

Vitamins

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Overview

- Vitamins in general
 - Different Types
 - Clinical Effect of Deficiency or Excess
 - DRVs
- Measurement of vitamins

Vitamins

- Organic micronutrients
- Disparate group of organic compounds essential for normal metabolism.
- Cannot be synthesised so must be obtained from the diet.
- Two groups
 - Water soluble
 - Fat soluble

Water Soluble Vitamins

- B Vitamins
 - B₁ = Thiamin
 - B₂ = Riboflavin
 - B₆ = Pyridoxine, pyridoxal and pyridoxamine
 - B₇ = Biotin
 - B₉ = Folic Acid
 - B₁₂ = Cobalamin
 - Niacin (nicotinic acid/nicotinamide)
 - Pantothenic acid
- Vitamin C = Ascorbic acid

Fat Soluble Vitamins

- Vitamin A = Retinol
- Vitamin D = Ergocalciferol (vitamin D₂) and Cholecalciferol (vitamin D₃)
- Vitamin E = Tocopherols and Tocotrienols
- Vitamin K
 - K₁ = Phylloquinone, Phytomenadione
 - K₂ = Menaquinone
 - K₃ = Menadione

Vitamin A

- Three major functions
 - Present in rods and cones of the retina.
 - Cofactor for making glycoproteins
 - Required for normal epithelial cell function and bone growth.
- Stored in the liver – transported to liver in chylomicrons and away via retinol-binding protein or prealbumin.
- Food sources include liver, fish, egg and milk.

Carotenes

- Retinol can be made from some carotenoids, most importantly from β -carotene (provides $\sim 1/4$ of dietary intake).
- Carotenoids are found in plant products, particularly carrots and green veg.
- β -carotene \rightarrow Retinal \rightarrow Retinol

Vitamin A Deficiency

- Deficiency
 - Defective night vision
 - Xerophthalmia leading to keratomalacia and blindness
 - Major cause of blindness in the world.
 - Poor growth of bones and teeth.
 - Increased susceptibility to infections.

Vitamin A Excess

- Excess
 - Toxic in excess.
 - Coarsening and loss of hair.
 - Skin problems
 - Bone fragility
 - Teratogenic (not β -carotene).

B Vitamins

- Isolated deficiencies of B Vitamins in developed countries uncommon (except for folate and B_{12})
- Generally non-toxic in excess – readily excreted in urine as water soluble – except pyridoxine
- Only limited body storage except B_{12}
- Present in wide variety of animal and plant based foods except B_{12} (only found in animals)

Vitamin B_1 - thiamin

- Coenzyme, intermediary metabolism especially carbohydrates.
- Deficiency – problem for chronic alcoholics, malnutrition secondary to inadequate food intake.
 - Beri-beri – peripheral neuropathy (dry Beri-beri), chronic deficiency, cardiac failure leads to oedema (wet Beri-beri)
 - Wernicke-Korsakoff syndrome – severe, acute deficiency = medical emergency. Confusion, loss of recent memory, peripheral neuropathy.

Vitamin B_2 - Riboflavin

- Prosthetic groups for numerous metabolic pathways
- Deficiency
 - No specific deficiency syndrome has been described
 - When it does occur often in conjunction with other nutrient deficiencies.
 - Angular stomatitis
 - Red inflamed tongue
 - Corneal vascularisation and lens opacity

Niacin

- Present as nicotinamide adenine dinucleotide (NAD) and NADP
- Hydrogen acceptor and donor in numerous metabolic reactions.
- Deficiency
 - Pellagra – glossitis, dermatitis, diarrhoea and dementia
 - Can be seen as part of carcinoid syndrome.

Vitamin B₆ - Pyridoxine

- Coenzyme for more than 60 enzymes, especially involved in amino acid metabolism
- Deficiency – very rare
 - Glossitis
 - Polyneuropathy
 - Sideroblastic anaemia seen in chronic alcoholics
 - Drugs e.g. isoniazid and penicillamine

Vitamin B₇ - Biotin

- Prosthetic group for carboxylase enzymes
- Deficiency – very rare
 - Dermatitis
 - Problem if raw eggs are eaten – they contain avidin that binds biotin with high affinity

Pantothenic acid

- Present in bodies as coenzyme A
- Essential for metabolism of carbohydrates, fats and proteins.
- Major component of the Krebs cycle
- Deficiency
 - No specific naturally occurring syndrome

Vitamin B₉ – Folic acid

- Major active form is tetrahydromethylfolate (THF)
- Used for single carbon transfers in multiple metabolic reactions and essential for DNA synthesis
- Deficiency
 - Due to dietary insufficiency, malabsorption, excess utilisation (e.g. lactation) or loss (e.g. dialysis).
 - Drugs e.g. methotrexate
 - Macrocytosis
 - Megaloblastic anaemia

Vitamin B₁₂

- It is a cobalamin – contains cobalt
- Coenzyme – essential for the synthesis of DNA
- Stored in the liver
- Deficiency
 - Macrocytic, megaloblastic anaemia
 - Neurological disorder
 - Vegans may be at risk
 - Pernicious anaemia and malabsorption major causes

Vitamin C – ascorbic acid

- Reducing agent, acting as an antioxidant and scavenger of free radicals
- Essential for formation of collagen and synthesis of carnitine, serotonin, dopamine and bile salts
- Promotes the absorption of inorganic iron
- Found particularly in citrus fruits, tomatoes and leafy vegetables.

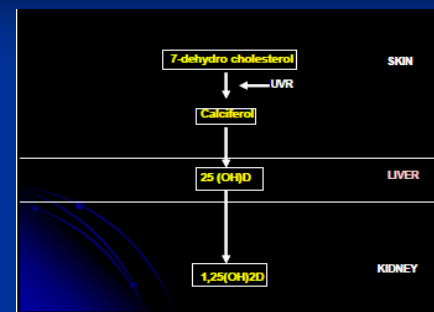
Vitamin C Deficiency

- Scurvy
 - Perifollicular haemorrhages
 - Swollen gums
 - Easy bruising
 - Spontaneous haemorrhage
 - Failure of wound healing
 - Anaemia
- Treat by giving ascorbate

Vitamin D

- Ergocalciferol is semi-synthetic, present in food fortified with vitamin D
- Cholecalciferol is produced in the skin by the action of UV radiation
- Also present in dairy products and egg yolk
- Endogenous synthesis is the major source

Production



Vitamin D Function

- Traditionally involved with bone metabolism and calcium homeostasis
- Now thought to have many other roles including cancer, immune modulation, cardiovascular disease, multiple sclerosis and diabetes
- Active hormone is calcitriol
 - Acts on gut and bone with PTH

Vitamin D Deficiency

- Deficiency
 - Rickets in children
 - Osteomalacia in adults
 - Bone pain, tenderness and myopathy
- Risk factors
 - Dietary deficiency (e.g. exclusively breast fed)
 - Low exposure to sunlight
 - Malabsorption
 - Drugs

Vitamin D Deficiency

- Deficiency
 - Calcitriol deficiency seen in chronic renal failure
 - Inherited disorders
 - Vitamin D-dependent rickets Type I – decrease hydroxylation to 1 α -25-OHD
 - Vitamin D-dependent rickets Type II – defect in the receptor for calcitriol

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Vitamin D Excess

- Excess
 - Not possible through excessive exposure to sunlight
 - Calcitriol is tightly regulated
 - However can have excessive 25-OHD which is thought to have some of the biological activity of calcitriol.
 - Supra-physiological supplementation
 - Sarcoidosis
 - Hypercalcaemia leading to metastatic calcification

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Vitamin E

- Powerful antioxidant
- Found in vegetable oil and cereals. Supplemented in formula milk
- Deficiency
 - Rare
 - Haemolytic anaemia
 - Thrombocytopaenia

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Vitamin E

- Excess
 - Predisposition to bleeding (interference with metabolism of vitamin K).
 - However low toxicity generally

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Vitamin K

- Essential for blood clotting
- Some vitamin K is synthesised by colonic bacteria
- Widespread availability in vegetables
- Deficiency
 - Rare
 - Bleeding tendency
 - Can occur in fat malabsorption

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Vitamin K and newborns

- Healthy newborns are at risk of vitamin K deficiency as a result of poor placental transfer of vitamin K and initial sterility of infants gut
- Breast milk is also a poor source
- Babies are given prophylactic Vitamin K shortly after birth to prevent haemorrhagic disease of the newborn

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Nutritional Requirements

- The amount of each nutrient needed by people to stay healthy is called the nutritional requirement.
- These are different for each nutrient and also vary between individuals and life stages, e.g. women of childbearing age need more iron than men.

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Nutritional Requirements

- Individual requirements of each nutrient are related to:
 - Age
 - Gender
 - level of physical activity
 - state of health
- Some people absorb or utilise nutrients less efficiently than others and so will have higher than average nutritional requirements.

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Dietary Reference Values

- COMA (Committee on Medical Aspects of Food and Nutrition Policy)
 - 1991 report – Dietary Reference Values (DRVs) for Food Energy and Nutrients for the UK
- COMA superseded by SACN (Scientific Advisory Committee on Nutrition)
- No real changes since 1991

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DRVs

- DRVs are estimates of the requirements for groups of people and are not recommendations or goals for individual people.
- There are three types of estimates:
 - Estimated Average Requirements (EARs)
 - Reference Nutrient Intakes (RNIs)
 - Lower Reference Nutrient Intakes (LRNIs).

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DRVs

Figure 1.1 Dietary reference values—definitions

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RNIs for Vitamins

Age	Thiamin mg/d	Riboflavin mg/d	Niacin (niacin acid equivalent) mg/d	Vitamin B6 mg/d	Vitamin B12 µg/d	Folate µg/d	Vitamin C mg/d	Vitamin A µg/d	Vitamin D µg/d
0-3 months	0.2	0.4	3	0.2	0.3	80	25	350	8.8
4-6 months	0.2	0.4	3	0.2	0.3	80	25	350	8.8
7-9 months	0.2	0.4	4	0.3	0.4	80	28	380	7
10-12 months	0.3	0.4	5	0.4	0.4	80	28	380	7
1-3 years	0.5	0.6	6	0.7	0.5	70	30	400	7
4-6 years	0.7	0.8	11	0.9	0.8	100	30	450	**
7-10 years	0.7	1.0	13	1.0	1.0	140	35	600	**
Males									
11-14 years	0.9	1.2	16	1.2	1.2	200	35	900	-
15-18 year	1.1	1.3	18	1.5	1.5	200	40	700	-
19-50 year	1.0	1.3	17	1.4	1.5	200	40	700	-
50+ years	0.9	1.3	16	1.4	1.5	200	40	700	**
Females									
11-14 years	0.7	1.1	12	1.0	1.2	200	35	600	-
15-18 year	0.8	1.1	14	1.2	1.5	200	40	600	-
19-50 year	0.8	1.1	13	1.2	1.5	200	40	600	-
50+ years	0.8	1.1	12	1.2	1.5	200	40	600	**
Pregnancy	+0.1***	+0.3	-	-	-	+100	+10	+10	10
Lactation									
0-4 months	+0.2	+0.5	+2	-	+0.5	+60	+30	+350	10
4+ months	+0.2	+0.5	+2	-	+0.5	+60	+30	+300	10

*10g niacin = 1mg niacin acid equivalent. **After age 50 the RNI is 10 µg/d for men & women. ***For last trimester only. Based on protein providing 14.7% of EAR for energy.

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Measurement of Vitamins

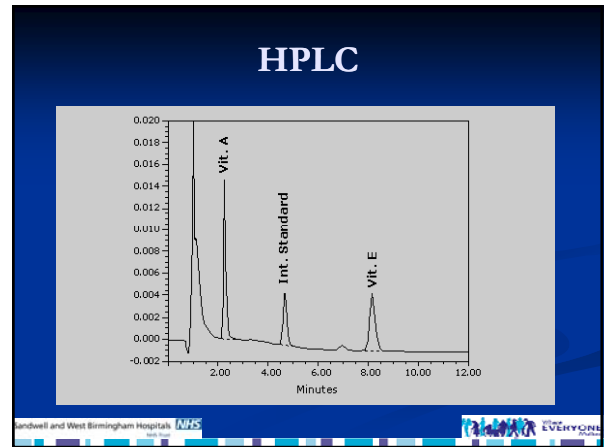
- Most vitamins can be measured
- Most commonly measured are
 - Vitamin A
 - Vitamin D
 - Vitamin E
 - Carotenes
 - B₁₂
 - Folate

Methodologies

- HPLC
- LC/MS/MS
- Immunoassay
 - RIA
 - EIA

HPLC

- High Performance Liquid Chromatography
 - Mobile Phase and Stationary Phase
 - High Pressure
 - Multiple detector types available

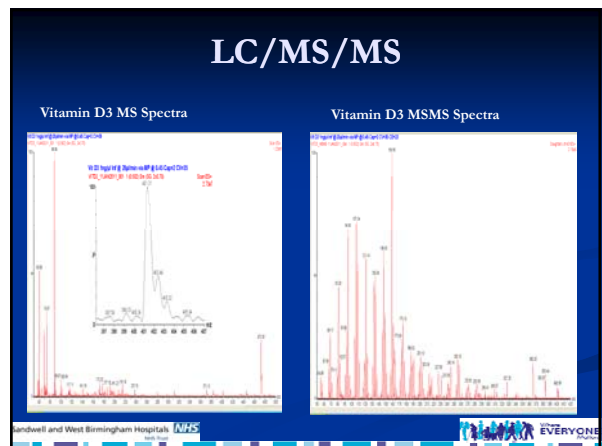
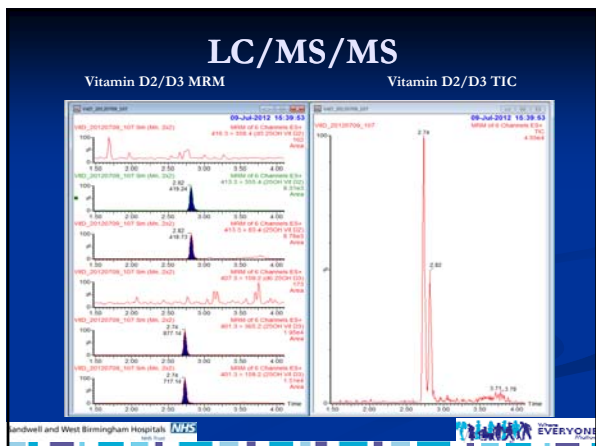
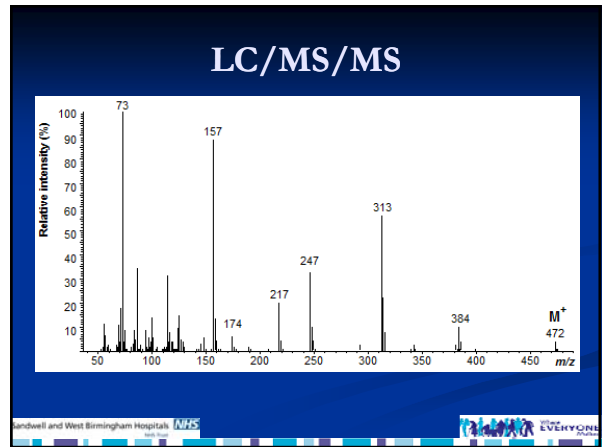
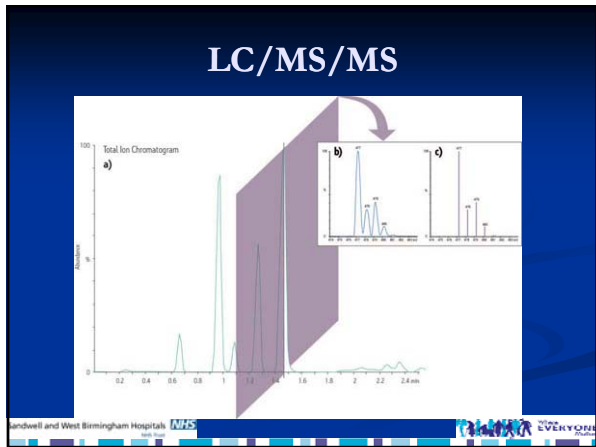
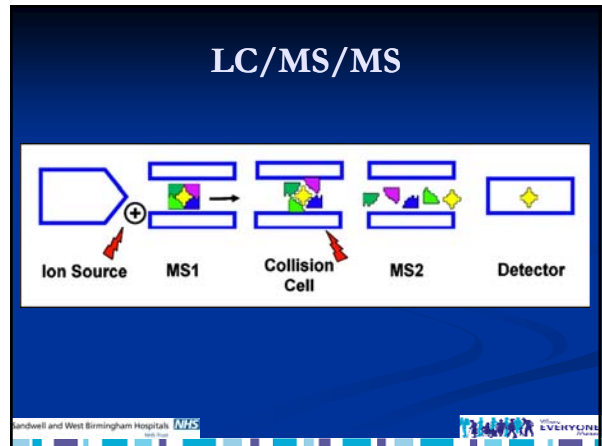
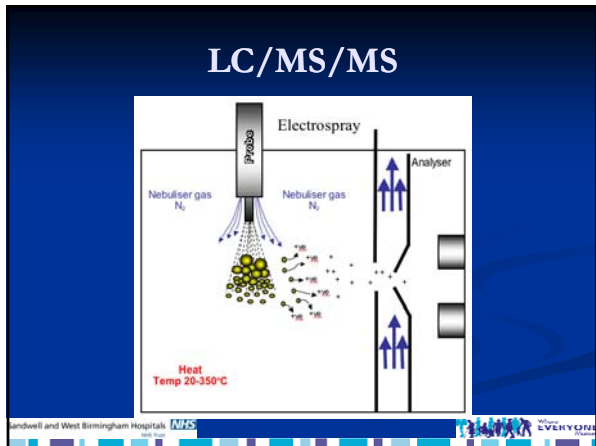


HPLC

Advantages	Disadvantages
Relatively Low Consumable Cost	Relatively High Equipment Cost
Can be automated	Skilled Operators
Multiple Detectors	Manual Extractions
Versatile Equipment	Lack of Specificity (co-eluting peaks)
Stable	Batched workload
Sensitive	Fairly Slow
	Low Throughput


LC/MS/MS

- Liquid Chromatography Tandem Mass Spectrometry
 - HPLC coupled to mass spectrometers
 - 3 MSs – 2 for detecting, one as a collision cell
 - 3 measuring parameters (at least) so often very specific methodology
 - Mass-to-charge ratio (m/z) – need ionised particles
 - Different operational modes




LC/MS/MS

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Multiple modes	

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Immunoassay

Advantages	Disadvantages
Open Access	High Equipment Cost
Quick	Expensive Reagents
Fully Automated Process	Interferences
High Throughput	Lack of Specificity

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