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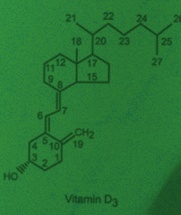
Rickets, scurvy and vitamins



Nobel Laureate Adolf Windaus (1876–1959)

Vitamins (a contraction of the old term 'vital amines') are organic compounds that, in limited quantities, represent vital nutrients for health. Lack of the vitamins C and D is responsible for scurvy and rickets, respectively, and shows what devastating effects this can have, even in the 21st century.

Scurvy

- Conditions similar to scurvy were known to ancient Egyptians.
- Name possibly derived from the Dutch 'scorbeck' or Danish 'schobect' meaning ulcers of the mouth.
- Not isolated to seamen as cases also seen on land; classic examples being in prisons during food shortage, and during the Irish potato famine.

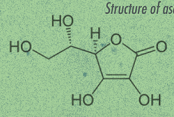
Cause

- Deficiency of dietary vitamin C, which is an essential nutrient for humans and involved in the maintenance of intercellular connective tissues, osteoid, dentine and collagen.
- Vitamin C also plays an important role as a cofactor, enzyme complement, co-substrate, reducing agent and an antioxidant in several biochemical reactions.
- Ascorbic acid (vitamin C) was first isolated in 1928 by Albert Szent-Gyorgyi, for which he was awarded the Nobel Prize for Physiology or Medicine in 1937.
- Humans are unable to synthesise vitamin C so must get their daily requirements from citrus fruit or vegetables.
- There is virtually no storage in the body, with excess being excreted in urine.
- Ascorbic acid is easily destroyed by heat and oxidation.

Symptoms

- Apparent within eight to 12 weeks of irregular or inadequate intake of vitamin C.
- Early-stage symptoms are malaise, fatigue and lethargy.
- Can lead to anaemia, myalgia, bone pain, easy bruising, swelling, petechiae, perifollicular haemorrhages, corkscrew hairs, gum disease, poor wound healing, mood changes and depression.
- Presentation can vary between individuals.

Structure of ascorbic acid



First controlled experiment

- 1747: James Lind, a British Royal Navy surgeon, conducted what was to be considered the first example of a controlled experiment aboard HMS Salisbury.
- Lind selected 12 men suffering from scurvy and divided them into six groups of two individuals. In addition to the daily rations they received, Lind provided oranges and lemons to one group, while the other group received cider, vinegar, seawater, or a mixture of garlic, mustard and horseradish. Those given the citrus fruits recovered quickly and fully, leading Lind to conclude that oranges and lemons prevented scurvy.
- 1753: Lind publishes a *Treatise on Scurvy* that is ignored by the Royal Navy, which orders a purgative, Ward's Drop and Pill, instead.
- 1795: Royal Navy finally issued daily lemon juice ration, but it was to be another 50 years before the Merchant Navy followed.

Birth of the soft drinks industry

- 1867: Rose's Lime Juice Cordial, the world's first soft drink, was produced in Leith Scotland by Lauchlan Rose. Sold to the navy and public, it was a financial success.
- Lime juice becomes a legal requirement for ships of the merchant marine in Britain, and sailors are nicknamed 'Limeys'.

Laboratory diagnosis

- Lack of ascorbic acid detected by a simple colorimetric test.

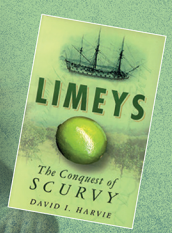
Treatment

- Vitamin C (ascorbic acid) supplementation provides full recovery within three months.

Current situation (2016)

- Cases of scurvy are still reported around the world.
- Risk factors include alcoholism, low socioeconomic status, and severe psychiatric illness leading to poor nutrition.

James Lind, a British Royal Navy surgeon who was the first to show that citrus fruits prevented scurvy



Rickets

- Sorano of Ephesus, a Greek physician in the 1st/2nd century AD is often credited with describing a case that had the features of rickets in infants.
- 1634: Rickets was given as the cause of death in the city of London Bills of Mortality, the first time the word appeared.
- 1645: David Whistler published his thesis on the disease of English children called rickets.
- Name possibly derived from the word 'rachitis' which is inflammation of the vertebral column. Alternative theory is that it was named after an apothocary called Rickets who successfully treated the disease.
- Osteomalacia in adults and rickets in children.
- Owing to its high prevalence in the UK, it became known as the 'English disease' or Morbum Anglorum but cases recorded throughout the world.

Lack of sun exposure

Rickets X-ray

Cause

- Deficiency of vitamin D, caused by reduced cutaneous synthesis due to lack of sun exposure or by a nutritional deficiency.
- Vitamin D is ingested in the diet in its two forms, ergocalciferol (D2), which is found in plants or plant products, or cholecalciferol (D3), mainly found in animal products such as fresh fish or cod liver oil.
- However, most vitamin D is produced from 7-dehydrocholesterol in skin through the action of UV irradiation. This is then converted to 25-hydroxyvitamin D3 in the liver and then to 1, 25 hydroxy vitamin D3 in the kidney.
- Vitamin D is involved in calcium homeostasis.
- Vitamin D metabolism is self-regulated through a negative feedback involving PTH, serum calcium and phosphate.
- Fat soluble.
- 1919: Sir Edward Mellanby discovered that cod liver oil could reverse rickets in experiments with dogs.
- 1928: Nobel Prize awarded to Adolf Windaus for his work on sterols and their connection with vitamins, including vitamin D. Other scientists also involved in its discovery including A Hess and O Rosenheim.

Symptoms

Children

- Widening of the wrists.
- Bowing of the distal radius and ulna.
- Delay in motor milestones.
- Pain.
- Hypocalcaemic seizures.

Adults

- Pain.
- Muscle weakness.
- Pathological fractures.

Laboratory diagnosis

- Serum bone profile and vitamin D serum assay.

Treatment

- Vitamin D supplementation.
- Calcium supplements.

Current situation (2016)

- Cases of rickets are still reported around the world.
- Cases reported in cultures that cover most of their skin.
- Risk during pregnancy, and recommendations include supplementation in at-risk women.
- Nutritional rickets has been reported as 2.9, 4.9, 7.5 and 24 per 100,000 in Canada, Australia, the UK and USA, respectively.

Timeline

Rickets

- 1st century AD: Sorano of Ephesus describes a case with features of rickets.
- 1509: Hans Burgkmair painted infant with appearance of symptoms of rickets.
- 1634: Rickets used for the first time in print as the cause of death of 14 children in the city of London.
- 1645: David Whistler defends thesis on rickets.
- 1650: Francis Glisson publishes book on rickets describing both clinical and anatomical features.
- 1889: BMA issued a report on the geographical distribution of rickets.
- 1889: Dr Theobold Palm, a GP, publishes data showing a relationship between prevalence of rickets and exposure to sun.
- 1918: Dr Kurt Huldschinsky successfully demonstrated how rickets could be treated with UV lamps.
- 1919: Sir Edward Mellanby discovered that cod liver oil could reverse rickets in experiments with dogs.
- 1921: Hess and Unger showed the importance of sunlight in curing rickets.
- 1922: Vitamin D name given by McCollum to Sir Edward Mellanby's 'accessory factor'.
- 1928: Nobel Prize awarded to Adolf Windaus for his work on sterols, including his work on Vitamin D.
- 1932: Vitamin D2 structure identified by Askew *et al.*
- 1937: Vitamin D3 structure identified by Windaus and Bock.
- 1978 Esveld *et al.* proved that D3 production arises in skin.

Scurvy

- 1497–98: First outbreak of scurvy on a naval voyage recorded by Portuguese explorer Vasco De Gama while sailing around the Cape of Good Hope.
- 1519–1522: Ferdinand Magellan's expedition suffers greatly while circumnavigating the world.
- 1534–35: French explorer Jacques Cartier and some crew members survive scurvy with help from the Iroquois wintering along the St Lawrence (drink boiled bark/leaves of white cedar tree).
- 1577: Explorer Francis Drake records several cases of scurvy.
- 1586: Thomas Cavendish attributes scurvy to an infection of the blood and liver.
- 1588: Spanish Armada hit hard by scurvy outbreaks.
- 1593: First recorded use of lemons to 'cure' scurvy by Sir Richard Hawkins.
- 1601–1630s: James Lancaster defeats scurvy aboard the Red Dragon on the first East India Company voyage. Lemon water is a common scurvy preventative on East India Company voyages. The Dutch East India company uses citrus juice and grows gardens on board ships.
- 1605: French naval surgeon Lescarbot blames scurvy on poor food.
- 1630s: East India Company issues tamarinds and oil of vitriol for scurvy instead of lemon juice.
- 1747: James Lind conducts the first clinical trial in medical history aboard the Salisbury and claims that citrus is a virtual specific for scurvy. Anthony Addington publishes *An Essay on the Sea Scurvy* advocating sea water and blood-letting as scurvy cures.
- 1755: Charles Bisset releases a *Treatise on Scurvy* advocating alcohol, sugar and rice.
- 1768: James Cook sails the Endeavour to Tahiti and insists on cleanliness in the men's quarters, and a diet that includes sauerkraut with salt meat. Although, the last voyager to arrive in Tahiti had about a hundred cases of scurvy on board, Cook had not a single case.
- 1795: Sir Gilbert Blane convinces the British Admiralty to issue a daily ration of lemon juice, virtually eliminating scurvy aboard naval ships.
- 1867: Scottish merchant Lauchlan Rose begins marketing sweetened lime juice.
- 1907 – 1912: Scurvy is produced in guinea pigs by Axel Holst and Theodor Frolich.
- 1912: Casimir Funk at the Lister Institute in London coins the term 'vitamine' to describe vital nutritional components of food.
- 1932: Hungarian Albert Szent-Gyorgyi isolates ascorbic acid.

Forgotten, but not gone: old diseases that can still bite

Produced by members of the History Committee for Congress 2017