Vitamin D

The Sunshine Superhormone

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Biochemistry

Vitamin D is not a true vitamin, as it is not an essential dietary factor - it is actually a hormone precursor that is normally produced in the skin through the action of sunlight (UVB) on 7-dehydrocholesterol.

Vitamin D3, made in the skin, is transported to the liver where it is metabolised to 25-hydroxyvitamin D [25(OH)D; aka calcidiol], the major circulating form. Further metabolism occurs in the kidney (and throughout the body) to form the highly biologically active 1,25-dihydroxyvitamin D [1,25(OH)2D; aka calcitriol].

Vitamin D is stored in fat, and excess oral vitamin D is excreted in the bile.

It is largely through historical accident that vitamin D was classified in the early 1920s as a vitamin rather than a steroid hormone. The molecular structure of vitamin D is closely related to that of classic steroid hormones (e.g. oestradiol, progesterone, testosterone, DHEA and cortisol). 1,25(OH)2D is the most potent steroid hormone in the human body, active at 1/1,000,000,000,000 of a gram!

Actions

- **Regulates blood calcium levels**
  - Stimulates intestinal calcium absorption
  - Stimulates bone calcium release
  - Stimulates resorption of calcium from the kidneys
- **Increases magnesium absorption**
- **Regulates osteoblasts** (bone-building cells)
  - 1,25(OH)2D stimulates differentiation of osteoblasts (but high levels may have inhibitory effect)
- **Regulates osteoclasts** (bone resorbing cells)
  - 1,25(OH)2D [toxic levels] stimulates formation and function of osteoclasts
  - 24,24(OH)2D inhibits formation and function of osteoclasts
- **Stimulates synthesis of osteocalcin** (a bone protein)
- **Maintains healthy cartilage**
  - Regulates chondrocyte proliferation and proteoglycan synthesis
- **Helps maintain optimal muscle strength**
- **Antioxidant**
- **Anti-inflammatory**
  - Inhibits cyclooxygenase-2 (COX-2)
  - Lowers CRP and IL-6, two measures of inflammation in the body
- **Reproduction**
  - Essential for normal reproductive function in both sexes
  - important for spermatogenesis and maturation of spermatozoa
  - Important for implantation and successful maintenance of pregnancy
  - Crucial for normal foetal growth and optimal development of the foetal brain, lungs, skeleton and immune system
- **Anti-cancer properties**
  - **Antiproliferative** (inhibits cancer cell proliferation)
  - **Prodifferentiating** (induces cancer cell differentiation)
  - **Proapoptotic** (induces apoptosis - programmed cell death)
  - **Antiangiogenic** (inhibits angiogenesis - new blood vessel formation)
  - **Antimetastatic** (inhibits metastasis)
  - **Immunomodulating**
  - Inhibits COX-2
  - potentiates the anticancer effects of many cytotoxic and antiproliferative anticancer agents
  - Down-regulates oestrogen receptor levels and decreases growth-stimulatory effect of oestradiol on breast cancer cells

- **Blood sugar control**
  - Improves insulin sensitivity
  - Stimulates insulin secretion
- **Inhibits leptin secretion by adipose tissue**
- **Modulates immune function**
  - Enhances activity of immune cells that have vitamin D receptors
  - Regulates synthesis and action of naturally occurring defensin molecules against bacterial antigens
  - Regulates antimicrobial peptides in the skin
  - Also dampens immune activity in some circumstances
- **Cardiovascular**
  - Regulates blood pressure; **i**nhibits rennin synthesis in the kidney
  - Improves endothelial function; modulates vascular tone
  - Improves cardiac function
  - Antihypertrophic role in the heart
  - May suppress cardiovascular risk markers (e.g. CRP)
  - Anti-atherosclerotic activity
- **Thyroid**
  - Affects thyroid function
- **Multiple functions in the nervous system**
  - brain development
  - adult brain function
  - neuroprotective
  - antiepileptic effects
  - anticalcification effects,
  - neuro-immunomodulation
  - interplay with neurotransmitters and hormones
  - modulation of behaviors
  - brain ageing
- **Has mood modulating effects**
  - Helps relieve symptoms of depression
- **Involved in energy metabolism**
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- **Important for normal balance**
- **Promotes production of IGF-1** (insulin-like growth factor)
- **Regulates proliferation and differentiation of keratinocytes** (skin cells)
- **Important in the maturation of the hair follicle**
- **Anti-thrombotic (reduces blood clots)**

Most tissues and cells in the body have receptors for vitamin D (VDRs), including:

- Bone (osteoblasts, osteoclasts, bone marrow)
- Cartilage (chondrocytes)
- Muscle
- Kidney
- Adrenal
- Thyroid
- Parathyroid
- Skin
- Hair follicles
- Fat cells (adipocytes)
- Immune cells
- Thymus
- Breast
- Ovary**,** uterus, cervix, fallopian tubes
- Placenta
- Testes, sperm
- Prostate
- Stomach, small intestine**,** colon
- Pancreas (beta cell)
- Liver
- Lung
- Heart and blood vessels
- Brain**,** pituitary
- Inner ear (semicircular canal)
- Cancer cells (many)

Sources

Sunlight: For people living in Australia, the main source of vitamin D is through exposure to sunlight. Studies have shown that between 90-100% of the daily requirement for vitamin D comes simply from being in the sun for about 15-20 minutes a day.

Dietary sources: Very few foods naturally contain vitamin D, and it is exceptionally difficult to obtain adequate levels of vitamin D solely from the diet. Oily fish, such as salmon, sardines, mackerel and herring are the best sources. Other food sources include shitake mushrooms, egg yolk and fortified foods.

Vitamin D deficiency

Vitamin D deficiency is a global health problem. A significant number of Australians are deficient in vitamin D – it is a fallacy that Australians receive adequate vitamin D from casual exposure to sunlight.

Risk factors for vitamin D deficiency

- ***Inadequate sun exposure***
  - Time spent outdoors
  - Excessive 'Slip, Slop, Slap'-ing (using sunscreen can reduce your body's

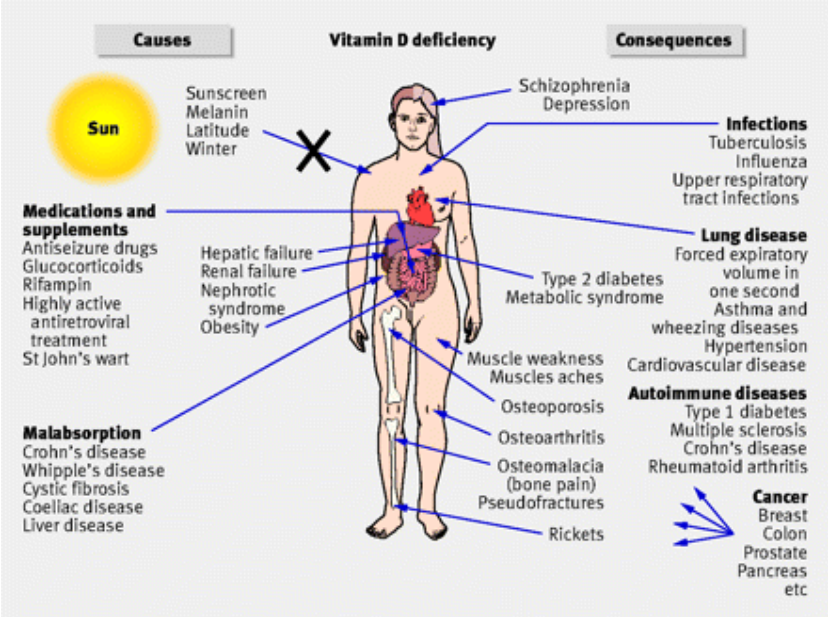
vitamin D production by almost 100%)
  - Infants (especially if solely breast fed)
  - Elderly
  - Dark skin
  - Religious/cultural (covered-up style of dress)
  - Latitude
  - Seasonal variation
  - Global dimming (due to atmospheric pollution)
- ***Washing after sun exposure***
- ***Ageing***
- ***Obesity***
- ***Pregnancy***
- ***Smoking***
- ***Malabsorption*** e.g. cystic fibrosis, coeliac disease, Crohn's disease
- ***Liver disease*** (impaired conversion of vitamin D to 25-hydroxy vitamin D)
- ***Kidney failure*** (impaired conversion of 25-hydroxy vitamin D to 1,25-dihdroxy vitamin D)
- ***Calcium deficiency*** - results in increased 25-hydroxy vitamin D inactivation in the liver
- ***Some drugs*** – statins, anticonvulsants, cholestyramine, colestipol, orlistat, ketoconazole
- ***Vitamin A excess*** – may antagonize the actions of vitamin D
- ***Burn injury***
- ***Psychiatric disorders***
- ***Genetic variability*** – accounts for 25-50% of the variation of vitamin D levels

What are the consequences of lack of vitamin D?

Vitamin D deficiency (***hypovitaminosis D***) is associated with numerous health problems, including:

- Increased inflammation (elevated CRP)
- Muscle weakness and pain - hypovitaminosis D myopathy (HDM)
- Rotator cuff muscle degeneration
- Poor physical performance
- Loss of muscle mass with ageing (sarcopenia)
- Falls in the elderly
- Aches and pains, non-specific musculoskeletal pain
- Fibromyalgia (vitamin D deficiency is often misdiagnosed as fibromyalgia)
- Fatigue
- Chronic low back pain
- Osteomalacia bone pain; tenderness on pressing sternum, shinbone, or forearm bone
- Sensitive, aching or 'throbbing' teeth
- Rickets
- Osteopaenia, osteoporosis
- Osteoarthritis
- Sweaty head as child
- 'Hurting hair' during childhood (pain in the scalp when hair is brushed or combed)
- Easily tired legs in a child
- Growing pains in childhood
- Periodontal disease, gingivitis
- Dental decay (caries)
- Anxiety
- Depression
- Seasonal affective disorder (SAD)
- Bipolar disorder
- Schizophrenia
- Insulin resistance (syndrome X, metabolic syndrome)
- Insulin deficiency
- Pre-diabetes (impaired glucose tolerance)
- Diabetes – type 1 and type 2
- Diabetic retinopathy
- Obesity
- Polycystic ovary syndrome (PCOS)
- Premenstrual syndrome
- Pelvic floor disorders / urinary incontinence in women
- Infertility (in men and women)
- Pre-eclampsia
- Low-birth weight
- Seizures in newborns
- Hypocalcaemia (low blood calcium)
- Auto-immune diseases, including multiple sclerosis, type 1 diabetes, rheumatoid arthritis, Sjogren's syndrome, lupus, Graves' disease, Hashimoto's disease, Crohn's disease, autoimmune prostatitis
- Increased susceptibility to infection
- Influenza, swine flu
- Methicillin-resistant Staphylococcus aureus (MRSA) nasal carriage
- HIV disease progression
- Psoriasis
- Rosacea
- Atopic dermatitis
- Hair loss (alopecia)
- High blood pressure (hypertension)
- Peripheral arterial disease
- Heart attack (myocardial infarction)
- Left ventricular hypertrophy
- Congestive heart failure
- Cardiomyopathy
- Stroke
- Asthma
- Chronic obstructive pulmonary disease (COPD)
- Cystic fibrosis
- Renal disease
- Multiple sclerosis
- Parkinson's disease
- Impaired cognitive function in elderly
- Alzheimer's disease
- Motor neurone disease
- Migraine
- Tension headache
- Retinitis pigmentosa, cataracts, myopia, keratoconus
- Hearing loss, otosclerosis, cochlear deafness
- Age-related macular degeneration
- Increased risk of 17 types of cancer, including breast, prostate, colon, ovarian, endometrial, oesophageal, Hodgkin's and non-Hodgkin's lymphoma, bladder, gallbladder, gastric, pancreatic, rectal, renal, testicular, vulvar, and skin

Causes and consequences of vitamin D deficiency (from *BMJ* 2008;336:1318-1319)



What should my vitamin D level be?

A blood level of 25-hydroxyvitamin D (25OHD) is the best indicator of vitamin D status.

25OHD level (nmol/L):

- <100 = Deficient ☹
- 100-200 = Ideal ☺
- 135-225 = Normal in sunny countries
- >250 = Excessive ☹
- 500+ = Potentially toxic ☹

Treatment of vitamin D deficiency

Adequate sun (UVB) exposure (20 minutes/day, without sunscreen)

Diet: increase consumption of oily fish

Vitamin D supplementation:

Vitamin D3 (cholecalciferol) is the natural form of vitamin D in humans and animals.

To correct a deficiency, 4,000-15,000 IU of D3 a day for 3 months, may be required; thereafter, 2,000-10,000 IU/day will generally be sufficient as a maintenance dose (depending on sun exposure). Maintenance vitamin D supplementation may be taken as a single weekly dose.

Toxicity

Vitamin D toxicity is also known as ***hypervitaminosis D***. All known poisonings with vitamin D3 reflect misuse on an industrial scale. All reports of iatrogenic (doctor-caused) vitamin D intoxification of adults have involved large doses of vitamin D2 or calcitriol.

- **Safe level** (25OHD) < 250 nmol/L
- **Potentially toxic level** (25OHD) 500+ nmol/L [requires a sustained daily intake >/= 40,000 IU]

Resources / further reading

www.vitamindcouncil.org
www.thevitamindcure.com
www.vitamindrevolution.com

The Vitamin D Solution: A 3-Step Strategy to Cure Our Most Common Health Problem. Michael F Holick; Hudson Street Press, 2010

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