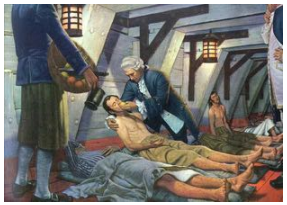
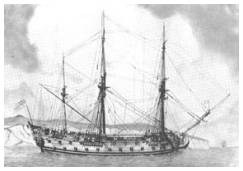
ANBI 141 Evolution of the Human Diet

Lecture 9: Vitamins



Pascal Gagneux October 20, 2022

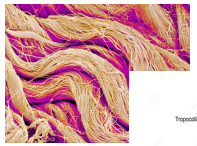
Scurvy: long voyages and bleeding gums and worse

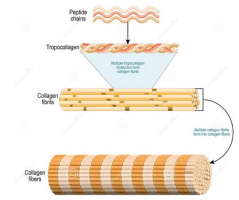


HMS Salisbury

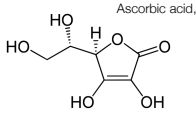
The first clinical trial James Lind? The real story is likely more complicated:
Scottish surgeon named James Lind (October 4, 1716 – July 13, 1794) began to unravel the secrets of scurvy. Born in Edinburgh, Lind entered the Navy as an apprentice doctor, though without qualifications. In March 1747, he was appointed surgeon of the HMS Salisbury, a 50-gun ship in charge of patrolling the English Channel. “The most sudden and visible good effects were perceived from the use of oranges and lemons,” Lind wrote in 1753 in his historical work A Treatise of the Scurvy. “One of those who had taken them being at the end of six days fit for duty … The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.” “Citrus as a scurvy cure was known for over century,” says Bown. In fact, the remedy was recognized in 1497 by the Portuguese Vasco da Gama, in 1593 by Englishman Richard Hawkins, and in 1614 by fellow Englishman John Woodall, who in his manual The Surgeon’s Mate recommended eating oranges, lemons, limes and tamarinds. In fact, others before Lind had already advanced such proposals, starting with the Persian physician Al-Razi who, in the ninth century, bled one group of patients and not the other in order to check the results. A century before Lind, others such as the Flemish Jan Baptist van Helmont, Englishman George Starkey or the German Franz Mesmer had already begun comparing like with like. The original design of these trials did not evolve further until the nineteenth century with the introduction of the double-blind trial and the twentieth century when placebos were concluded.

Vitamin C





Ascorbic acid, vitamin C



Vitamin C is an essential nutrient involved in the repair of tissue and the enzymatic production of certain neurotransmitters. It is required for the functioning of several enzymes and is important for immune system function. It also functions as an antioxidant (i.e. it counters the negative effect of oxidative stress within tissues).

Practice question: What tissue is heavily affected by lack of vitamin C?

Connective tissue (collagen synthesis).

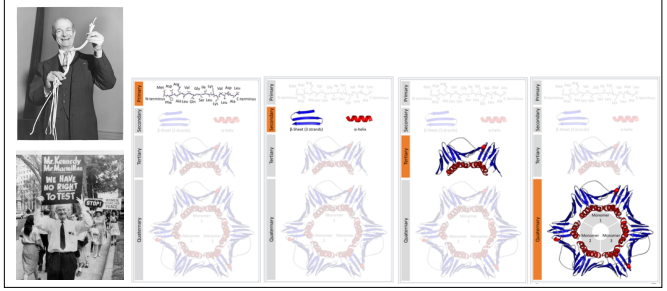
Preventing scurvy: sauerkraut

On his first voyage, the captain stocked his ships with sauerkraut and pickled carrots to prevent scurvy. He used reverse psychology to get the crew to eat the sauerkraut, initially announcing that this specialty was going to be reserved for the officers only.

Practice question: How did Captain Cook get his crews to eat sauerkraut?

Reverse psychology.

Linus Pauling tangent



Linus Pauling, American biochemist and double Nobel Laureate (Chemistry and Peace) was a big proponent of high doses of Vitamin C to prevent infections and support the immune system. Among his many achievements were the discovery of how linear polypeptides/proteins form higher order conformations as they become building block and molecular machines. He also was influential in stopping atmospheric nuclear tests.

Practice question: How can a linear polypeptide give rise to a 3 dimensional molecular machine?

Answer: The linear molecule can fold and bend to take on secondary, tertiary and quaternary conformations.

Practice question: What are the parallels between a complex basket and a functional protein molecule?

Answer: Like the basket, the protein is made out of long “fiber” = polypeptides. These form a

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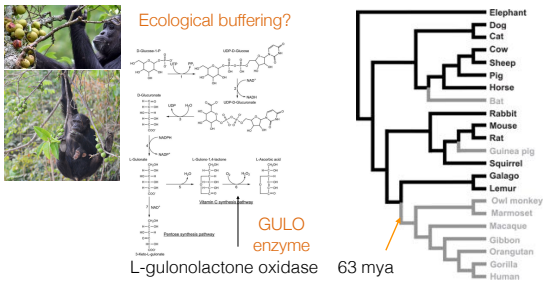
Vitamin C Synthesis: fruit driven loss?

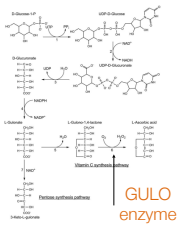


Eating fruit seems to have allowed for the loss of vitamin C synthesis genes.Thus primate behavior buffered loss-of-function mutations in the gene encoding the GULO enzyme until all populations inherited only the dysfunctional DNA sequence.

Practice question: How could an entire group of mammals evolve to lose the function of an enzyme?

Via ecological buffering: e.g. fruit rich-diets making the need to synthesize ones own vital C obsolete. (use it or lose it!)

Vitamin C Synthesis: present in most mammals

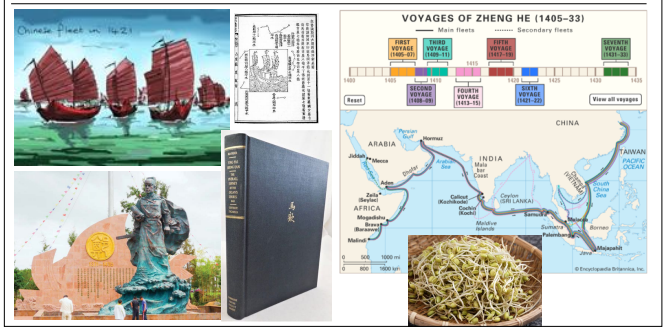


L-gulonolactone oxidase is active in goats!

Goats unlike humans but like many other mammals can make their own vitamin C because they did not lose the function of their GULO enzyme. Goats make much more vitamin C when they are stressed!

Practice question: Is there a gene for vitamin C?
Answer: No, vitamin C is not a protein encoded in a particular DNA sequence, but there is a gene encoding an enzyme that can make vitamin C.

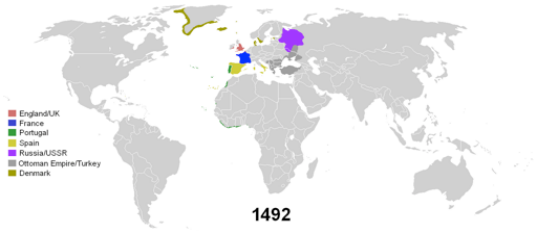
Earlier solutions to Scurvy?



One of the Chinese fleets carried a historian, Ma Huan, whose diaries ("The overall survey of the ocean shores", 1433) recorded how the fleets solved the problem. Apparently, these diaries record that, unlike the supplies of weevil-ridden, ship's biscuit carried on the later British fleets, the Chinese supply ships carried staples of soy beans, wheat, millet and rice, which could be stored for long periods without loss of nutritional value. These could be cooked fresh. In addition, the ships carried chickens, fed by the cereals, for fresh eggs and meat. The soy beans were of particular importance. All the ships carried open tubs in which the soy beans were sprouted in sunlight, developing large quantities of riboflavin, niacin and, most importantly, vitamin C. Daily consumption of sprouted soy would provide more than enough vitamin C to prevent scurvy. Zheng He (Chinese: 鄭和; 1371 – 1433 or 1435) was a Chinese mariner, explorer, diplomat, fleet admiral, and court eunuch during China's early Ming dynasty. He was originally born as Ma He in a Muslim family, and later adopted the surname Zheng conferred by Emperor Yongle.

Practice question: How did ancient Chinese navigators avoid the problem of scurvy?
Answer: By sprouting soy beans on board.

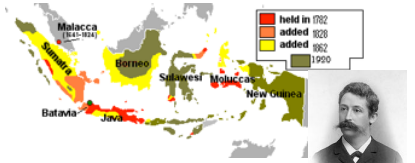
Colonial History



Much of what we eat was profoundly shaped by colonial history, which resulted in crops being moved all around the world.
It also lead to many important t insight into nutrition and the important role of certain nutrients

Practice question: What does the discovery of vitamins have to do with colonialism?
Vitamins were discovered in the Dutch Indies in the context of beriberi disease.

Dutch Indies and Dietary Vitamins



Christiaan Eijkman, Dutch physician

Beriberi, , vitamine B1 (thyamine) deficiency syndrome

After reading accounts from Eijkman in Indonesia, Funk tried to isolate the substance from brown rice it was niacin vitamin B3 even though he thought it would be thiamine..

Polish American Scientist Casimir Funk

Christiaan Eijkman attempted to find the pathogen responsible for feet, breathing problems and heart failure – by injecting chicks with the blood of soldiers who had the disease. Although some animals became ill, he realized that they were all fed on leftovers from the soldiers' meals. The soldiers were fed on white rice, which had the 'polishings' removed to increase its shelf life. He showed that restoring the rice polishings to the diets of the chickens restored their health. Eijkman later discovered that in prisons where brown rice was eaten, beriberi was almost unknown, providing good support for his work. Gowland Hopkins showed that illness could be caused by lack of nutrients in the diet in 1912. He investigated the nutritional needs of rats and mice, feeding young rats on casein, lard sucrose, starch and minerals. Half the group also received 2ml of milk daily. Those receiving the milk grew well, and after 2 weeks he switched the groups. The rats which now had milk in their diet began to grow normally, and after staying at the same weight for two weeks, the other group began to fall ill. He suggested that the basic diet must lack some fundamental nutrient (later termed vitamin A), and that this problem was similar to diseases caused by poor diet in humans.

Practice question: what is the advantage of white (polished rice) over brown?
Better storage life, does not go rancid.

"Vital amines" - Casimir Funk 1912

anti-beriberi: B vitamins

anti-scorbutic: Vitamin C

anti-pellagra:vitamin B3 and tryptophan

anti-rachitic: Vitamin D

Sudden realization that different foods contain key nutrients that despite they low abundance, played crucial roles for human health.

Practice question: What was the solution of maize eating people of Central America to avoid pellagra?
Treating the corn with lime stone to make the niacin and tryptophan available.

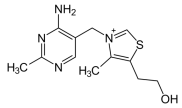
“Vital amines” - Casimir Funk 1912

anti-xerophtalmia: vitamin A

Bitot’s spots: vitamin A

Deficiency in vitamin A can be deadly to infants and can lead to blindness.

Vitamin B : beriberi



Thyamine

B3
Niacin

B9
Folate

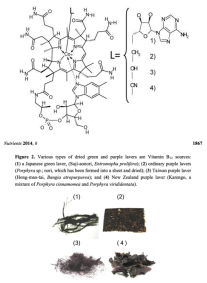
B12
Cobalamin

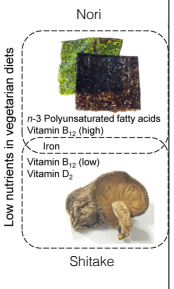
B VITAMIN TYPE	BEST FOOD SOURCES
Thiamin (B1)[ix]	Pork, liver, whole grain and enriched breads and cereals, dried peas, beans and lentils
Riboflavin (B2)[x]	Milk, yogurt, cottage cheese, meat, leafy greens, whole grains and enriched breads and cereals
Niacin (B3) [xi]	Milk, eggs, poultry, fish, whole grains and enriched breads and cereals, nuts, all protein foods
Pyridoxine (B6)[xii]	Whole grains, bananas, potatoes, legumes, fish, meat, poultry
Folic Acid[xiv]	Spinach, orange juice, lentils, asparagus, artichokes, avocado, leafy greens, wheat germ, whole grains
Biotin[xv]	Most foods
B12[xvi]	Meat, poultry, fish, dairy products, eggs, fortified soy and rice milk
Pantothenic Acid[xvii]	Most foods

There are 8 different B vitamins. All are water soluble, like vitamin C.
The fat soluble vitamins are A D E and K.

Practice question: Which are the water soluble vitamins?
B’s and C

Vitamin B12: Veganism can be a risk



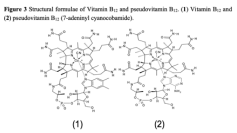


Watanabe *et al.* ***Nutrients*** 2014

Why is vitamin B12 insufficiency a risk for vegans?
Most plants do not make this vitamin, only animals and microbes, cyanobacteria and marine algae.

Practice question: Which common non-animals foods contains vitamin B12?
Answer: Nori (Japanese green laver) and shiitake mushrooms.

Vitamin B12 and pseudovitamin B12!



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Chlorella algae food supplement

Pros and Cons of Vegetarian diets:

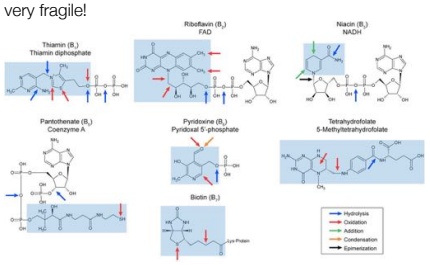
Table 1. Nutrient imbalance in vegetarian diets.

Rich	Low
Fiber	Vitamin A
Vitamin C	Vitamin D_3
Vitamin E	Vitamin B_{12}
Folate	Iron
Magnesium	Cholesterol
n-6 Polyunsaturated fatty acids	*n*-3 Polyunsaturated fatty acids
Carbohydrates	Saturated fatty acids

Watanabe *et al.* ***Nutrients*** 2014

B vitamins found in plants and representative cofactors derived from them

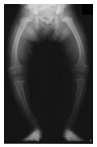
B vitamins are very fragile!



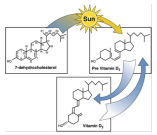
Andrew D. Hanson et al. Plant Physiol. 2016;172:2082-2097

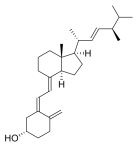
B-vitamins are relatively fragile: Structures and damage reactions of the seven B vitamins found in plants and of representative cofactors derived from them. The vitamin moieties are highlighted in blue. Note that folates generally have a short γ-linked poly-Glu chain attached to the glutamyl moiety. Color-coded arrows show the site and nature of spontaneous chemical or enzymatic damage reactions that each vitamin/cofactor can undergo in vivo.

Vitamin D



Rickets





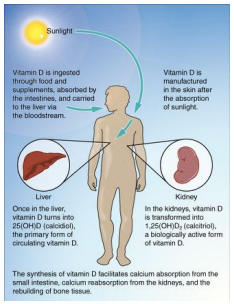
Vitamin D2: Ergocalciferol

Cholecalciferol is one of the five forms of vitamin D - vitamin D3. It is a secosteroid - a steroid molecule with one ring open. Vitamin D is important for the absorption of calcium from the stomach and for the functioning of calcium in the body. Cholecalciferol is used to treat or prevent many conditions caused by a lack of vitamin D, especially conditions of the skin or bones.

However, vitamins, by definition are essential organic compounds which cannot be synthesised by the body and must be ingested - but cholecalciferol is synthesized by the body, and functions as a prehormone. Cholecalciferol itself is inactive: it is converted to its active form by two reactions: the first in the liver, the second in the kidney, to form calcitriol, whose action is mediated by the vitamin D receptor. This receptor regulates the synthesis of hundreds of enzymes and is present in virtually every cell in the body.

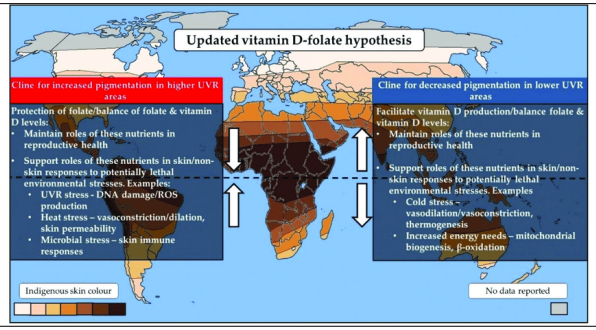
Practice question: what condition indicate vitamin D deficiency?
Answer: Rickets (rachitis), softening and associated deformation of bones.

Vitamin D



Practice question: Which cell types are affected by vitamin D?
Answer: Most cell types in the body.

Skin pygmentation, Vitamin D, and folate



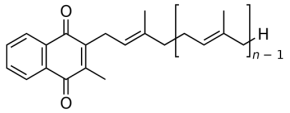
An update of the vitamin D–folate hypothesis. Vitamin D and folate have disparate sensitivities to UVR; whilst vitamin D may be synthesized following UVR exposure, folate may be degraded. The vitamin D–folate hypothesis proposes that the two clines of skin pigmentation evolved as a balancing mechanism to maintain levels of these photosensitive vitamins. In maintaining adequate levels of vitamin D and folate, roles of these nutrients in reproductive health would be preserved. Protection of vitamin D and folate levels may have offered additional advantages in the form of these nutrients themselves having roles in maintaining the skin as a barrier against environmental stresses. Vitamin D also exerts roles in adipocytes that may be of importance in colder environments. These additional roles are consistent with precepts of other prominent theories for the evolution of skin pigmentation (skin mutagenesis, skin barrier, and energy conservation hypotheses). UVR: ultraviolet radiation; ROS: reactive oxygen species. Map adapted from Chaplin (2004).

Practice question: What is the vitamin D-folate hypothesis?

Answer: The proposition that changes in skin pigmentation evolved to balance levels of these photosensitive vitamins.

Vitamin K

blood clotting
Koagulationsvitamin



Vitamin K: menaquinone
from phylloquinone in green plants

The Danish biochemist Henrik Dam was working on how chicks synthesize their own cholesterols, but some of the chicks in the study became ill. They developed severe internal hemorrhages when their blood became unable to clot as usual. Dam found that the problem could be prevented by the introduction of certain substances, such as green leaves and liver, to their diet, but did not appear to match up to a deficiency for any of the known vitamins. The new nutritional factor was named vitamin K, and was synthesized by the American biochemist Edward Doisy. The discovery of vitamin K was able to prevent severe hemorrhaging, particularly in jaundiced patients and newborn infants.

Practice question: What does the K in vitamin K refer to?
C(K)oagulation, blood clotting.

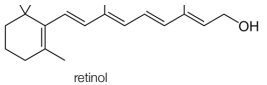
How do vitamins make it from your gut into your body?

Fat soluble or water soluble?
Size?

Active transport by specific transport proteins on gut cells: vitamin C
Passive absorption of fatty vitamins: e.g. Vitamin D
Need for specific 'shuttle" proteins: retinol binding proteins e.g. Vitamins A,
Vitamins can be "drunk" by cells: pinocytosis, e.g. B12

Practice question: Are all vitamins taken up in the gut by the same mechanism?
No, some are absorbed passively, others are actively transported across cells to reach the blood stream.

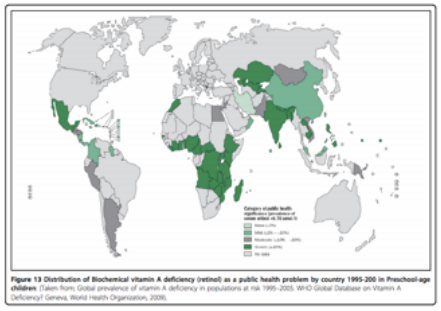
Vitamin A



retinol

Feeding rats with and without milk.. A number of researchers were studying the nutritional requirements of mammals in the early 1900's. Experiments were carried out on the diets of young rats and mice, beginning with simple dietary mixtures and finding out what more was needed. For a long time researchers thought that failures in growth resulted from ingredients in the diet becoming denatured. The first clear evidence that a lack of particular components of the diet could be harmful was presented in 1912 by Gowland Hopkins, who had previously isolated and demonstrated the essential nature of the amino acid tryptophan. Hopkins fed young rats on casein, lard, sucrose, starch and minerals. Half of the rats also received milk daily. Those receiving the milk grew well, and after two weeks the group receiving the milk was switched. He found that those receiving the milk grew normally and those now lacking did not continue to develop well. He explained this by the basic diet was lacking in some essential organic nutrient, and felt that similar problems may be present in human diseases related to diet. Hopkins did not investigate his "milk factor" further, but a researcher in the USA, Elmer McCollum found that given a purified diet rats began to loose weight after 10 weeks, but would recover if given butter fat, but not olive oil. In 1914 he found that the active component could be separated from the rest of the butter fat, as it was soluble in ether. He called this nutrient "factor A". He termed a nutrient which had been isolated from rice polishings by Casimir Funk in 1911 "factor B". These fat soluble factors were later to become vitamins A and B, a term coined by Casimir Funk as a contraction of "vital amine". It was subsequently found that not all vitamins are amines. Vitamin deficiency in both humans and rats causes malnutrition and deficiency of vitamin A can result in serious eye damage.

Vitamin A



According to the WHO, an estimated 250 million preschool children are vitamin A deficient. An estimated 250,000 to 500,000 vitamin A-deficient children become blind every year; half of them die within 12 months of losing their sight. The deficiency seriously impacts children and pregnant women. Breastmilk is a natural source of vitamin A, so breastfeeding in high-risk countries is encouraged. Children with vitamin A deficiencies are more likely to die from diarrheal diseases and the measles. Pregnant women with the vitamin deficiency experience night blindness problems in their third trimester when both baby and mother require a lot more nutrients. Distribution of Biochemical vitamin A deficiency (retinol) as a public health problem by country 1995-2005 in Preschool-age children: (Taken from; Global prevalence of vitamin A deficiency in populations at risk 1995–2005. WHO Global Database on Vitamin A Deficiency? Geneva, World Health Organization, 2009)

Practice question: What food item in South America is fortified with vitamin A?

Sugar.

Death toll of vitamin A deficiency

Vitamin A-deficiency	
Global population mortality (in millions)	
Vitamin A-deficiency	1.9-2.7
HIV/Aids	1.7
Tuberculosis	1.4
Malaria	0.75

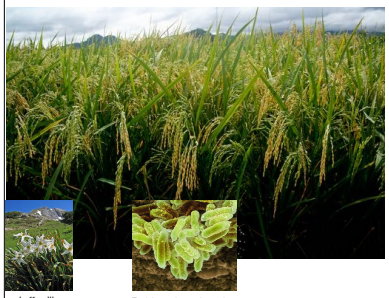
*Courtesy of Ingo Potrykus

Vitamin A deficiency is deadlier than HIV!

Practice question: Which kills more people every year, HIV/AIDS or Vitamin A deficiency?

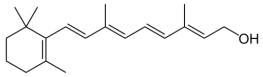
Answer: Vitamin A deficiency.

Combating vitamin A deficiency – Golden Rice



daffodil

Erwinia uredovora bacterium



retinol

Ingo Potrykus, at Swiss University ETH
Peter Beyer, U. Freiburg

Golden rice was created by transforming rice with two beta-carotene biosynthesis genes:

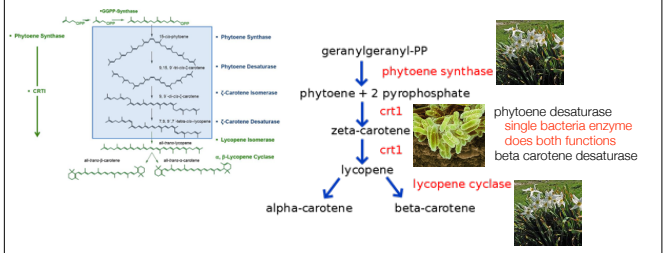
psy (phytoene synthase) from daffodil ('Narcissus pseudonarcissus')

crtI (phytoene desaturase) from the soil bacterium Erwinia uredovora

(The insertion of a **lcy** (lycopene cyclase) gene was thought to be needed, but further research showed it is already produced in wild-type rice endosperm.)

The psy and crtI genes were transferred into the rice nuclear genome and placed under the control of an endosperm-specific promoter, so that they are only expressed in the endosperm. The exogenous lcy gene has a transit peptide sequence attached, so it is targeted to the plastid, where geranylgeranyl diphosphate is formed. The bacterial crtI gene was an important inclusion to complete the pathway, since it can catalyze multiple steps in the synthesis of carotenoids up to lycopene, while these steps require more than one enzyme in plants. The end product of the engineered pathway is lycopene, but if the plant accumulated lycopene, the rice would be red. Recent analysis has shown the plant's endogenous enzymes process the lycopene to beta-carotene in the endosperm, giving the rice the distinctive yellow color for which it is named. The original golden rice was called SGR1, and under greenhouse conditions it produced 1.6 µg/g of carotenoids.

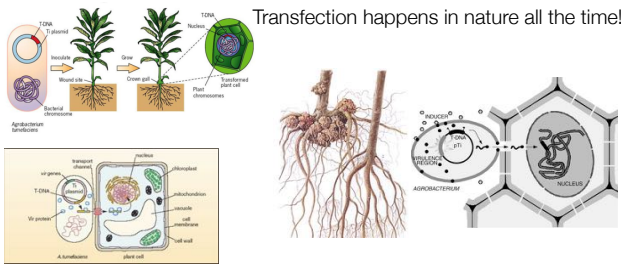
Vitamin A synthetic pathway – Golden Rice



Filling a biosynthetic gap: Pathway elements in green are functional in wild-type rice grains. Thus the GGPP precursor molecule is being synthesized and lycopene can be cyclized. Elements in blue, including the blue box, are effectively absent. Introduction of the enzymes phytoene-synthase and the bacterial desaturase CRTI fills the biosynthetic gap created by the absence of the blue elements.

Practice question: What was the source of the genes transferred to golden rice to cause rice to make beta carotene?
Daffodil and bacterium.

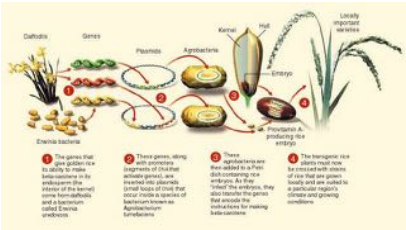
Natural *Agrobacterium tumefaciens* transformation



Bacteria have evolved ways to shuttle genes into plants in order to manipulate the plant to their advantage. genetic engineers use these bacteria as gene shuttles when they insert foreign genes into a crop that they they to engineer.

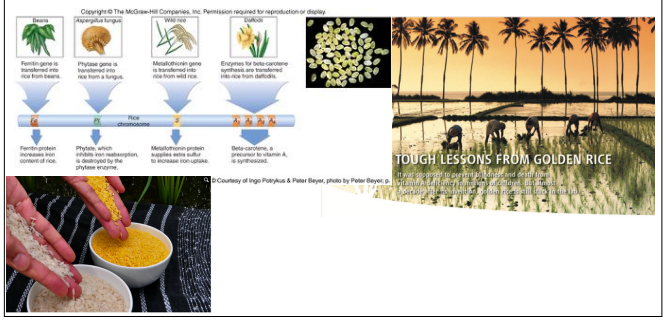
Practice question: Does transfer of foreign DNA (from one species to another) occur in nature?
Yes, via viral or phage infection and by bacteria that use plasmids (circular DNA carrying genes useful to the bacterium).

Four genetic engineering steps:



A japonica variety of rice was engineered with three genes necessary for the rice grain to produce and store beta-carotene. These included two genes from the daffodil plant and a third from a bacterium. Researchers used a plant microbe to ferry in the genes into the plant cells. The incorporation of these genes allows the rice plant to modify certain metabolic pathways in its cells to produce precursors of Vitamin A, which was previously not possible. This was considered a technical milestone, as most agronomic traits engineered to date have only required the introduction of a single gene.The Golden Rice project, which began in the early 1990's, was a result of a collaborative effort between the Swiss Federal Institute of Technology (ETH-Zurich) and the University of Freiburg, Germany. Ingo Potrykus and Peter Byer are its main developers. Funding was obtained from ETH-Zurich itself, the European Commission's agricultural research program, and the Rockefeller Foundation.

A few more additions:



Practice question: Why has the production of golden rice not really taken off?
Answer: Lack of social acceptance has created huge hurdles.

Frankenfood?

146 Nobel Laureates are urging everyone to acknowledge that GMO technology is basically safe and should be supported and encouraged for the sake of the developing world, who desperately need better yielding crops with added nutritional value.

https://supportprecisionagriculture.org/

Greenpeace otherwise known for embracing scientific reasoning has not backed off it s campaign against all GMO crops including golden rice.
Dr. Patrick Moore, an ecologist, co-founder and former director of Greenpeace has quit and now actively promotes golden rice. So does Micheal Pollan, the famous food writer and UC Berkley Professor of Journalism.

June 29th 2016

To the Leaders of Greenpeace, the United Nations and Governments around the world

The United Nations Food & Agriculture Program has noted that global production of food, feed and fiber will need approximately to double by 2050 to meet the demands of a growing global population. Organizations opposed to modern plant breeding, with Greenpeace at their lead, have repeatedly denied these facts and opposed biotechnological innovations in agriculture. They have misrepresented their risks, benefits, and impacts, and supported the criminal destruction of approved field trials and research projects.

We urge Greenpeace and its supporters to re-examine the experience of farmers and consumers worldwide with crops and foods improved through biotechnology, recognize the findings of authoritative scientific bodies and regulatory agencies, and abandon their campaign against "GMOs" in general and Golden Rice in particular.

Scientific and regulatory agencies around the world have repeatedly and consistently found crops and foods improved through biotechnology to be as safe as, if not safer than those derived from any other method of production. There has never been a single confirmed case of a negative health outcome for humans or animals from their consumption. Their environmental impacts have been shown repeatedly to be less damaging to the environment, and a boon to global biodiversity.

Greenpeace has spearheaded opposition to Golden Rice, which has the potential to reduce or eliminate much of the death and disease caused by a vitamin A deficiency (VAD), which has the greatest impact on the poorest people in Africa and Southeast Asia.

The World Health Organization estimates that 250 million people, suffer from VAD, including 40 percent of the children under five in the developing world. Based on UNICEF statistics, a total of one to two million preventable deaths occur annually as a result of VAD, because it compromises the immune system, putting babies and children at great risk. VAD itself is the leading cause of childhood blindness globally affecting 250,000 - 500,000 children each year. Half die within 12 months of losing their eyesight.

WE CALL UPON GREENPEACE to cease and desist in its campaign against Golden Rice specifically, and crops and foods improved through biotechnology in general;

WE CALL UPON GOVERNMENTS OF THE WORLD to reject Greenpeace's campaign against Golden Rice specifically, and crops and foods improved through biotechnology in general; and to do everything in their power to oppose Greenpeace's actions and accelerate the access of farmers to all the tools of modern biology, especially seeds improved through biotechnology. Opposition based on emotion and dogma contradicted by data must be stopped.

How many poor people in the world must die before we consider this a **"crime against humanity"**?

Sincerely,

Letter signed by over 100 Nobel laureates.

Unnatural?

Proc. Natl. Acad. Sci. USA
Vol. 87, pp. 7777–7781, October 1990
Medical Sciences

Dietary pesticides (99.99% all natural)*

(carcinogens/mutagens/chatogens/coffee)

BRUCE N. AMES†‡, MARGIE PROFET†, AND LOIS SWIRSKY GOLD†§

Table 2. Some natural pesticide carcinogens in food

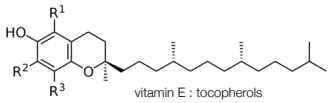
Rodent carcinogen	Conc., ppm	Plant food
5-/8-Methoxypsoralen	14	Parsley
	32	Parsnip, cooked
	0.8	Celery
	6.2	Celery, new cultivar
	25	Celery, stressed
p-Hydrazinobenzoate	11	Mushrooms
Glutamyl *p*-hydrazinobenzoate	42	Mushrooms
Sinigrin* (allyl isothiocyanate)	35–590	Cabbage
	250–788	Collard greens
	12–66	Cauliflower
	110–1,560	Brussels sprouts
	16,000–72,000	Mustard (brown)
	4,500	Horseradish

Many common vegetables have high levels of natural pesticides.

The argument that a technology is to be rejected because it is unnatural is deeply problematic: reading is unnatural, so are reading glasses, books, stoves, bicycles and surf boards.
Plants have evolved their own highly toxic and carcinogenic pesticides rather naturally.
Fiddler leaf fern also contain carcinogens. **Ptaquiloside** is a norsesquiterpene glucoside produced by bracken ferns (majorly Pteridium aquilinum) during metabolism it causes gastric cancer in cattle and people.

Vitamin E

fertility in rats
cardio vascular
AMD
LOAD



vitamin E : tocopherols

Vitamin E (aplha-tocopherol) was discovered nearly 100 years ago because it was required to prevent fetal resorption in pregnant, vitamin E-deficient rats fed lard-containing diets that were easily oxidizable. The human diet contains eight different vitamin E-related molecules synthesized by plants; despite the fact that all of these molecules are peroxyl radical scavengers, the human body prefers alpha-tocopherol. The biological activity of vitamin E is highly dependent upon regulatory mechanisms that serve to retain alpha-tocopherol and excrete the non-alpha-tocopherol forms.

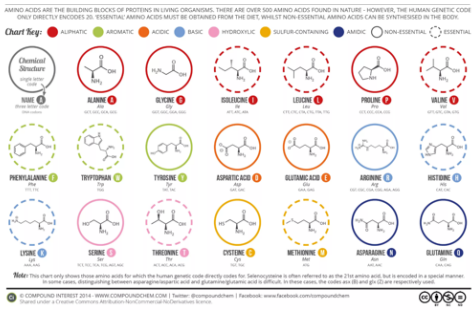
Nixtamalizing corn and making tortillas.

Essential Amino acids

Essential Amino Acid	Main Food Source
Histidine	Eggs, soy protein, Parmesan, sesame, peanuts
Isoleucine	Eggs, soy protein, tofu, white fish, pork, Parmesan
Leucine	Eggs, soy protein, white fish, Parmesan, sesame
Lysing	Eggs, soy protein, white fish, Parmesan, smelts
Methionine	Eggs, soy protein, white fish, sesame, smelts,
Cysteine	Eggs, soy protein, sesame, mustard seeds, peanuts
Phenylatanine	Eggs, soy protein, peanuts, sesame, white fish
Tyrosine	Eggs, soy protein, parmesan, peanuts, sesame
Threonine	Eggs, soy protein, white fish, smelts, sesame
Tryptophan	Eggs, soy protein, sesame, winged beans, chia seeds
Valine	Eggs, soy protein, parmesan, sesame, beef

Conditionally essential AA are amino acids that become essential under certain conditions: disease, pregnancy, hard physical labor etc.

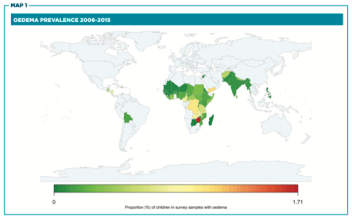
Essential Amino acids



Practice question: What is an essential amino acid?
Answer: Amino acids (building blocks of proteins) that have to be taken up from the diet.

Kwashiorkor: "the sickness the baby gets when the new baby comes"

Severe Acute Malnutrition: lack of protein led to accumulation of fluids in the tissues



> The percentage of children with oedema is highest in Zimbabwe (1.71), Yemen (1.10), The Democratic Republic of Congo (1.04), and Zambia (0.81)

UNICEF. 2016

Weaning is traumatic in most mammals. In Humans how live in poverty but with sufficient calories from farmed food, early weaning and sudden shift to carbohydrate but protein poor food causes severe protein deficiency that can result in kwashiorkor disease.

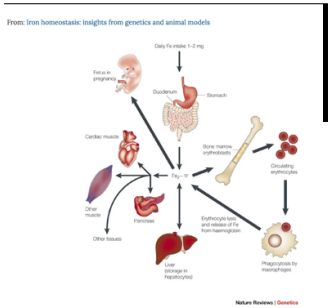
Practice question: Is Kwashiorkor a disease of vitamin deficiency?
No, it is a disease of protein deficiency.

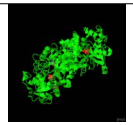
Iodine

In the high Alps (Switzerland, Austria, Italy and France) up tp 90% of people suffred from goitres and 2% were affected by cretinism, after being born to a mother who had a goiter from sever iodine deficiency.
Doctor Johann Jakob Guggenbühl with his patients Lithography after a photo by Carl Durheim, from Guggenbühl's "Die Heilung und Verhütung des Cretinismus und ihre neuesten Fortschritte, Berne 1853

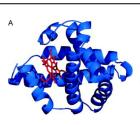
Practice question: Why is iodine deficiency so common in mountain regions?
Answer: Because the local environment has been leached of iodine.

Iron

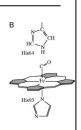




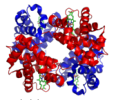
transferrin



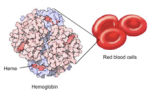
myoglobin



heme



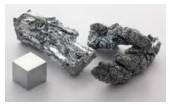
hemoglobin

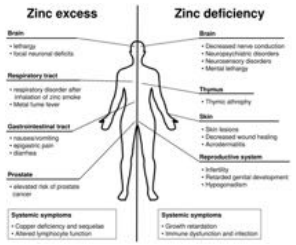


The normal distribution of iron within the body is shown. Adults typically have 3–5 g in total. About 0.5–2 mg of dietary iron is absorbed each day through the proximal small intestine. This intake is balanced by loss of a similar amount of iron, through blood loss and the sloughing of skin and mucosal cells. Most iron is found in the erythroid bone marrow and in mature erythrocytes, contained within the haem moiety of haemoglobin. Iron for new red-blood-cell synthesis is primarily supplied by reticuloendothelial macrophages, which recycle iron from old red blood cells. Circulating iron is bound to transferrin. Around 0.1% of the total body iron is found in this transit compartment. Transferrin delivers iron to developing erythroid precursors, as well as to other tissues of the body. Stored iron is primarily found in the hepatocytes of the liver. The distribution of iron is altered in response to pregnancy, iron deficiency and iron overload. (TF, transferrin.)

Practice question: what protein is responsible for sequestering iron in the human body?
Transferrin

Zinc



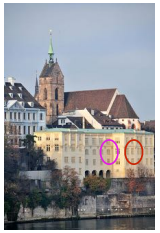


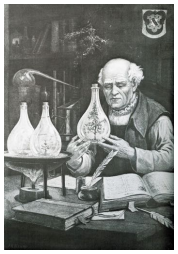
Zinc is a common element in human and natural environments and plays an important part in many biological processes. Zinc, which is defined as an essential trace element, or a micronutrient, is essential for the normal growth and the reproduction of all higher plants and animals, and of humans. In addition, it plays a key role during physiological growth and fulfills an immune function. **It is vital for the functionality of more than 300 enzymes, for the stabilization of DNA, and for gene expression.**

Paracelsus (1493-1541)

"The dose makes the poison"
(Latin: sola dosis facit venenum)

Friedrich Nietzsche





Paracelsus was the first to point out the relation between goitrous parents and their mentally disabled children.

Burnt medical books by Galen and Ibn Sina, rocked the establishment.

Philippus Aureolus Theophrastus Bombastus von Hohenheim
"The dose makes the poison" (Latin: sola dosis facit venenum)

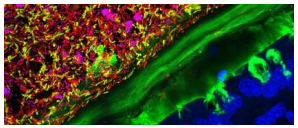
Red circle my office where I wrote my master's thesis on Chimpanzee Mother-offspring behavior in 1991.
Purple circle, Friedrich Nietzsches office when he was chancellor of Basel University.

Vitamin factory within us?

Table 1
Estimated maximal % of daily reference intake (DRI) of B vitamins that could be provided by the gut microbiota (from Magnusdottir et al. [56])

Vitamin	Intracellular concentration (mmol/gDW)	DRI[a] (mg/day)	HGM_{ratio}	%DRI from HGM
Biotin	9.0×10^{-5}	0.03	0.40	4.5
Cobalamin	8.5×10^{-4}	0.0024	0.42	31
Folate[b]	5.0×10^{-3}	0.4	0.43	37
Niacin[b]	3.3×10^{-3}	15	0.63	27
Pantothenate	2.3×10^{-4}	5	0.51	0.078
Pyridoxine[b]	5.8×10^{-4}	1.3	0.50	86
Riboflavin	9.0×10^{-4}	1.2	0.65	2.8
Thiamin[b]	8.7×10^{-4}	1.15	0.56	2.3

[a]Dietary reference intakes (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and Its Panel on Folate, Other B Vitamins, and Choline, 1998). Values averaged for male and female references intakes (ages 19–50)
[b]Atomic mass for dihydrofolic acid, nicotinic acid, pyridoxine 5′-phosphate, and thiamine monophosphate



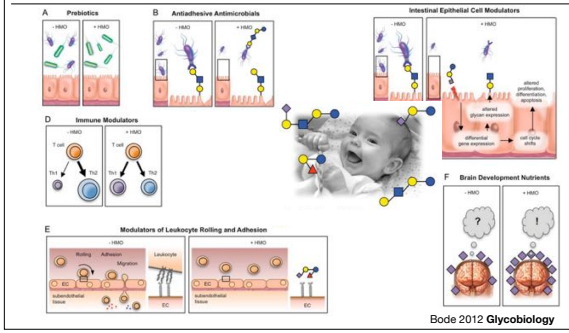
Microbes Mucus gut cells

Rowland *et al.* ***Europ. J Nutr*** 2018

A better understanding of our gut microbiota could lead to improvement of internal vitamin production.

Practice question: How do our gut epithelial cells keep the microbes in the gut at bay?
By secreting a thick layer of mucus.

Human Milk Oligosaccharides -Protective Effects

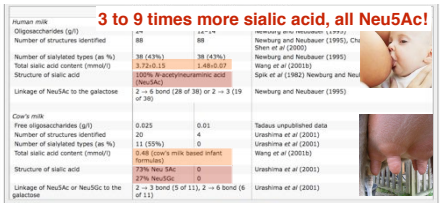


Bode 2012 **Glycobiology**

Human milk contains many bioactive substances including vitamins and functional antibodies. It also contains about 70 g/liter of lactose and 5–10 g/liter of free oligosaccharides. More than 130 different glycan species have been identified with lactose at the reducing end, including poly-N-acetyllactosamine units. Some glycans are α2-3- and/or α2-6-sialylated and/or fucosylated in α1-2, α1-3, and/or α1-4 linkages. In contrast, bovine milk, the typical mainstay in human infant formulas, contains much smaller amounts of these glycans. These differences may account for some of the physiological advantages seen for breast-fed versus formula-fed infants. The glycans may also favor growth of a nonpathogenic bifidogenic microflora and/or block pathogen adhesion that causes infections and diarrhea. Surprisingly, a substantial number of human milk oligosaccharides remain almost undigested in the infant's intestine and are excreted intact into the urine. Whether supplementing infant formula with specific, biologically active free glycans enhances infant health is unknown.

Practice question: How does human break milk favor a healthy human gut microbiome?
Answer: By providing molecules to feed the good and discourage the bad microbes.

Amount and type of oligosaccharides and sialic acid in breast and cow's milk



bovine formula: sialic acid poor, + antigenic sialic acid

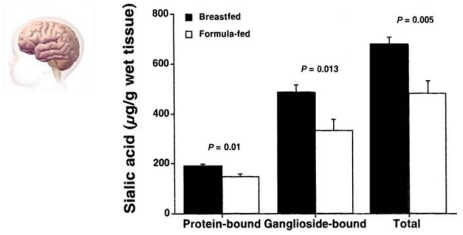
Wang B and Brand-Miller J. . ***Europ. J Clin Nutr*** 2007

In addition to being low in sialic acids, bovine milk contains non-human silica acid, against which most humans develop antibodies.

Practice question: which sugar is found in much higher concentrations in human milk than in cows' milk?

Answer: Sialic acid (a.k.a. N-Acetylneuraminic acida) an acidic, amino-sugar with crucial roles in neurodevelopment.

Brain sialic acid concentration; comparison of breast fed vs formula-fed infants: a sugar vitamin?



Wang B *et al.* ***Am J Clin Nutr*** 2003;78:1024-1029

There different content of sialic (N-Acetylneuraminic) acid of breast milk (high) and bovine milk (low) appears to affect the chemical composition of infant brain tissue.

Neu5Ac could thus be considered a **conditionally essential sugar** for infant brain development.

Summary

Some nutrients have to be consumed because our bodies cannot make them.

Vitamins were only discovered in the 20th century.

Traditional human populations figured out ways to cover their vitamin needs before agriculture.

All vitamins can now be synthetically produced at low cost and added to various foods.

There are 13 essential vitamins: vitamins A, C, D, E, K, and 8 B vitamins.

Before their discovery humans had to learn by trial and error which foods kept them healthy.

Millions of people still suffer from relative lack of vitamins and micronutrients.

Vitamin deficiencies are often result from ignorance and/or social injustice.

Genetic engineering can create crops that have high content of important vitamins, but face cultural resistance.

Animal experiments have been crucial to figure out the biological role of vitamins and other trace nutrients.

Our microbiome can potentially provide a large fraction of our vitamins.

Breast milk contains many vitamins and also essential sugars (the monosaccharide N-acetylneuraminic acid) and many oligosaccharides.