitamin D intake or/and inadequate sunlight exposure** reduces Ca absorption, esp. among the elderly
 - The efficiency of vitamin D production in older adults is lower

Calcium - Availability and Absorption

- Ca is absorbed only in an ionic form, an **acidic medium** increases its absorption
 - HCl secreted by the stomach lowers the pH of the duodenum, increasing the absorption
 - Thus taking Ca supplements with meals increases its absorption
 - Ageing is associated by achlorhydria (lack of gastric acid secretion) which results in less gastric acidity and reduced Ca absorption

Calcium - Availability and Absorption

- **Lactose** (sugar in milk) increases Ca absorption, however it is only significant in infants
- **Oxalic acid** in rhubarb, spinach, chard, beet greens forms insoluble calcium oxalate in the digestive tract-decreasing Ca absorption
 - Spinach is a rich source of Ca, however the bioavailability of spinach Ca is low

Calcium- Availability and Absorption

- **Phytic acid (phytate)** , a **phosphorous compound** found in outer husks of grains combines with Ca forming calcium phytate, which cannot be absorbed
- **Dietary fibre may decrease** absorption but only in higher amounts
- Some **medications may** decrease absorption or increase Ca excretion leading to bone loss
- In individuals with **fat malabsorption**-Ca forms fatty acids-Ca soaps, which decreases absorption
- Unless the intake of **dietary phosphate (P)** is very high, Ca absorption does not seem to be impaired by dietary P

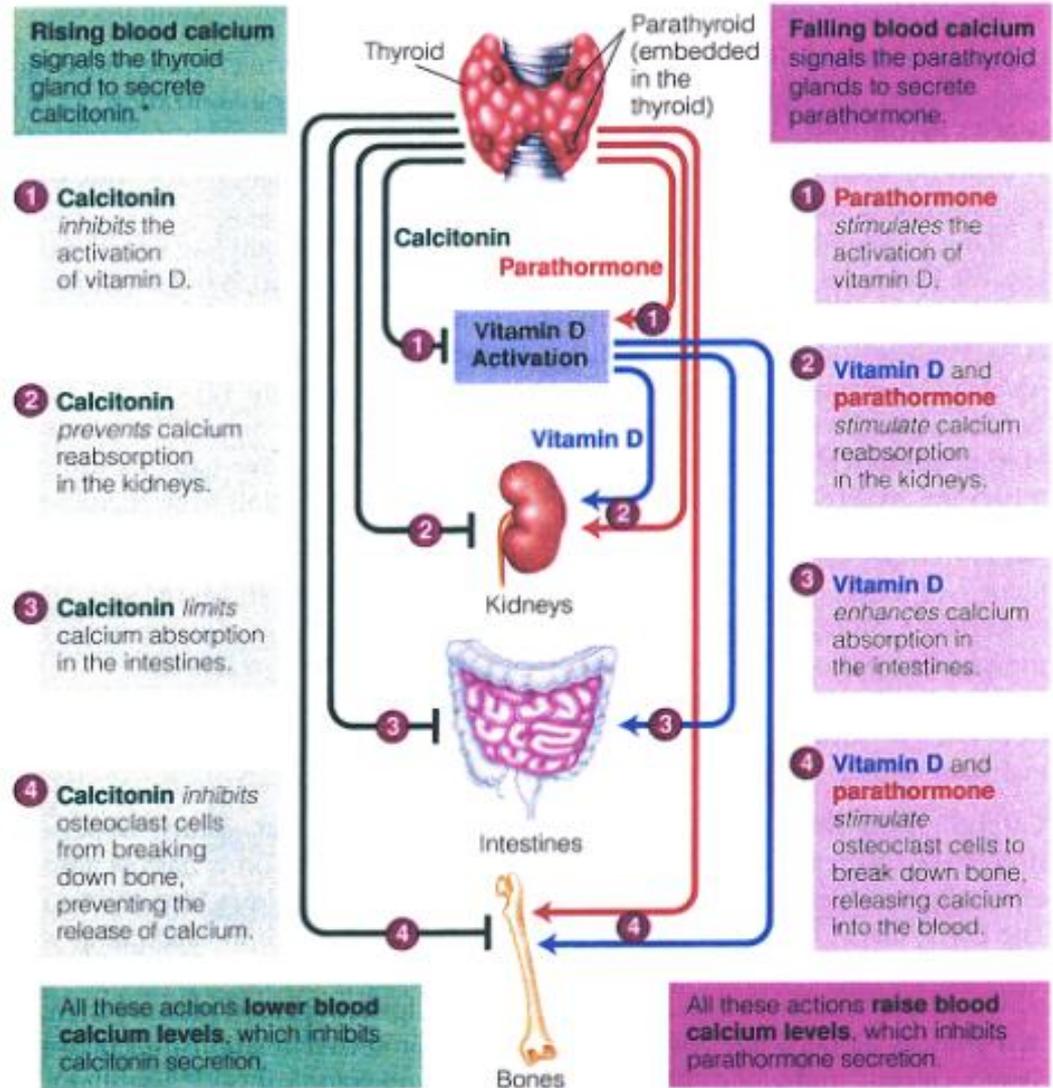
Calcium Metabolism

- 99% of body Ca is found in mineralised tissues (bones and teeth)-as calcium phosphate and calcium carbonate
- The rest-1% is found in extra cellular fluid, muscle and other tissues
- Ca levels in blood are tightly regulated by:
 - **Hormones such as parathyroid hormone (PTH),**
 - **Vitamin D 1.25-dihydroxycholecalciferol**
 - **Calcitonin**
- These serve to decrease or increase the entry of Ca into the blood

(Mahan and Escott –Stump 2008; Strain and Cashman 2002)

Calcium Metabolism

Only in extreme situations (e.g. severe malnutrition or hyperparathyroidism) is the serum Ca concentration below or above normal range; normally Ca balance is tightly regulated by hormones

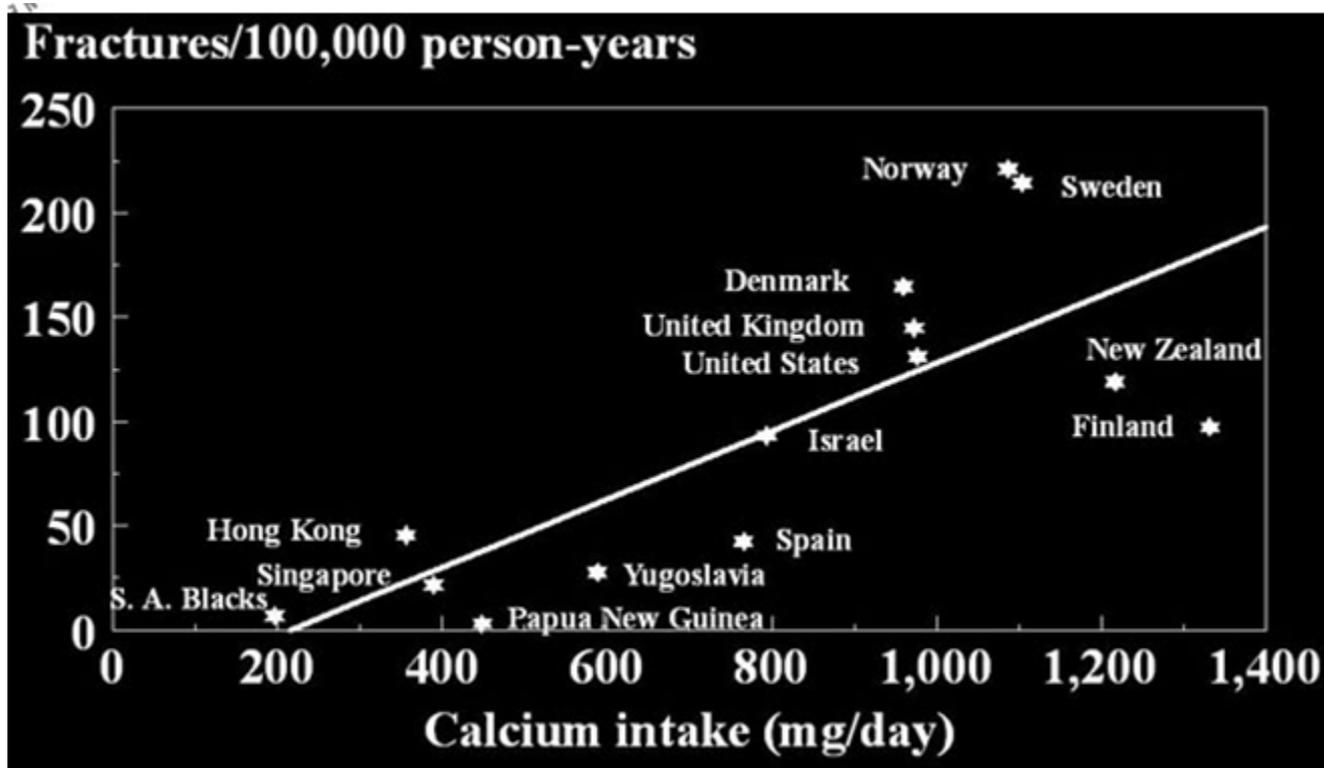


Calcium Excretion

- **Urinary Ca excretion varies throughout life cycle:**
 - It is usually lowest during rapid skeletal growth (adolescents)
 - In menopause-Ca excretion increases
- **Dietary factors increasing urinary calcium excretion:**
 - Diet **high in animal protein** (meat, poultry, fish, cheese) due to the generation of acids (sulphuric acid) from sulphur-containing amino acids abundant in animal products
 - **High caffeine intake** (several cups of coffee a day)
 - **A high-salt diet** (more evidence still needed)

(Mahan and Escott –Stump 2008;)

Calcium Wasting Factors



Higher Ca intakes are NOT the causes of the higher fracture rates, rather they are accompanied by higher protein, salt consumption, lower physical activity and sun exposure

(Frassetto 2000; Abelow 1992)



Calcium Wasting Factors

Focus: High Protein Diets and Calcium Excretion

- High protein intake increases urinary Ca excretion = **protein-induced hypercalciuria; 3 mechanisms:**
- Excess amino acids → urea, a powerful diuretic- → increase in glomerular filtration rate → increase in Ca excretion
- Excess amino acids → decrease in kidney reabsorption of calcium
- Liver metabolizes the S-containing amino acids methionine and cysteine (abundant in animal proteins and isolated soy protein) to acid H₂SO₄ → reduction in blood pH → increased bone resorption → increased urinary Ca losses



Calcium Wasting Factors

- Every 10g dietary protein in excess of our needs increases daily urinary calcium loss by 16mg
- Doubling protein intake increases calcium loss by 50%
- Amount of calcium lost in the urine of a woman after eating a hamburger: 28 milligrams



(Massey 1998)

Calcium Wasting Factors

The relationship between urinary calcium excretion and protein intake is generally well accepted, however confirmation of the source of this excreted calcium is not.

The below meta-analysis and systematic review found little evidence to support a negative relationship between protein intake and bone. In fact there was a slight positive association for protein intake and bone density.

Read more:

<http://ajcn.nutrition.org/content/90/6/1451.full>



Calcium Wasting Factors

- Among the **elderly women of Bantu** osteoporosis does not exist!
 - when the researchers were studying this population (in the 1970s) it was considered a scientific phenomenon
- They had a huge calcium drain, having an average of 10 children and nursing each child for 14 months.
- Their diet included 440 mg of calcium per day, 30%-50% of the Western recommendation; huge amount of physical activity, adequate sun exposure
- Their protein consumption was 50 g/d protein (their diet was mostly plant-based)
- When they move to Western civilization and their dietary and lifestyle pattern changes and they develop osteoporosis



(Walker 1965; Walker et al 1972)

Calcium - Metabolic Functions

- **Building Bone Mass:** adequate Ca, especially in the prepubertal and adolescent years - is critical to permit optimal gains in bone mass
 - The critical period to acquire adequate bone mass and density is during teenage years, and in this period Ca intakes should be optimised
- **Preserving Bone Mass:** sufficient Ca intakes are critical in postmenopausal women to maintain bone health
 - Oestrogen promotes bone formation and lowering levels can precipitate osteoporosis

Calcium - Metabolic Functions

Focus: Childhood Calcium Intake and Adult Bone Density

- Although **adequate** Ca intake during adolescence is one of the conditions for healthy bones in adulthood; **high calcium intakes per se do not protect from future fractures**
- **Metaanalysis, Journal of the American Academy of Paediatrics:**
 - 37 good quality studies on Ca and dairy product intakes during childhood and future bone health
 - 10 showed: Ca supplements and dairy increase bone mineral density in children; however the **effect is very small**
 - 27 showed: **no effect**
 - **Conclusion: ‘Neither consumption of dairy products, nor total dietary Ca has shown even a modestly consistent benefit for child or young adult bone health’**

What has shown the benefit:

Highest physical activity in childhood!



(Lanou et al 2005)

Calcium - Metabolic Functions

- **Blood Clot Formation:**

- Ca is required as a cofactor for numerous enzymatic reactions in the process of blood clot formation

- **Weight Control**

- High dietary calcium is associated with decreased prevalence of being overweight or obese
- **Mechanism:**
 - Depression of PTH and 1.25 hydroxyvitamin D, which leads to inhibition of lipogenesis (fat formation) and increased lipolysis (fat burning)
 - Increased excretion of faecal fat due to soap formation

Calcium - Metabolic Functions

Other Functions at Cellular Level:

- Ca affects cell membrane stability
- It influences the transport of ions across membranes of cell organelles
- It helps the release of neurotransmitters
- It affects the activation of intracellular enzymes
- It is required for nerve transmission
- Adequate Ca intake **might help lower blood pressure**

(Mahan and Escott-Stump 2008; Rolfes et al 2006)

Metabolic Functions

Other Functions at Cellular Level:

- It regulates heart muscle function and smooth muscle contractibility:
 - The proper balance of Ca, Na, K and Mg maintains **muscle tone and controls nerve irritability**
 - A significant increase in the serum calcium level can stop the heart and cause respiratory failure
 - A significant decrease-**tetany** (contraction) of skeletal muscles

(Mahan and Escott-Stump 2008)

Calcium - Specific Therapeutics

- **Bone loss:** in premenopausal women over age 40, following Western diet bone loss can be reduced significantly by supplementing with 1000 mg calcium/day
- But in the 5 years immediately after menopause, calcium supplementation has very little effect on bone loss
 - Right after the onset of menopause, the rapid loss of oestrogen causes a high bone resorption rate, which increases serum calcium levels and therefore decreases intestinal absorption of calcium at that time

Calcium - Specific Therapeutics

Bone loss:

- After this period, calcium supplementation has a significant benefit on bone loss among Western women with numerous Ca –wasting lifestyle factors
- The typical rate of bone loss in postmenopausal women who are not taking calcium supplements is 2% per year
- Calcium 1000-1600 mg/day (as carbonate, citrate, lactate gluconate, or citrate malate) decreases this rate by 0.25% to 1% annually
- **For optimum results, optimal vitamin D status through sun exposure or supplementation (400IU/d) and avoidance of Ca –wasting lifestyle factors should be recommended**

(Maton et al 1999; Koo et al 1999; Nieves 1998; Castelo-Branco 1999; Jackson et al 2006)

Calcium - Specific Therapeutics

- **Foetal bone mineralization:** calcium supplementation in pregnant women who have low dietary Ca intake (less than 560 mg per day), increases foetal bone mineralization and density; however, in women with adequate dietary intake, calcium supplementation does not offer any additional benefit; 300-1300 mg/day beginning at week 20-22 –**always consult patient's doctor first!**
- **Premenstrual syndrome (PMS):** there seems to be a link between low dietary calcium intake and symptoms of PMS; taking calcium 1-1.2 grams daily seems to significantly reduce depressed mood, water retention, and pain associated with PMS
- **Dyspepsia:** taking **calcium carbonate** 0.5-1.5g orally as an antacid is effective for treating dyspepsia

(Maton et al 1999; Koo et al 1999; Thys-Jacobs 1998)

Calcium - Specific Therapeutics

- **Hypertension:** dietary Ca may protect against hypertension; restricting Na without increasing Ca (along with K, and Mg) is not enough to optimally reduce high blood pressure
 - The DASH diet, very successful in lowering blood pressure, was not particularly low in sodium but high in Ca, K and Mg
 - The Dietary Approaches to Stop Hypertension (DASH) study-emphasized high fruit, vegetable, whole grain, and beans along with low meat intake with adequate Ca through plant foods and low fat dairy

Calcium - Deficiency

- A low Ca intake during the growing years limits the bones' ability to reach their optimal mass and density
 - Most people achieve their peak bone mass by their late 20s
 - Dense bones best protect against age-related bone loss
 - Adults lose bone beginning in the early 30s
 - Unlike other diseases-bone loss is asymptomatic, and even blood calcium levels offer no clues as Ca levels remain constant in the serum despite suboptimal intakes

Remember: adequate Ca intake is not a guarantee for healthy bones; equally as important is avoidance of Ca-wasting lifestyle factors!

Factors That Might Affect Individual Requirements

- Insufficiency can easily develop among:
 - Pregnant and lactating women
 - Adolescents who eat a junk-food diet
 - The elderly
 - Vegans eating vegan junk-foods with low whole food intake
- Insufficiency may also result from:
 - High caffeine and alcohol consumption
 - People on high animal protein diets (e.g. Atkins, Zone, etc.)
 - Gastrointestinal dysfunction

Factors That Might Affect Individual Requirements

- Symptoms suggesting inadequate calcium status:
 - Frequent fractures
 - Blood clotting problems
 - Chronically low blood Ca levels (although it might indicate other abnormality, e.g. Vit. D deficiency)
 - Muscle cramps, twitches and symptoms of hypertension

Meeting Your Ca Needs

It is possible to achieve 1000mg from both dairy or plant foods. You need to eat more plant foods, but they come in a healthier package:

- broad beans-100g
- broccoli-1 cup
- 5 dried figs
- 2 cups of lettuce
- tofu (80g)
- chickpeas -1 cup
- soy milk (1 cup)

EQUALS:

- saturated fat: 1g
- cholesterol: 0g
- sodium: 219mg
- fibre, phytonutrients- plenty!

- milk 1%-2 cups
- cheese- 2 slices

EQUALS:

- saturated fat : 12.5g
- cholesterol: 64g
- sodium: 546 mg
- phytochemicals, fibre-none!



Calcium - Toxicity

- Excessive calcium intake from supplements in the long-term has been shown to increase risk of :
 - Kidney stone formation
 - Hypercalcaemia (high blood Ca levels) and renal insufficiency
 - Impaired absorption of Fe, Zn, Mg, P
- Excessive Ca intakes from diet (mainly dairy products-very concentrated sources of Ca) and supplements have been shown to increase the risk of:
 - **Prostate cancer**
 - The mechanism: excessive Ca suppresses the synthesis of 1.25 hydroxyvitamin D; vit D suppresses prostate cancer cell proliferation

Tolerable Upper Intake Level for Adults: 2500mg/day



Calcium - Drug Interactions

- **Biphosphonates** (a class of drugs that prevents bone loss): Ca supplementation decreases the absorption of those drugs
 - **Biphosphonates** include: (Fosamax), etidronate (Didronel), ibandronate (Boniva), risedronate (Actonel), and tiludronate (Skelid)
- **Calcipotriene** is a vitamin D analogue used topically for psoriasis. It can be absorbed in sufficient amounts to cause hypercalcaemia; theoretically, combining calcipotriene with calcium supplements might increase the risk of hypercalcaemia (high blood calcium)
- **Digoxin** (drug used for heart conditions): hypercalcaemia increases the risk of fatal cardiac arrhythmias with digoxin; Ca supplements should be consulted with GP

(Peters et al 2001; Bourke et al 1997; Vella et al 1999)



Calcium - Drug Interactions

- **Hypothyroid medications (levothyroxine):** calcium reduces levothyroxine absorption
- **Quinolone and Tetracycline Antibiotics:** taking calcium at the same time as quinolones/tetracyclins reduces their absorption
 - **Quinolones:** include ciprofloxacin (Cipro), levofloxacin (Levaquin), ofloxacin (Floxin), moxifloxacin (Avelox), gatifloxacin (Tequin), gemifloxacin (Factive), and others
 - **Tetracyclines:** include demeclocycline (Declomycin), doxycycline (Vibramycin), and minocycline (Minocin).



Drug Interactions

- **Thiazide Diuretics:** reduce calcium excretion by the kidneys
- Using thiazides along with moderately large amounts of calcium increases the risk of **milk-alkali syndrome** (hypercalcaemia, renal failure)
- Advise patients to consult their physician about appropriate calcium doses

Magnesium

Forms:

- Magnesium (Mg) is the second most common cation found in the body
- It is evenly distributed between skeleton (50-60%) and soft tissues (40-50%)
- Bone magnesium pool is exchangeable and may serve to maintain serum or soft-tissue magnesium concentrations in times of need
- 99% of body magnesium is **inside cells**



Food Sources of Magnesium

Magnesium is mostly concentrated in plant foods, the richest sources involve:

– Dark leafy green vegetables (& all green vegetables)

– Legumes

– Nuts and seeds

– Whole grains

– Soybeans & tofu



Reference Nutrient Intakes

- The RDA for Mg has been revised upwards for most groups and is currently EU RDA 375mg
- According to these guidelines most Europeans (and Americans alike) are not meeting their magnesium recommendations
- However, the significance of this is still being debated, as there is not a universally accepted reliable magnesium status assessment tool, which makes it difficult to determine the actual consequence of this apparent low intake

(Strain and Cashman 2002)

- The Food Safety Authority of Ireland Working Group has not set a RDA for magnesium, except for infants 0-12 months, where the RDA is 55-80 mg/d (UK).

- (FSAI 1999)

Reference Nutrient Intakes (mg/day)

(Geissler and Powers 2005; FSA 2007; USAD 2009)

Age	UK recommendation	US recommendation
0-6 months	60	30
7-9 months	75	75
10-12	80	75
1-3 years	85	80
4-6 years	120	130
7-10 years	200	130
Males 11-14 years	280	240
Males 15-18 years	280	410
Males 19-50+ years	300	420
Females 11-14 years	280	240
Females 15-18 years	300	360
Females 19-50 years	300	320
Females 50+ years	270	320
Pregnancy	no increment	350
Lactation	+ 550	310

Mg in Selected Foods

Food per 100g	mg
Pumpkin Seeds	535
Flaxseeds	392
Brazil nuts	376
Tahini	362
Soybeans	280
Mung Beans	267
Buckwheat	231
Sundried Tomatoes	194
Tofu	181
Oats	177
Dried Corn	149
Beef steak	23



Dosage of Mg

- Supplemental Range: 300 - 1000mg in divided doses
- High doses of Mg can cause diarrhoea, abdominal discomfort and cramping.
- RDAs – see table

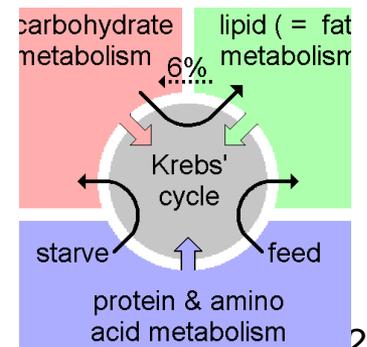
Age	Magnesium
0.5-1yrs	40-60mg
1-10yrs	80-170mg
11-24yrs	280-300mg
Adult (EU)	375mg
Lactation	355mg

Magnesium - Availability and Absorption

- Mg is absorbed in the small intestine
- In normal healthy humans Mg absorption ranges from 20-70% from a meal
- Due to chemical similarity between Mg and Ca, **large** changes in vitamin D status affect Mg status as well
- Phosphate (especially from high-phytate containing foods) and Ca may be an inhibitor of Mg absorption
- Protein and fructose may enhance Mg absorption

Magnesium - Metabolic Functions

- Magnesium participates in hundreds of enzyme systems where it acts as a **catalyst**:
 - Its major role is in the reaction that adds the last phosphate to the high-energy compound ATP; making it **essential in energy production**
 - As a component of ATP metabolism, Mg is essential for:
 - **The use of glucose**
 - **Synthesis of fat, protein and nucleic acids**
 - **The cell's membrane transport systems**



(Rolfes et al 2006)

Metabolic Functions

- Together with **Ca**, it is involved in:
 - **Blood clotting:**
 - Ca promotes blood clotting, Mg inhibits it
 - **Muscle contraction**
 - **Regulating blood pressure**
 - **Lung function**
- Mg also **prevents dental caries** by holding Ca in tooth enamel
- It is essential in the functioning of the **immune system**



Magnesium - Metabolic Functions

Ion transport across cell membranes

- Magnesium is required for the active transport of K and Ca ions across cell membranes. As a result of Mg's role in ion transport systems, magnesium affects the conduction of nerve impulses, muscle contraction, and normal heart rhythm
- Cell signalling requires MgATP for the phosphorylation of proteins and the formation of the cell-signalling molecule cAMP. cAMP is involved in many processes
i.e. secretion of parathyroid hormone

Magnesium - Specific Therapeutics

- **Constipation:** taking magnesium orally is helpful as a laxative for constipation; magnesium citrate, sulphate, and hydroxide salts are typically used for this indication;
 - Remember: changing a patient's diet is the most effective way to help constipation and should always be the first step
- **Dyspepsia:** taking magnesium orally as an antacid reduces symptoms of gastric hyperacidity; magnesium carbonate, hydroxide, oxide are used
- **Coronary artery disease:** taking magnesium orally may reduce angina attacks in people with coronary artery disease; **always consult the GP**

Magnesium - Specific Therapeutics

- **Diabetes:** higher **dietary magnesium** intake is associated with a reduced risk of developing type 2 diabetes
- A 100 mg/day increase in dietary magnesium intake might be associated with a 15% risk reduction for developing type 2 diabetes; 100mg of Mg is contained in:
 - 4 slices of whole grain bread
 - 1 cup of beans
 - 1/4 cup of nuts
 - 1/2 cup of cooked spinach
 - 3 bananas

Magnesium - Specific Therapeutics

- **Diabetes:** results of clinical studies using magnesium supplements in patients with type 2 diabetes or insulin resistance have been mixed
 - Some research suggests magnesium supplements can decrease fasting blood glucose and improve insulin sensitivity
 - However, other research suggests no effect of magnesium on insulin or glucose levels
- **Kidney stones:** taking magnesium orally (as magnesium hydroxide) may prevent the recurrence of kidney stones

Magnesium - Specific Therapeutics

- **Metabolic Syndrome:** higher magnesium intake **from diet** is associated with a 27% lower risk of developing metabolic syndrome in healthy women and a 31% lower risk in healthy young adults
- **Migraine headaches:** taking high-dose magnesium citrate orally (600mg/day) seems to reduce the frequency and severity of migraine headaches; however, other research suggests that magnesium doesn't have any effect
- **Osteoporosis:** epidemiological research suggests that **high dietary** magnesium intake is related to greater bone mineral density

Magnesium - Specific Therapeutics

- **Premenstrual syndrome (PMS):** taking magnesium orally (200-360 mg/d) seems to relieve symptoms of PMS; magnesium supplementation can improve symptoms including mood changes and fluid retention in some patients with PMS
- **Stroke:** there is some evidence that increasing **dietary magnesium** intake might decrease the risk of stroke in men; however, there is no proof that taking magnesium supplements has this same effect
- **Hypertension:** Mg is critical to heart function and **high dietary Mg** seems to protect against hypertension and heart disease; in Mg deficiency the walls of the arteries and capillaries tend to constrict

(Bendich et al 2000; Ascherio et al 1998; Rolfes et al 2006)

Magnesium - Deficiency

Mg deficiency is uncommon, however lowered Mg status is very common!

Some symptoms include:

- Muscle cramps, twitches, weakness
- Anxiety, nervous tension, tension headaches, depression, irritability, insomnia, behavioural disturbances, seizures
- Fatigue, chronic fatigue syndrome
- Heart arrhythmias, hypertension, MIs, palpitations, cold hands and feet, atherosclerosis
- Poor immunity, free radical damage, decreased membrane integrity
- Asthma
- PMS
- Osteoporosis
- Reduced pain threshold

Factors That Might Affect Individual Requirements

- Deficiency of Mg in humans is rare, mostly it is associated with the presence of other illnesses
- Poor magnesium status has been found in patients with:
 - **Cardiovascular disease**
 - **Renal disease**
 - **Diabetes mellitus**
 - **Hypertension**
 - **Athletes**
- Reasons to suspect magnesium insufficiency
 - Alcoholism
 - The elderly with eating difficulties
 - Pregnant women with poor dietary habits
 - Anyone with poor dietary habits!

(Gropper et al 2005; Liska et al 2004)



Magnesium -Toxicity

- Magnesium ingested from foods has not been shown to exert any adverse effects
- Excessive intakes from supplements in the long-term have been shown to cause:
 - Diarrhoea
 - Nausea
 - Abdominal cramping

Tolerable Upper Intake Level for Adults: 400mg/day of non-food magnesium



Magnesium - Drug Interactions

- **Biphosphonates (drugs that prevent loss of bone mass) :** magnesium can decrease bisphosphonate absorption; advise patients to separate doses of magnesium and these drugs by at least 2 hours
- **Calcium Channel Blockers** (anti-hypertension drugs): magnesium inhibits calcium entry into smooth muscle cells and may therefore have additive effects with calcium channel blockers; severe hypotension can occur when high doses of Mg are given with these drugs
- **Potassium-sparing diuretics:** also have magnesium-sparing properties, which can counteract the magnesium losses and lead to excessive magnesium levels when taken with Mg supplements
 - they include (miloride (Midamor), triamterene (Dyrenium), and spironolactone (Aldactone))



Magnesium - Drug Interactions

- **Quinolone Antibiotics:** magnesium can form insoluble complexes with quinolones and decrease their absorption
- **Tetracyclin antibiotics:** magnesium can form insoluble complexes with tetracyclines and decrease their absorption and antibacterial activity
- Advise patients to take these drugs at least 2 hours before, or 4 to 6 hours after, magnesium supplements

(Dunn et al 2001; Hansten et al 1997; Ryan et al 1987)



Zinc

Forms:

- Zinc (Zn) is the most abundant intracellular trace element
- Human body contains 2g of Zn of which about 60% is in skeletal muscles and 30% in bones, 4-6% in skin
- Zn in those tissues is not accessible at times of deprivation
- Body has no specific zinc reserve and is dependent on a regular dietary supply of the element





Food Sources of Zinc

- Zinc is highest in protein-rich foods like oysters, meats, poultry and liver
- Legumes and whole grains are also good Zn sources when eaten in considerable quantity
 - in a typical Western diet, phytate content is not high enough to impair Zn absorption
- Vegetables vary in Zn content depending on the soil in which they are grown
- Oysters, seafood
- Pumpkin seeds, sunflower seeds, cashews
- Fresh root Ginger
- Whole grains
- Beef, lamb, liver



(Strain and Cashman 2002; Osiecki 2004)

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
0-12 months	(UK) 4.0-5.0
1-3 years	4
4-6 years	6
7-10 years	7
Males 11-14 years	9
Males 15-17	9
Females 11-14	9
Females 15-17	7

(FSAI 1999)

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	9.5
Males 65+	9.5
Females 18-64	7
Females 65+	7
Pregnancy	7
Lactation	12

Reference Nutrient Intakes (mg/day)

Age	UK recommendation	US recommendation
0-6 months	4	2
7 months-3 years	5	3
4-6 years	6.5	5
7-10	7	5
Males 11-14 years	9	8
Males 15-18 years	10-15	11
Males 19-50+ years	10-15	11
Females 11-14 years	10-15	8
Females 15-18 years	10-15	9
Females 19-50+	10-15	8
Pregnancy	19-20	11
Lactation	0-4 months + 6 4+ months +2.5	12

(Geissler and Powers 2005; FSA 2007; USDA 2009)

Zinc Sources in Selected Foods

Food per 100g	mg
Oysters Raw	90-200
Beef Liver	7.8
Pulses raw	0.2-5.0
Beef	4.3
Whole Wheat Flour	2.9
Pork	2.4
Brown Rice	2.0
Chicken	1.1
Wheat Flour	0.6-0.9
Green Leafy Vegetables	0.2-0.6
Cod, plaice, whiting	0.3-0.5
Potatoes	0.2-0.3

(FSA 2007; USDA 2009)

Dosage of Zinc

- RDAs – see table
- Supplemental Range: 10-100mg (divided doses will avoid any side effects)
- Watch out for copper deficiencies as Zn supplementation interferes with Cu absorption and metabolism



Age	Zinc
Infant	5mg
Child (under 10 yrs)	7-10mg
Adult (EU)	10mg
Pregnancy	19mg

(Osiecki 2004; FSA 2007; EUFIC 2011)

Zinc – Availability and Absorption

- The bioavailability of Zn depends on dietary enhancers and inhibitors:
 - **Enhancers:**
 - low Zinc status-the more is needed, the more is absorbed
 - **Inhibitors:**
 - Phytates, oxalates and polyphenols bind Zn and make it less available
 - Excess iron, copper and calcium may inhibit Zn absorption
- Absorption from a mixed animal and plant based diet-20-30%
- Absorption from a plant-based diet (high in phytates)-15%

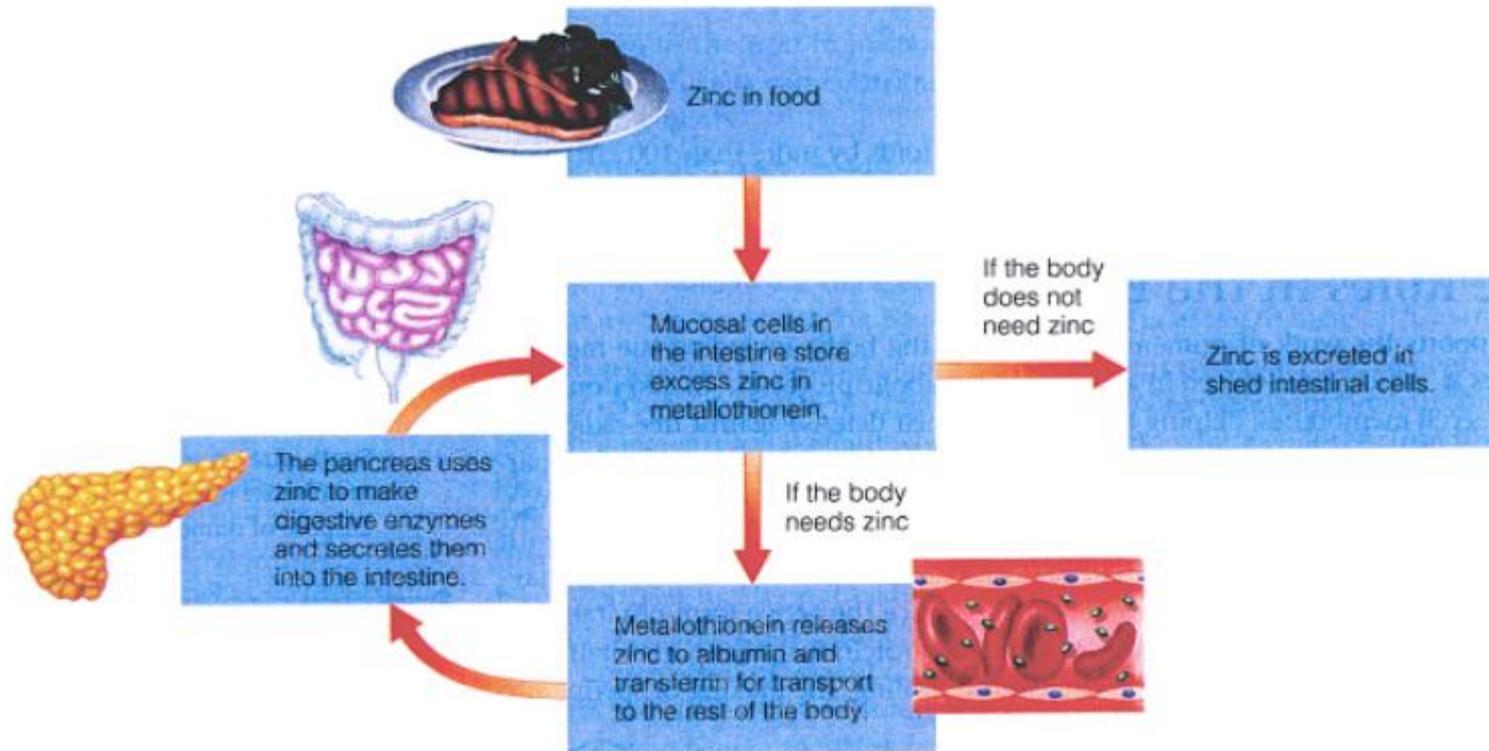
(Strain and Cashman 2002)

Metabolism of Zinc

- Upon absorption Zn is retained by a storage protein-**metallothionein**
- **Metallothionein** regulates zinc absorption by holding it in reserve until the body needs zinc-then metallothionein releases it into the blood where it can be transported around the body
- Some Zn reaches the pancreas where it is incorporated into digestive enzymes, released during meals
 - This Zn is recycled back to the pancreas through **enterohepatic Zn circulation**

Enterohepatic Zn Circulation

Some zinc from food is absorbed by the small intestine and sent to the pancreas to be incorporated into digestive enzymes that return to the small intestine. This cycle is called the enteropancreatic circulation of zinc.



(Rolfest et al 2006)

Zinc - Metabolic Functions

Zn is a component of numerous **metalloenzymes** (at least 70). E.g:

- **Superoxide Dismutase (SOD)** –which serves in cell antioxidant defences
- **Alcohol Dehydrogenase** – important in the conversion of alcohols to aldehydes (e.g. breakdown of consumed alcohol)
- **Carboxypeptidase**-secreted by the pancreas needed for the digestion of protein
- **Other enzymes** involved in:
 - Haem synthesis
 - Digestion of folate (poor Zn status can diminish folate absorption)
 - Nucleic acid synthesis (DNA, RNA)

Zinc -Metabolic Functions

Zn is also involved in:

- **Cell growth and cell replication**
- **Sperm formation**
- **Bone formation**
- **Skin integrity**
- **Cell-mediated immunity**
- **Carbohydrate metabolism** i.e Zn deficiency decreases insulin response, resulting in impaired glucose tolerance
- **Basal Metabolic Rate (BMR)** i.e. a decrease in thyroid hormones and BMR has been observed in subjects receiving a zinc-restricted diet

Zinc - Specific Therapeutics

- **Zinc deficiency:** taking zinc orally prevents and treats zinc deficiency; however, routine zinc supplementation is not recommended due to mineral-mineral interactions
- **Acne:** taking zinc orally (30mg) might help treat acne; research suggests that people with acne might have lower serum and skin zinc levels; clinical trials have been small, but most suggest that zinc can improve acne
- **Age Related Macular Degeneration (AMD):** large scale population studies suggest that increasing **dietary intake of zinc** might reduce the risk of developing AMD

Zinc - Specific Therapeutics

- **Attention deficit - hyperactivity disorder (ADHD):** taking zinc orally in combination with conventional treatment might modestly improve symptoms of hyperactivity, impulsivity, and impaired socialization, but not attention deficit in some children with ADHD; zinc sulphate 55 mg was used in those studies (**always consult the GP**)
- **Common cold:** using zinc oral lozenges seems to help decrease the duration of the common cold in adults; the majority of studies show a significant decrease in the duration of symptoms when adults take zinc gluconate or acetate lozenges providing 9-24 mg elemental zinc per dose; lozenges should be taken every 2 hours while awake, starting within 48 hours of symptom onset
 - However, not all studies have been positive

(Akhondzadeh et al 2004; Bilici et al 2004; Godfrey et al 1992; Petrus et al 1998; Douglas et al 1997)

Zinc - Specific Therapeutics

- **Hypogeusia** (lack of taste): taking zinc orally (25mg) might be effective for taste dysfunction in some patients with zinc depletion
- **Osteoporosis**: lower **dietary zinc** intake and zinc serum levels seem to be associated with lower bone mineral density (BMD) in men and women

(Henkin et al 1976; Atik 1983)

Zinc - Deficiency

Zn deficiency can be caused by:

- A diet very high in unrefined grains and unleavened breads due to their high phytate content with little Zn-rich food sources like meats or pulses
 - Bread fermentation increases Zn absorption
- Malabsorption
- Starvation
- Increased losses via urinary, pancreatic or secretions



(Mahan and Escott-Stump 2008)

Zinc- Deficiency

Symptoms include:

- **Short stature**
- **Decreased taste acuity – loss of taste or smell**
- Delayed wound healing, skin lesions, itchy skin
- Alopecia (hair loss)
- Alcohol intolerance
- **Immune system impairment** (even mild Zn deficiency)
 - decreased immune cell activity, atrophy of the thymus
- Anorexia nervosa, depression, over the top stress response, learning disorders, poor memory
- Reproductive disorders, infertility, stretch marks
- **Hypogonadism**
- Mild anaemia (which may reflect coexisting Fe deficiency from the same cause)

(Mahan and Escott-Stump 2008; Osiecki 2004)

Factors That Might Affect Individual Requirements

- Groups at increased risk of insufficiency:
 - Patients with alcoholism
 - Pregnant women
 - Older adults
 - Athletes
- Insufficiency symptoms may include:
 - Sleep disturbances, slow wound healing, dandruff, reduced appetite, skin disorders

(Mahan and Escott-Stump 2008)



Zinc -Toxicity

- High doses (40-45-mg) of Zn may cause:
 - Vomiting
 - Diarrhoea
 - Headaches
 - Exhaustion

Tolerable Upper Intake Level for Adults: 40mg/day – based on the interference with copper metabolism- an effect that in animals leads to degeneration of the heart muscle!

(Rolfes et al 2006)



Zinc - Drug Interactions

- **Penicillamine** (used as a form of immunosuppression to treat rheumatoid arthritis) : Zinc forms an insoluble complex with penicillamine, interfering with penicillamine absorption and activity
- **Quinolone Antibiotics and Tetracyclin Antibiotics:** quinolones and tetracyclins form complexes with zinc in the gastrointestinal tract, reducing absorption their absorption and that of and zinc if taken at the same time

Phosphorus

- Phosphorus (P) is the second most abundant mineral in the body
- About 85% of it is found combined with Ca in the hydroxyapatite crystals of bones and teeth
- Phosphorus is never found free in nature
- It is mostly found bound to oxygen as phosphate (PO_4^{3-})

(Strain and Cashman 2002; Rolfes et al 2006)

Food Sources of Phosphorus

- Phosphate is an essential constituent of all known plant and animal tissues and thus widely distributed in all foods
- Diets that provide enough energy and protein also supply adequate phosphorus-**dietary deficiencies of phosphorus are unknown**
- Foods especially rich in phosphorus include:
 - Beans and legumes
 - Dairy
 - Meats
 - Processed foods (especially soft-drinks)



(Strain and Cashman 2002; Rolfes et al 2006)

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
0-12 months	No value
1-3 years	300
4-6 years	350
7-10 years	450
Males 11-14 years	775
Males 15-17	775
Females 11-14	625
Females 15-17	625

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	550
Males 65+	550
Females 18-64	550
Females 65+	550
Pregnancy	550
Lactation	950

Reference Nutrient Intakes

- The RDA for phosphorus for adults =700mg/day
- No adverse effects of high dietary phosphorus intakes have been reported
 - In the past a high intake of dietary phosphorus (mostly from soft drinks) was blamed for bone loss; today we know that it is the displacement of calcium-rich foods by soft drinks and not their phosphorus content that is responsible for bone loss
 - **Tolerable Upper Intake Level for Adults: 4000mg/day**

(Oseiki, n.d.)

Phosphorus Sources in Selected Foods

(Linus Pauling Institute 2011)

Food	Serving	Phosphorus (mg)
Milk, skim	1 cup	247
Yogurt, plain nonfat	1 cup	385
Cheese, mozzarella; part skim	28g	131
Egg	1 large, cooked	104
Beef	840mg	173
Chicken	840mg	155
Turkey	840mg	173
Fish, halibut	840mg	242
Fish, salmon	840mg	252
Bread, whole wheat	1 slice	57
Bread, enriched white	1 slice	25
Carbonated cola drink	340mg	40
Almonds	23 nuts	134
Peanuts	28g	107
Lentils	1/2 cup, cooked	178

Dosage of Phosphorus

- RDAs – see table
- Supplemental Range: 400-1400mg



Age	Phosphorus
0-1 yrs	300-500mg
1-10yrs	800mg
11-14yrs	1200mg
Adult (EU)	700mg
Pregnancy	1200mg
Lactation	1200mg

Phosphorus - Availability and Absorption

- P absorption ranges from 50-70%
- There appears to be no adaptive mechanism to improve P absorption at low intakes (unlike Ca)
- P absorption is reduced by aluminium-containing antacids and excessive calcium carbonate supplementation



(Strain and Cashman 2002)

Phosphorus- Metabolic Functions

Anything requiring Phosphate:

- Bone growth
- Intracellular fluids
- Calcium homeostasis, maintains blood pH
- Component of DNA & RNA, Phosphoproteins/lipids (cell membranes), nucleic acids
- Energy metabolism, ATP (adenosine tri-phosphate) production
- Muscle contraction, creatine phosphate
- Phosphorylation reactions



Phosphorus- Toxicity

- Phosphorus intakes from natural foods will not lead to toxicity
- However, phosphorus from regular consumption of processed foods (as additives, mainly soft drinks) could possible lead to hyperphosphataemia (high P in the blood)
- This could result in decreased Ca absorption as P can complex Ca in the chyme
- Polyphosphates from food additives can interfere with Zn, Cu and Fe absorption

(Rolfes et al 2006; Strain and Cashman 2002)

Potassium

Introduction/Absorption

- Potassium (K) is the principal cation inside the body cells
- **Potassium, sodium and chloride** comprise the **principal electrolytes** within the body
- More than 90% of potassium is absorbed from the diet
 - Olive oil can increase the absorption
 - Fibre can slightly decrease the absorption



(Strain and Cashman 2002; Rolfes et al 2006)



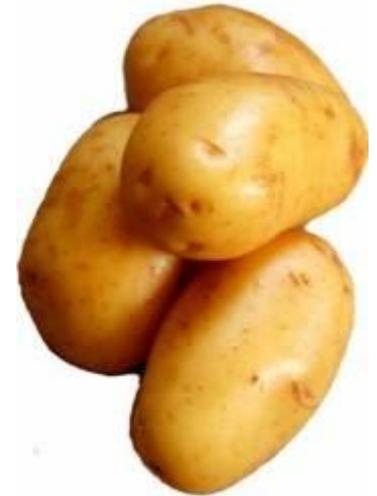
Food Sources of Potassium

Potassium is widely distributed in natural, unprocessed foods, the richest sources are fruits and vegetables:

- Apricots
- Avocado
- Banana
- Citrus fruits
- Dates and raisins
- Potatoes
- Almonds and sunflower seeds

Also in:

- Herring and sardines
- Milk



Food processing (leaching) and the addition of salt decreases K content

Reference Nutrient Intakes

- Adult requirements are estimated to be 2g/day
- However, due to the high salt content of the Western diet, 3.5g-4.7/day is thought to be more adequate
- In order to meet this requirement, more fruits and vegetables need to be added to a typical Western diet
- Intakes of more than 6g may be dangerous for people with impaired renal function

(Strain and Cashman 2002; Rolfes et al 2006)

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
0-12 months	(UK) 700-850
1-3 years	800
4-6 years	1100
7-10 years	2000
Males 11-14 years	3100
Males 15-17	3100
Females 11-14	3100
Females 15-17	3100

Recommended Dietary Allowances

(mg/d)

Age	Irish Recommendations (1983, revised 1999)
Males 18-64	3100
Males 65+	3100
Females 18-64	3100
Females 65+	3100
Pregnancy	3100
Lactation	3100

Potassium in Foods and Dosages

- EU RDA for an adult is 2000mg per day
- Supplemental Range: 3-8gm

Potassium Content in 100mg	
Pinto Beans	1393mg
Potato	413mg
Banana	358mg
Winter Squash	347mg
Tomato	237mg
Cheddar Cheese	98mg
Corn Flakes	<u>79mg!</u>
Corn Raw	<u>270mg!</u>

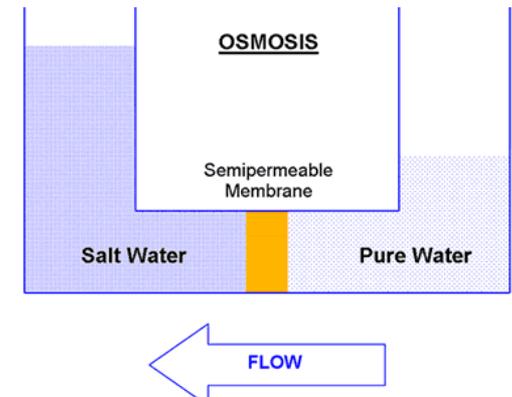
Potassium Metabolism

- An average 70kg male contains ca. 120g of potassium
- Various hormonal factors regulate potassium homeostasis
 - In **hyperkalaemia**: insulin, aldosterone and adrenaline promote uptake of K by body cells; aldosterone promotes K kidney excretion
 - In **hypokalaemia**: potassium is released from the cells

(Strain and Cashman 2002)

Potassium - Metabolic Functions

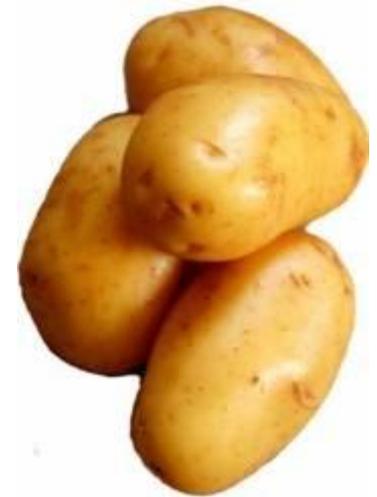
- Potassium, together with sodium and chloride, is the major determinant of **osmotic pressure** and **electrolyte balance**
- The concentration difference of potassium and sodium across cell membranes is critical for:
 - **Nerve transmission**
 - **Muscle function**
- Potassium is a cofactor for enzymes involved in **energy metabolism, glycogenesis, cellular growth and division**



Potassium Deficiency

Potassium deficiency symptoms:

- Muscle cramps
- Muscle fatigue and weakness
- Irregular heartbeat
- Fatigue mental
- Mental confusion
- Irritability
- Abnormally dry skin
- Insatiable thirst
- Insomnia
- Diarrhoea
- Low blood pressure



(Strain and Cashman 2002)

Potassium - Specific Therapeutics

- Low potassium intakes contribute to the development of high blood pressure
- High food potassium intakes (fruits, vegetables, beans) both prevent and correct hypertension
- Potassium rich fruits and vegetables also appear to reduce the risk of stroke-more so than can be explained by the reduction in blood pressure alone
- Decreasing salt intake combined with increasing K intake is more effective in correcting hypertension than decreasing salt intake alone

(Rolfes et al 2006; Strain and Cashman 2002)

Potassium - Deficiency

- Potassium levels are very tightly regulated by homeostatic mechanisms
- Deficiency results from excessive losses rather than deficient intakes:
- **Hypokalaemia** (low K levels in plasma) can result from:
 - Cushing's disease (excess steroids)
 - Diuretics that enhance potassium loss
 - Chronic renal disease
 - Diarrhoea
 - Vomiting
 - Laxative abuse



Potassium - Toxicity

- Potassium toxicity does not result from overeating foods high in potassium; therefore Upper Level was not set:
- It can result from: overconsumption of potassium salts or supplements (including some 'energy fitness shakes') or certain diseases and treatments
- Excess potassium from supplements can stop the heart; try increase potassium levels with foods!
- **Acute:** cardiac arrhythmias, CNS paralysis, diarrhoea, fever, polydipsia, renal necrosis, convulsions
- **Chronic:** cardiac and CNS depression, paralytic extremities, mental confusion, tingling, weakness, cardiac arrest, kidney failure, dehydration, adrenal insufficiency.

Sodium and Chloride

- One of the sodium salts-sodium chloride (table salt) is the major source of sodium in foods
- Sodium and chloride intakes in humans are closely matched
- Salt was of major importance in early civilisations and in prehistory
- Humans have special taste and salt appetite systems
 - This led to special culinary uses for salt
- Nowadays salt is used to modify flavour, alter the texture and control microbial growth in foods



(Strain and Cashman 2002)



Food Sources of Sodium & Chloride

- Sodium and chloride are present in most natural foods
- However the richest sources of both sodium and chloride are processed foods, where NaCl has been added



(Strain and Cashman 2002)

Reference Nutrient Intakes

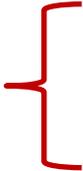
Diets consisting of natural foods (with no salt added at all) will provide adequate amounts of both sodium and chloride!

- Average minimum requirements for sodium-500mg/day
- Average minimum requirements for chloride-750mg/day
- Average Western sodium intake – 2000-14000 mg/day (with chloride following sodium intake slightly in excess)
- Recommended maximum sodium intake: 2300mg/day

(Strain and Cashman 2002; Rolfes et al 2006)

Sodium Intake in Various Populations (gm/day)

there is almost no hypertension among those communities



Japan in the 1960ties-highest rates of hypertension and therefore strokes in the world



Before 1982	Year	Intake	From 1988	Year	Intake
<i>Communities not using added salt</i>					
Brazil (Yanomamo Indian)	1975	0.06			
New Guinea (Chimbus)	1967	0.40			
Solomon Islands (Kwaio)		1.20			
Botswana (Kung bushmen)		1.80			
Polynesia (Pukapuka)		3.60			
Alaska (Eskimos)	1961	<4.00			
Marshall Islands in the Pacific		7.00			
<i>Salt-using communities</i>					
Kenya (Sambura nomads)		5-8	Mexico (Tarahumsa Indian)		3-10
Mexico (Tarahumsa Indian)	1978	5-8	Mexico, rural (Nalinalco)	1992	5.7
			Mexico, urban (Tlaplan)	1991	7.18
Denmark		9.8	Denmark	1988	8.00
Canada (Newfoundland)		9.9	Canada		8-10
New Zealand		10.1			
Sweden (Göteborg)		10.2			
USA (Evans Country, Georgia)		10.6	USA (Chicago)		7.7
Iran		10.9			
Belgium	1966	11.4	Belgium	1988	8.4
UK (Scotland)		11.5			
Australia		12.0			
India (north)		12-15	India		9-11.4
Federal Republic of Germany		13.1			
Finland (east)		14.3	Finland		10.6
Bahamas		15-30			
Kenya (Samburus, army)	1969	18.6			
Korea		19.9			
<i>Japan</i>					
Japan (farmers)	1955	60.3	Japan	1988	8-15
Japan (Akita)		27-30			
Japan	1964	20.9			

(Strain and Cashman 2002)

Sodium Content of Food & RDAs

EU has no established RDA for sodium

Sodium Content in 100gm	
Wheat flour	5mg
Crisp bread (Wheat)	264mg
French Baguette	670mg
Sausages	1131mg
Cheddar Cheese	629mg
Broccoli	33mg
Corn	<u>35mg</u>
Cornflakes	<u>949gm</u>

Age	Sodium
Infant	120mg
Adults < 18yrs	500mg
Adult	2.4-3g

Sodium and Chloride : Absorption and Metabolism

- Sodium (Na) is the major extracellular electrolyte and exists as a water-soluble cation: Na⁺
- Chloride (Cl) is also mainly found in extracellular fluid as the chloride anion Cl⁻
- Both are **easily absorbed** from the digestive tract (95-100% absorption rate)
- Average 70kg male has about 90g sodium with up to 75% contained in the mineral apatite of bone

(Strain and Cashman 2002)

Sodium and Chloride : Metabolism

- Plasma sodium is **tightly** regulated through a hormone system, which also regulates water balance, pH and osmotic pressure
- **Angiotensin** and **aldosterone**: conserve sodium by increasing sodium reabsorption by the kidney
- When Na levels go down, **renin** is secreted that generates **active angiotensin** in the circulation, which:
 - Stimulates vasoconstriction
 - Increases blood pressure
 - Decreases water loss
 - Stimulates aldosterone release



(Strain and Cashman 2002)

Sodium and Chloride : Metabolism

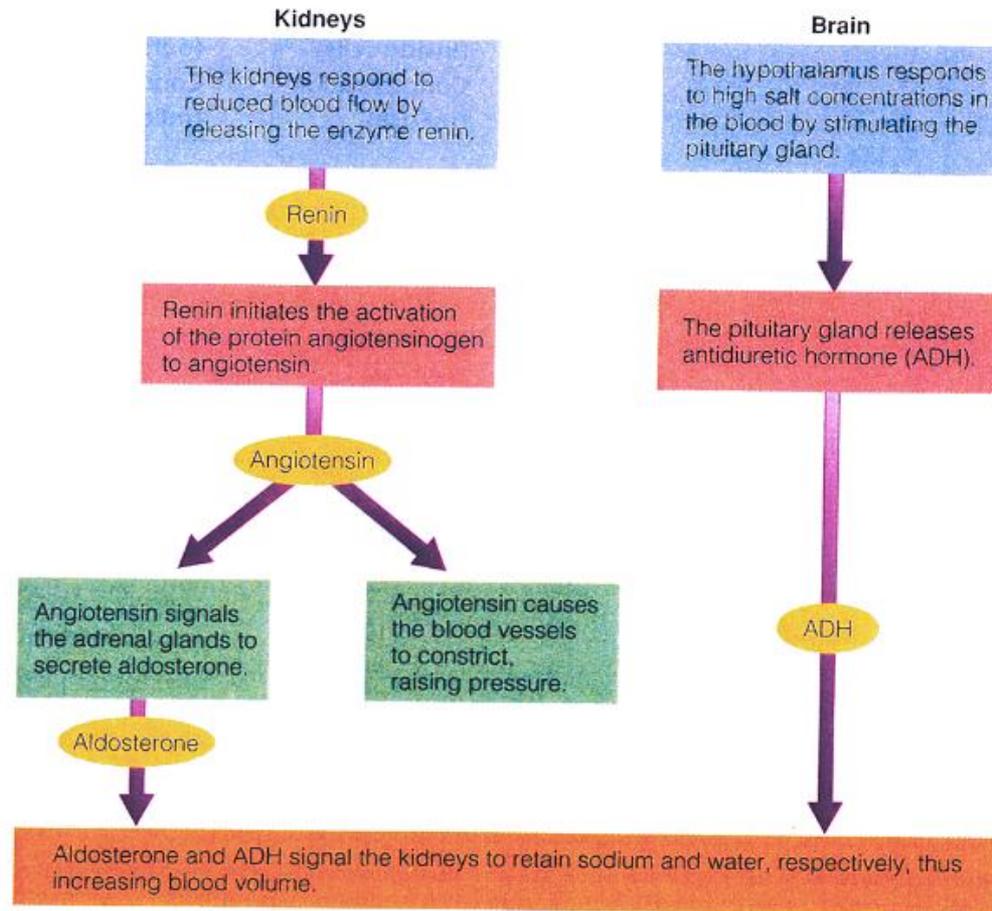
- **Atrial natriuretic** hormone counteracts sodium retention mechanisms by suppressing renin, aldosterone and angiotensin release
- A raised plasma sodium stimulates the release of **antidiuretic hormone** that stimulates renal reabsorption of water
- Chloride is passively distributed throughout the body and moves to replace anions lost from cells via other processes

Sodium and Chloride : Metabolic Functions

- Sodium is a principal cation of the extracellular fluid and the primary active **regulator of its volume**; chloride is a **passive regulator of the volume**
- Na and Cl help maintain **acid-base balance**
- Na is essential in **nerve impulse transmission**
- Na helps in **muscle contraction**
- Chloride is a constituent of a **hydrochloric stomach acid**

Specific Therapeutics

Sodium & Blood Volume



Specific Therapeutics

Sodium & Blood Volume

HYPERTENSION:

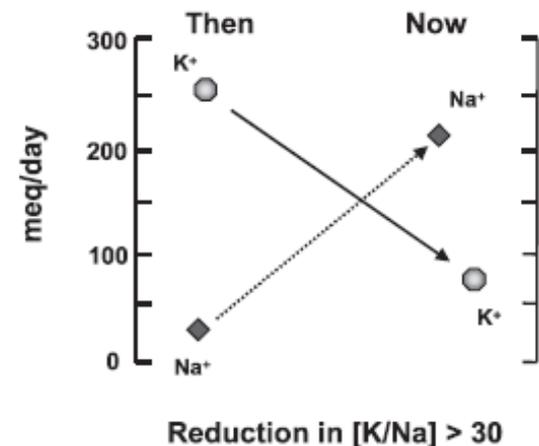
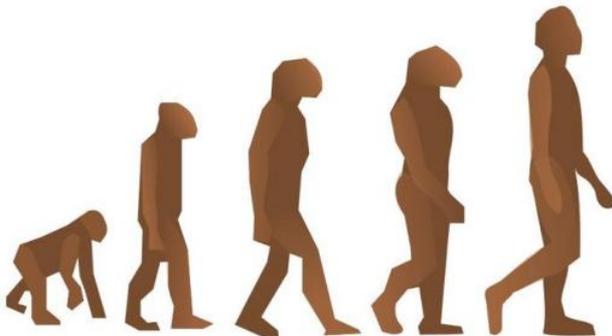
- Sodium is considered the primary factor responsible for high blood pressure
- Salt (NaCl) has a greater effect on blood pressure than either sodium or chloride alone
- Certain individuals appear to be particularly sensitive to high salt intakes:
 - Those with family history of hypertension
 - Those with chronic kidney disease
 - Those with diabetes
 - People of African origin
 - People over 50
 - Overweight people
 - Additionally, **low Ca, K, and Mg** intakes encourage the Na-induced hypertension





NaCl & Evolution

- During the long period of human evolution **no salt was added to foods** and therefore the body has evolved a very efficient mechanism conserving sodium
- At the same time, **potassium intake was high** and humans have developed efficient mechanisms to excrete excess K
- **K: Na ratio** in the original human diet: 10:1
- **K: Na ratio** in the Western diet: 1:3 (!)



(Frassetto et al 2001)



NaCl & Evolution

The more processed the food is, the less K and the more Na it contains

Table 9.7 Salting (g/100 g fresh weight) of foods in Western societies

	Na	K	Ca	Mg
<i>Maize-based products</i>				
Corn	4	284	55	41
Tortilla, rural	11	192	177	65
Breakfast cereals	866	101	3	11
Processed snacks	838	197	102	56
<i>Wheat-based products</i>				
Natural cereals	39	1166	94	343
Tortillas, wheat	622	73	11	17
Breakfast cereals	855	869	81	236
Processed bread (urban)	573	126	47	31
Salted bread, made locally (rural)	410	92	10	74
Sweet bread, made locally (rural)	97	93	87	18
Processed bread (rural)	344	79	213	18
Processed biscuits	582	80	16	17
<i>Pulses</i>				
Unprocessed, cooked	53	373	50	41
Processed, canned	354	371	27	79

(Strain and Cashman 2002)



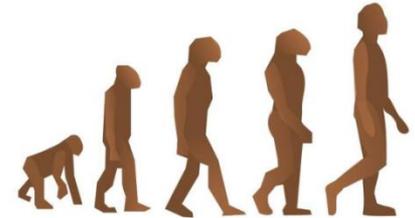
NaCl and Evolution

- Humans are better adapted physiologically to the diet our ancestors were exposed to during millions of years of hominid evolution
-
- Mismatch between our genetically determined nutritional requirements and our current diet:
 - The **deficiency of potassium alkali salts (K-base)** (present in plant foods that our ancestors ate in abundance)
 - The **exchange of those salts for sodium chloride (NaCl)**
 - This results in an increase of the net systemic acid load- **chronic metabolic acidosis** imposed by the Western diet



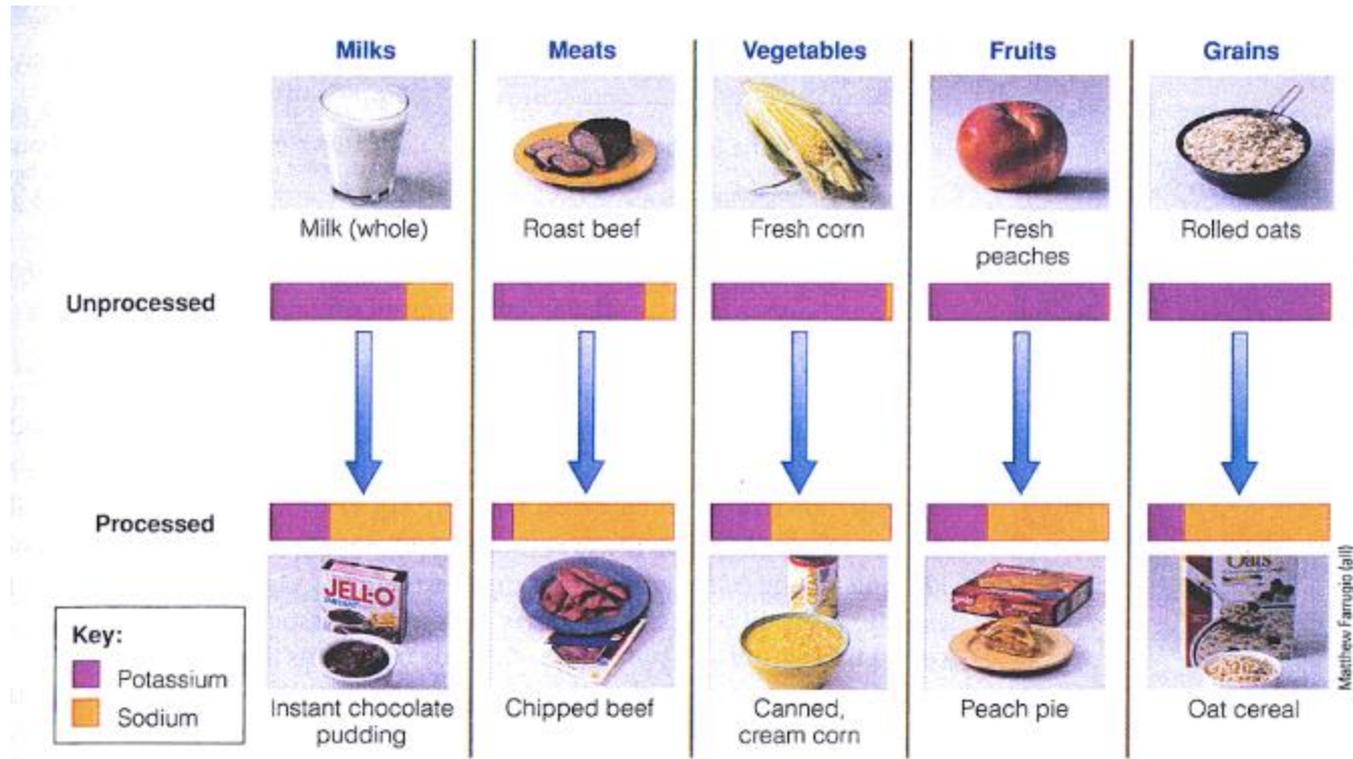
NaCl and Evolution

- It is thought that a lifetime of eating diets that deliver evolutionarily superphysiologic loads of acid to the body contribute to **chronic metabolic acidosis** that leads to:



- **Decrease in bone mass**
 - metabolic acidosis increases urinary Ca excretion
- **Increase the risk of kidney stones**
 - excess urinary Ca can promote stone formation
- **Decrease in muscle mass**
 - metabolic acidosis increases muscle protein degradation
- **Decrease of growth hormone secretion**

The Effects of Processing on Na/K Content



(Rolfes et al 2006)

Sodium and Chloride : Deficiency

Deficiency of sodium and chloride is very difficult to induce as the human body is very efficient at conserving sodium

- Low plasma sodium can be caused by a variety of clinical conditions:
 - Major trauma
 - Cachexia (wasting condition seen in advanced cancer patients)
 - Overuse of diuretics
 - Anorexia nervosa
 - Excessive water intake
 - Liver disease
 - Ulcerative colitis
 - Persistent diarrhoea
- Low plasma chloride can be caused by :
 - Vomiting
 - Chronic renal disease
 - Renal failure



Sodium and Chloride: Toxicity

- Ingestion of 1 ounce (28gm) of table salt (NaCl) was a traditional way to commit suicide in China
- Excessive salt intakes can contribute to:
 - Hypertension
 - Coronary artery disease
 - Stroke
 - Stomach cancer
 - Osteoporosis
 - Asthma

Thank you

(Rolfes et al 2006)