

MUDr. Eva Kudlová, CSc.

First Faculty of Medicine, Charles
University and
General University hospital in Prague



MALNUTRITION



Malnutrition: WHO definition

- Impaired health caused by a dietary deficiency, excess, or imbalance in a person's intake of energy and/or nutrients
 - Undernutrition
 - Micronutrient-related malnutrition
 - Overweight, obesity and diet-related noncommunicable diseases (such as heart disease, stroke, diabetes and some cancers)

International Classification of Diseases (ICD)

- Most in family IV. Endocrine, nutritional and metabolic diseases
 - Malnutrition E40 – E46 includes: kwashiorkor, marasmus, marasmic kwashiorkor, mild, moderate, severe protein-energy malnutrition

BUT e.g.

- **Nutritional anaemia** in III. **Diseases of the blood** and blood-forming organs and certain disorders involving the immune mechanism
- **Selenium deficiency**
 - Keshan disease (congestive cardiomyopathy) in IV. **Endocrine, nutritional and metabolic** diseases
 - Kashin Beck disease (chronic osteochondropathy) in XIII. Diseases of the **musculoskeletal** system and connective tissue

Malnutrition: Classification by origin

- Primary (exogenous):
 - ↓ or ↑ intake from food
- Secondary (endogenous):
 - impaired absorption, utilization

NOT malnutrition:

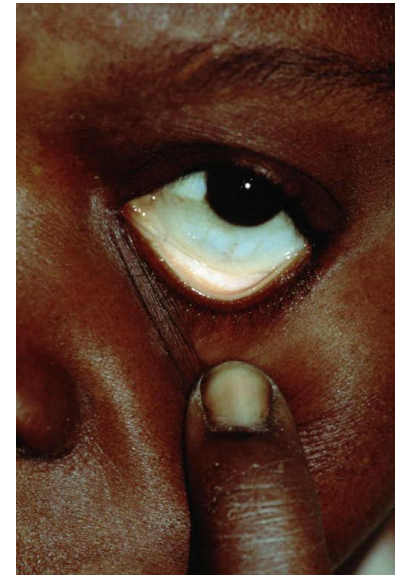
- Chapter V Mental and behavioural disorders (F00-F99)
 - F50 Eating disorders
 - F50.0 **Anorexia nervosa**
 - F50.2 **Bulimia nervosa**
- Chapter IV Endocrine, nutritional and metabolic diseases (E00-E90)
 - Metabolic disorders (E70-E90)
 - E86 Volume depletion incl. **Dehydration**, Depletion of volume of plasma or extracellular fluid, Hypovolaemia
 - E87 Other **disorders of fluid, electrolyte and acid-base balance**
 - E87.0 Hyperosmolality and hypernatraemia
 - E87.1 Hypo-osmolality and hyponatraemia



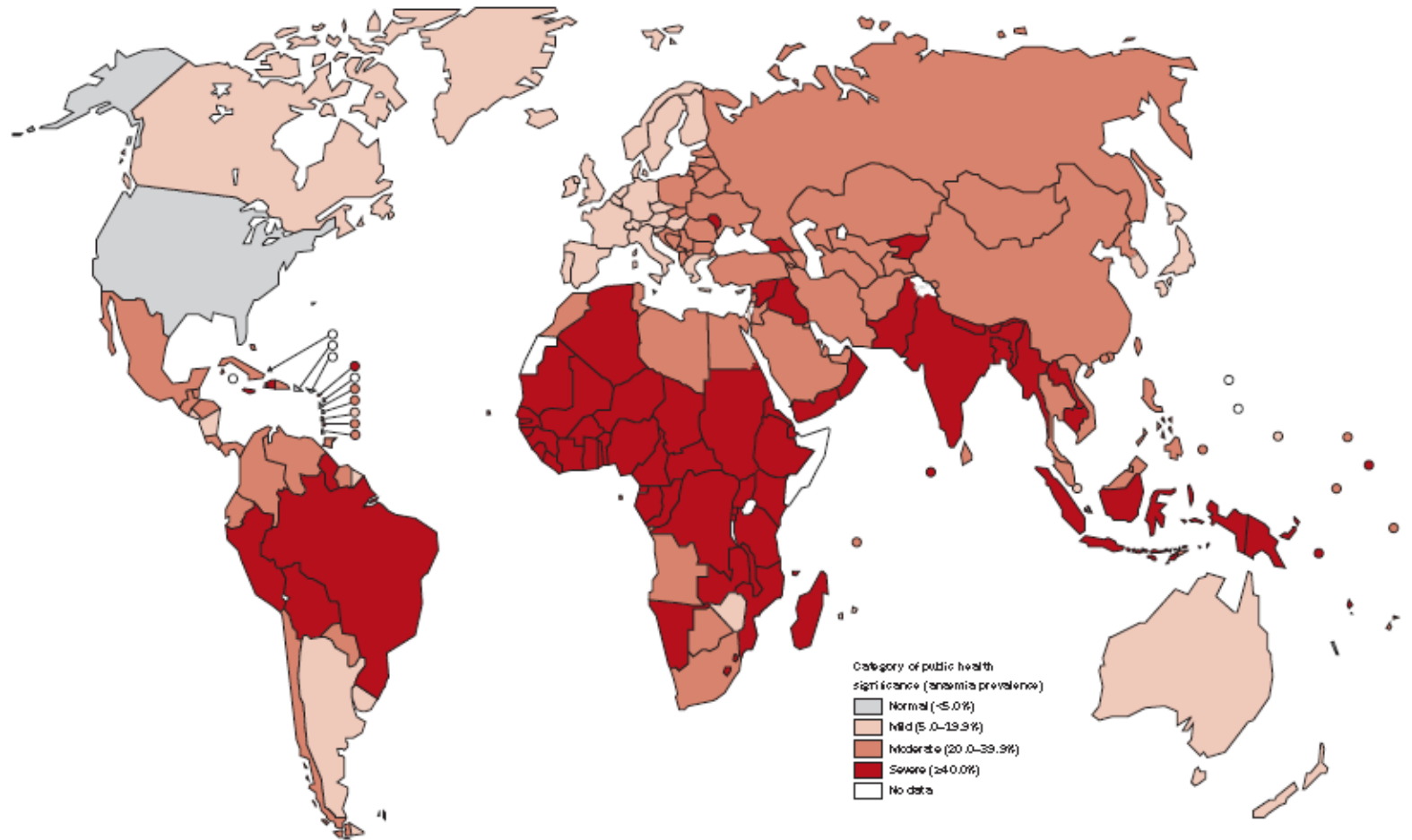
What are the most widespread
micronutrient deficiencies in the World?

Iron deficiency anaemia / IDA

- 1.6 billion low Hb level
- Highest prevalence South Asia & Sub-Saharan Africa



Anaemia as a public health problem: Preschool children

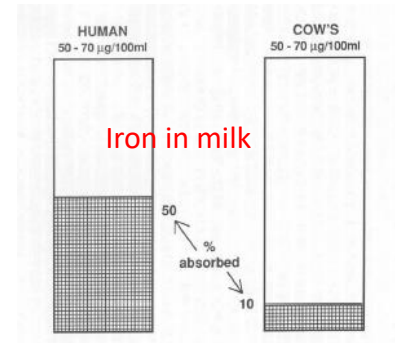


Anaemia

- **Low intake of iron**
 - Developing countries also lack of folate, vit. B2, B12, A, copper; some areas sickle cell anaemia
- **Poor absorption of non-haem Fe**
- **Increased requirement**
 - Growth
 - Pregnancy & lactation
- **Blood loss**
 - Menstruation
 - Helminthoses (Ankylostoma duodenale, Necator americanus, Ascaris lumbricoides, schistosomosis),
- **Acute & chronic infections, tumours**

Iron sources

- Breastmilk: little but up to 50% absorbed
- Haem Fe 20-30% absorbed
 - meat, offal (inner organs), fish, blood products
- Non-haem Fe <5% absorbed
 - Cereals, root crops, pulses, nuts, egg
- Some substances **enhance** (vit. C), some **inhibit** (phytate, fiber, polyphenols) **non-haem Fe absorption**



IDA: Risk groups

- Infants in transition from milk to family diet:
 - fast growth, little Fe in milk
- Women - high requirement
 - Menstruation
 - Pregnant,
 - Breastfeeding
- Seniors: low intake, losses

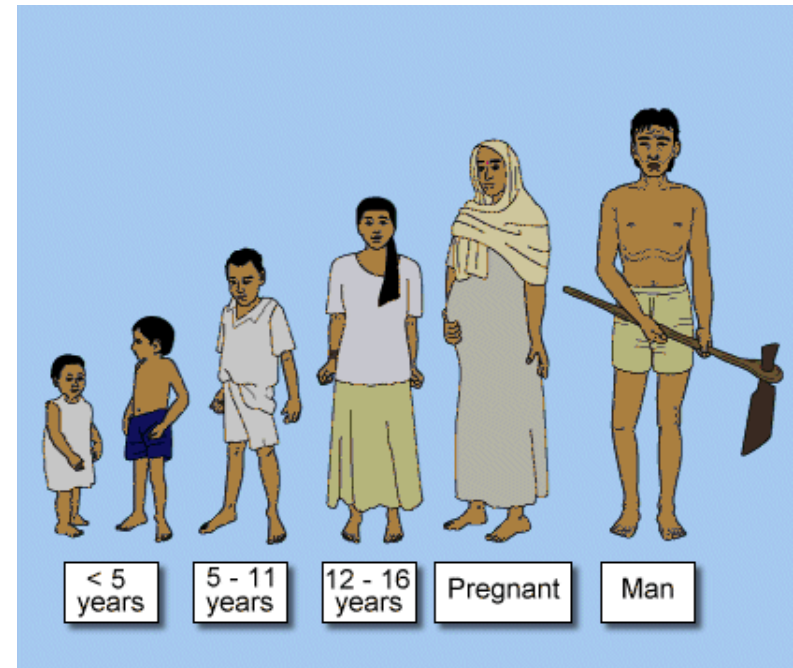
Iodine deficiency

- The **most common cause of preventable brain damage and mental retardation**
- A public health problem in 47 countries
- Low intake 2 billion people
 - 52% Europe
 - 47% East Mediterraen
 - Goitre 740 milions
 - Cretinismus 16,5 milions
 - Less severe brain damage 49.5 milions



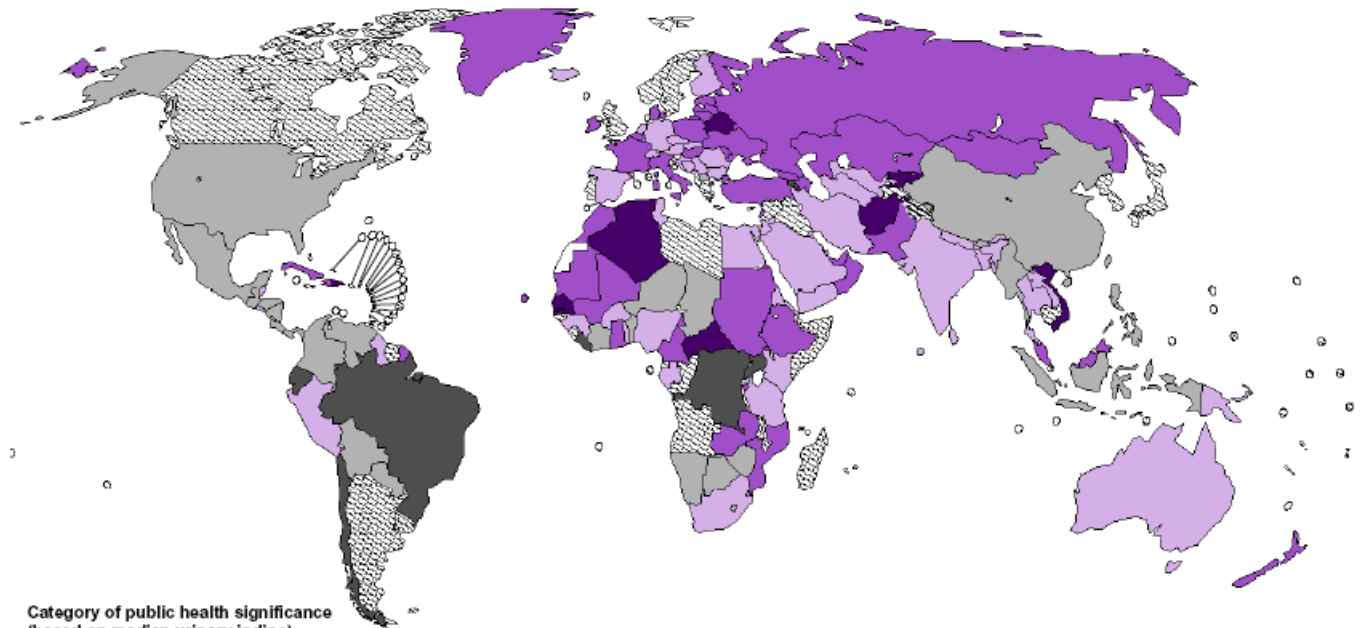
Spectrum of clinical effects

- Is due to
 - Varying degrees of ID
 - Different life stages
- The spectrum includes:
 - Impaired mental function
 - Retarded physical development
 - ↓ Fertility
 - ↑ Stillbirth
 - ↑ Congenital anomalies
 - ↑ Perinatal mortality



Iodine deficiency

Degree of public health significance of iodine nutrition based on median urinary iodine: 1993-2006



Category of public health significance
(based on median urinary iodine)

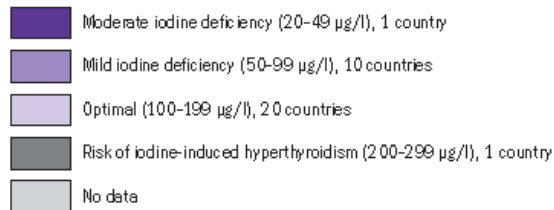
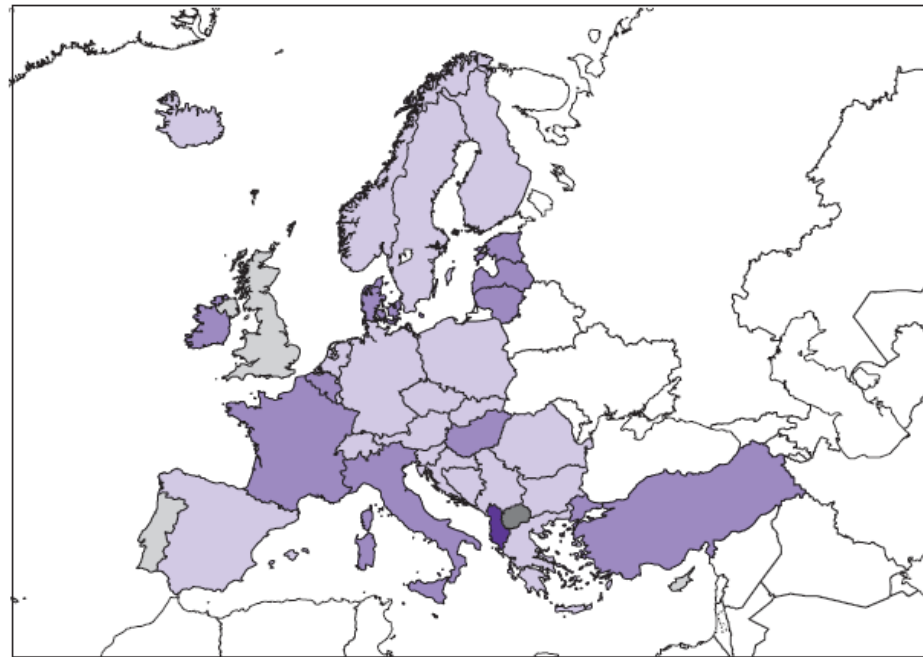
- Moderate iodine deficiency (20-49 µg/l)
- Mild iodine deficiency (50-99 µg/L)
- Optimal (100-199 µg/l)
- Risk of iodine induced hyperthyroidism (200-299 µg/l)
- Risk of adverse health consequences (>300 µg/l)
- No data

Source:

de Benoist B et al. Iodine deficiency in 2007: Global progress since 1993. Food and Nutrition Bulletin, vol 29, no. 3, 195-202, September 2008.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2009. All rights reserved.

Iodine deficiency in Europe



Iodine deficiency risk groups

- When higher demand:
 - Rapid growth
 - Growth and maturation of almost all organ systems
 - Bone growth demand
 - Pregnancy, Lactation

Sources of iodine

- Food and water in varying amounts
 - Iodine is high in sea water, so in seafood
 - Greater in meat and other animal products than in plants
- Iodized salt 25 mg KI/kg
- The amount of iodine available to the thyroid gland depends on
 - Amount of iodine in soil on which food was grown
 - Amount of goitrogens in food



Goitrogens

- **Action**

- Reduce the amount of iodine that the thyroid takes up from the blood OR
- Influence the synthesis of thyroid hormones

- **Sources**

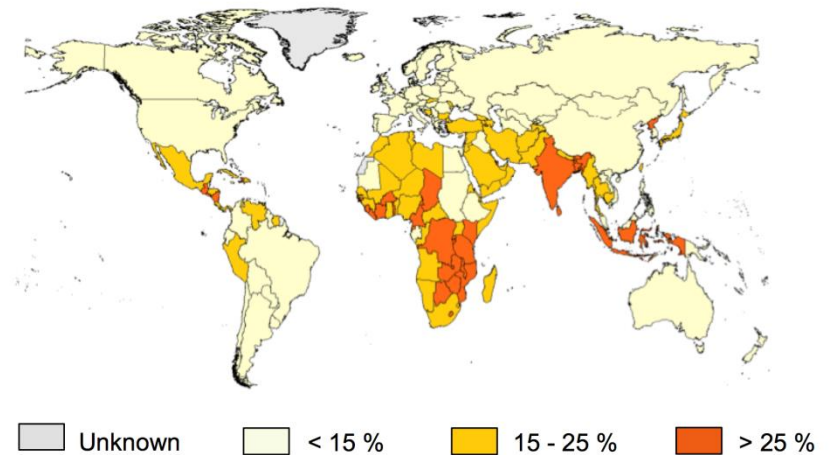
- Some root crops e.g. cassava, sweet potatoes
 - Genus Brassica vegetables e.g. cabbage, kale
 - Maize, bamboo shoots, lima beans
-
- Particularly important where the staple food contains goitrogens
 - Can threaten fetal development because they can pass across the placenta.



Zinc deficiency: prevalence

- Severe: not common
- Mild: 20% global population
 - 9 % USA, Canada 33 % South-east Asia
 - Up to 100 % pregnant women + children in developing countries

Estimated country-specific prevalence of inadequate zinc intake



- Plasma zinc concentrations are a nonspecific biomarker
- Estimates of inadequacy are largely based on the prevalence of child stunting, estimates of dietary intakes, and the availability of zinc from the food supply

Zinc deficiency: signs

- Severe:
 - Hypogonadismus, dwarfism (Middle east)
 - Acrodermatitis enteropathica (malabsorption)
- Mild
 - impaired immune functions
 - intrauterine growth retardation
 - neural tube defects in the foetus
 - dermatitis
 - affects taste acuity



Acrodermatitis enteropathica

Zinc: sources



- More readily absorbed from animal sources than plant sources.
- Meat and other protein rich foods
- Seafood - excellent source
- Whole grain breads, cereals and dried beans
 - BUT phytates in grains can decrease its absorption



Vitamin A deficiency
WHAT ARE THE SIGNS?



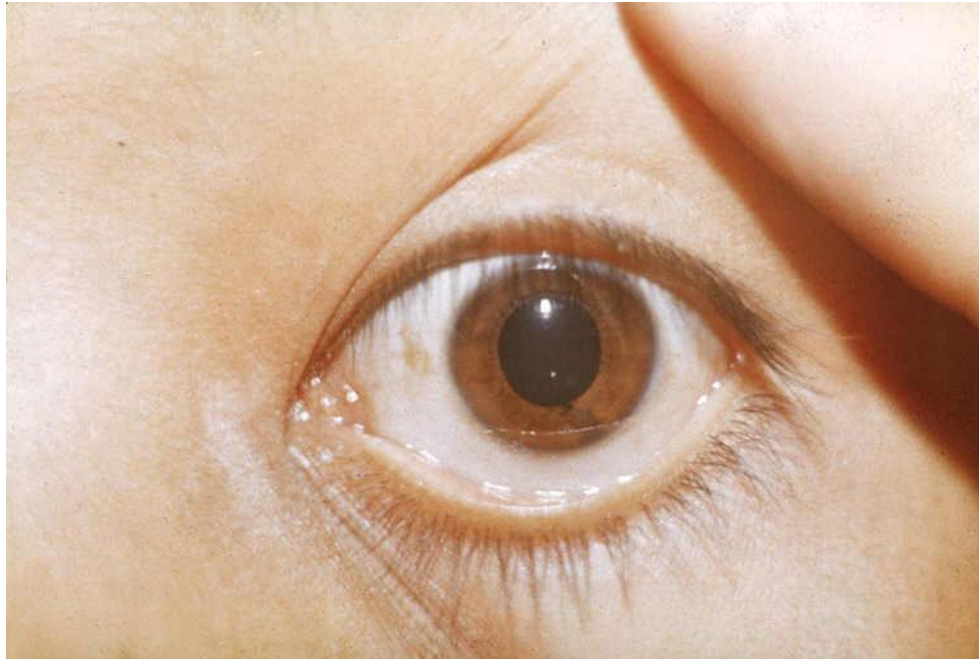
A: Xerophthalmia - night blindness

XN

- Reduced rhodopsin in the rods of retina



A: Xerophthalmia - xerosis of conjunctiva X1A



A: xerophthalmia – corneal scar XS

- Right eye enlarged:
corneal staphyloma
- Left eye smaller:
phtisis bulbi
- Both eyes blind



Vitamin A deficiency in children <5 years in developing countries

Blindness:

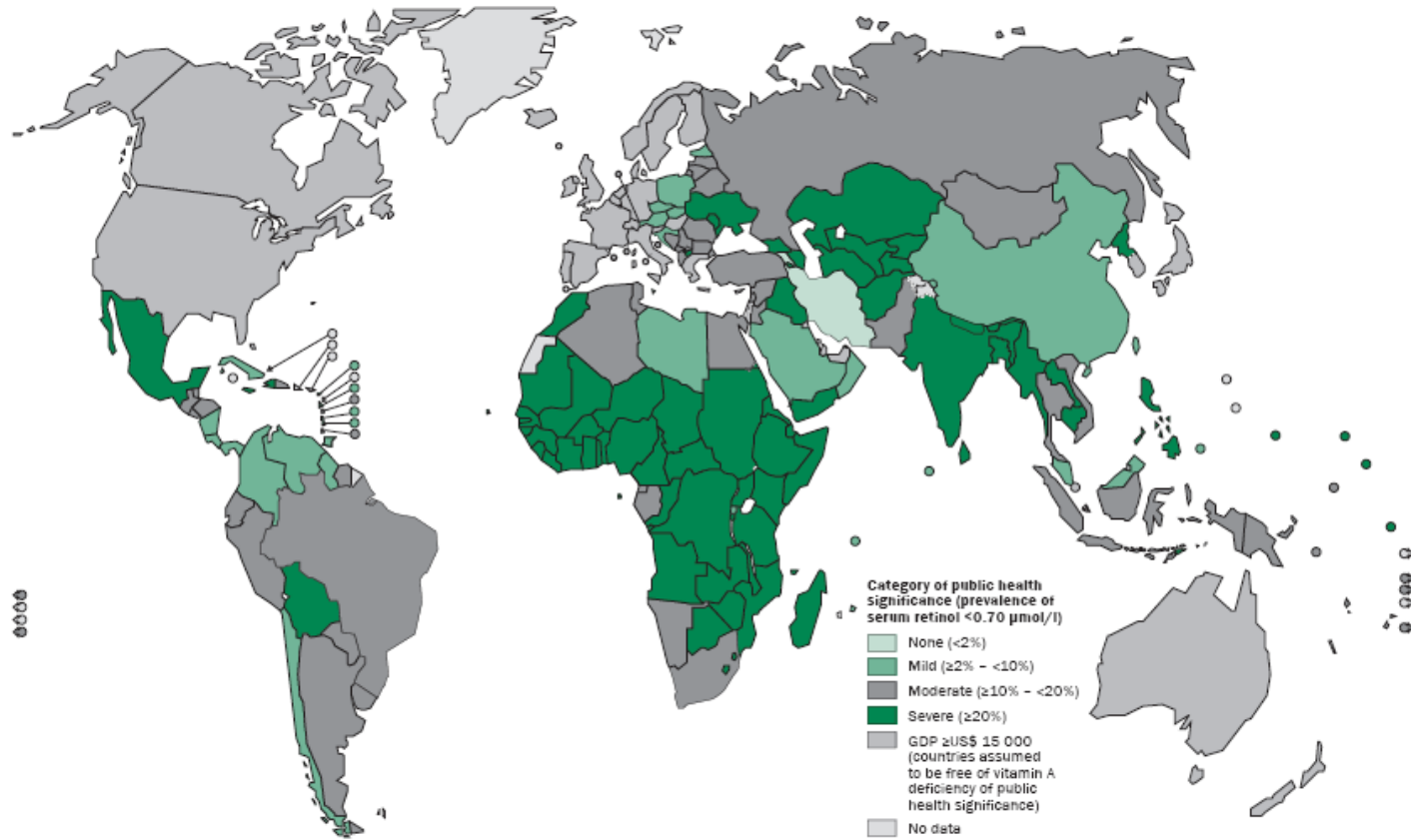
250 - 500 000/year • ½ die within one year

Xerophthalmia:
5.2 million

Subclinical deficiency:
190 million

- Contributes to the death of 1-3 million children; mostly diarrhoea, ARI & measles.
- Even mild deficiency increases the severity of disease and case fatality rate.

Low plasma retinol levels



Sources of vitamin A and beta carotene

Vitamin A

- Animal foods



Beta carotene

- Vegetable foods: Leafy vegetables, yellow, orange & red fruits and vegs



Vitamin A supplementation



Vitamin D deficiency
WHAT ARE THE SIGNS?



Vitamin D deficiency

Rickets in children

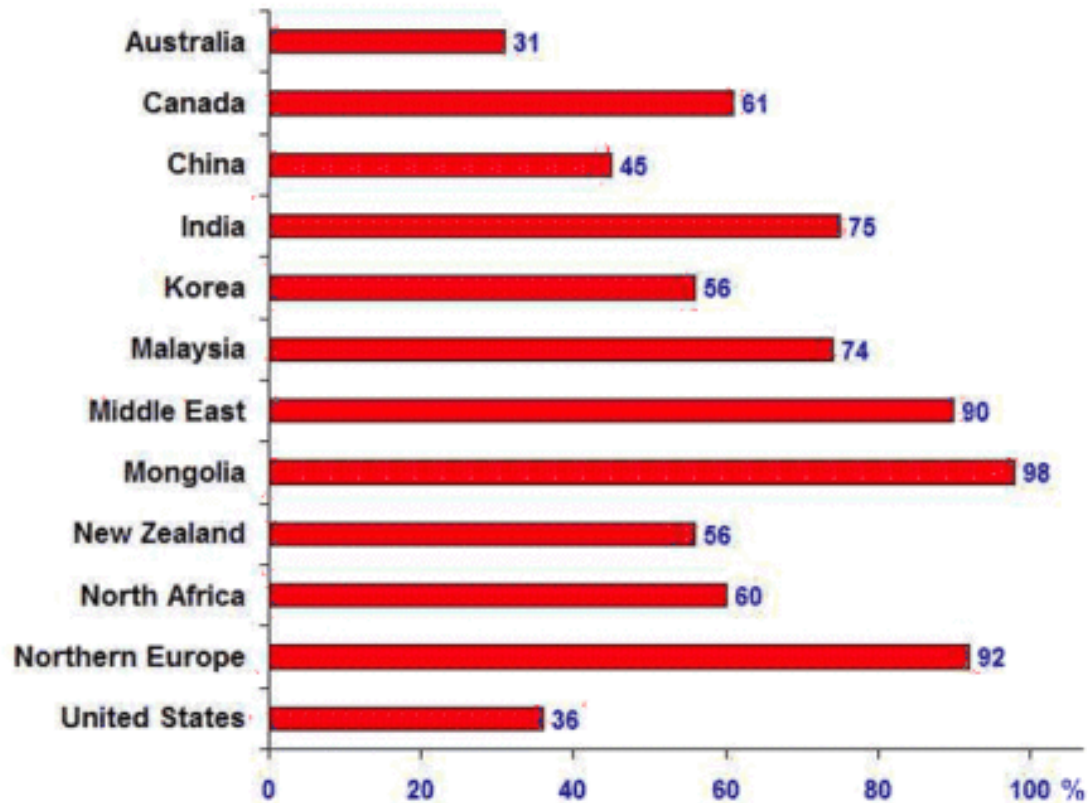


Osteomalacia in adults



Vitamin D deficiency

Many countries have large % of population with less than 20 ng of vitamin D



[Wahl DA](#) et al. A global representation of vitamin D status in healthy populations. [Arch Osteoporos.](#) 2012;7:155-72.

Vitamin D: people at risk

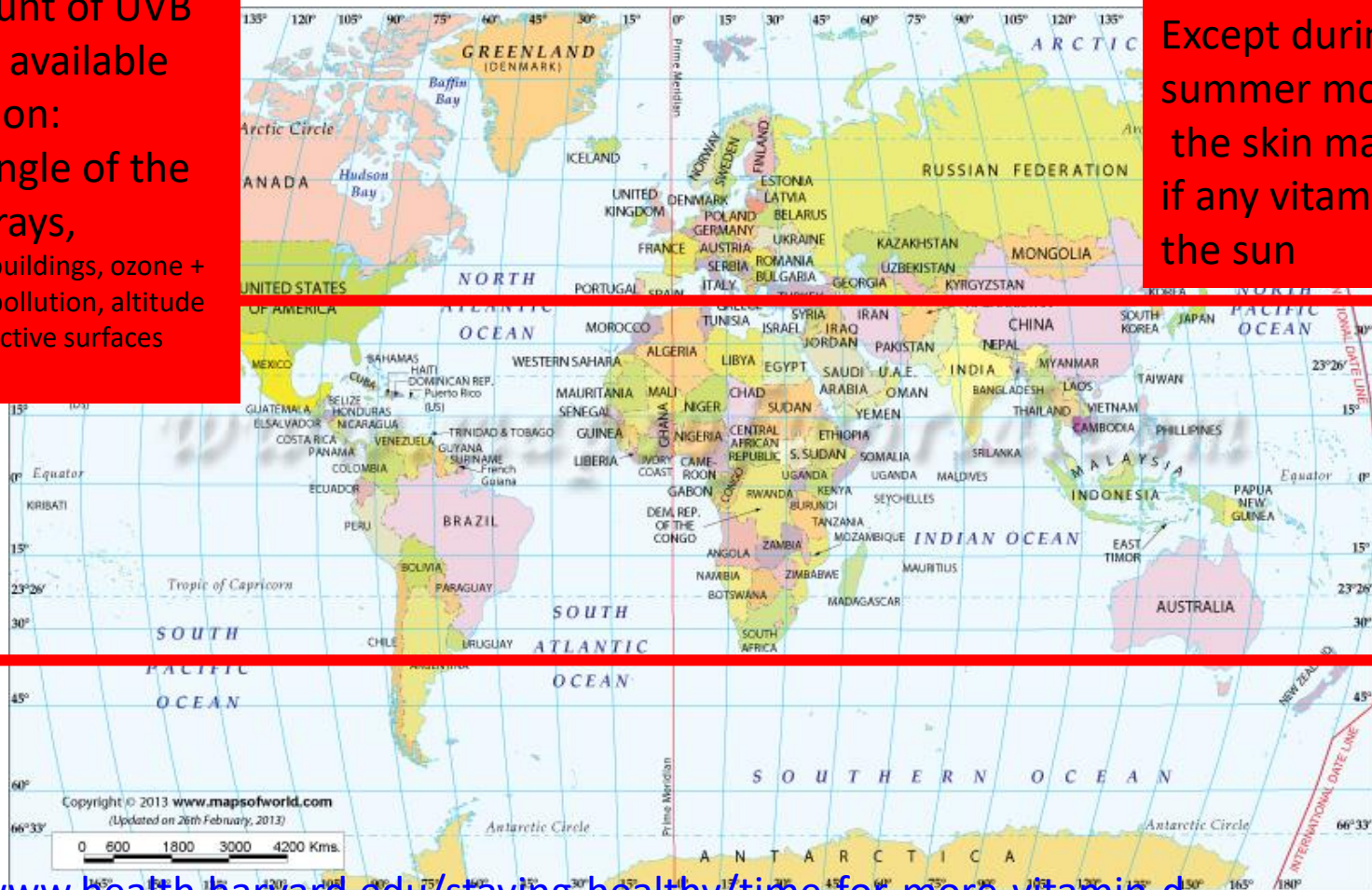
- Living at high latitudes
- Naturally dark skin - especially if resettled
- Have limited sun exposure:
 - Avoid the sun
 - Nightshift workers
 - Confined indoors or institutionalised
 - Wear covering clothing
- Use sunscreen lotions
- Seniors

Vitamin D deficiency risk: Latitudes above 37° N or below 37 ° S

The amount of UVB radiation available depends on:

- the angle of the sun's rays,
- Clouds, buildings, ozone + aerosol pollution, altitude and reflective surfaces (snow)

Except during the summer months, the skin makes little if any vitamin D from the sun



<https://www.health.harvard.edu/staying-healthy/time-for-more-vitamin-d>

<https://www.mapsofworld.com/world-maps/world-map-with-latitude-and-longitude.html>

Vitamin D: Role

- Ca – P homeostasis:
 - Increased resorption Ca in gut → increases Ca²⁺ in plasma → bone deposition
 - Increased re-absorption of phosphate in kidneys
- Other roles – explored
 - Receptors for vitamin D everywhere – even in tissues not associated with Ca-P homeostasis
 - Calcitriol influences the transcription of 5 % of the human genome
 - Observational studies: Potential preventive and therapeutic role of vitamin D in:
 - cancer
 - autoimmune diseases
 - DM 1. & 2.
 - cardiovascular diseases
 - hypertension
 - neuropsychiatric disorders
 - pre-eclampsia
 - infectious diseases (known for a long time)

Vitamin D: Causality or consequence?

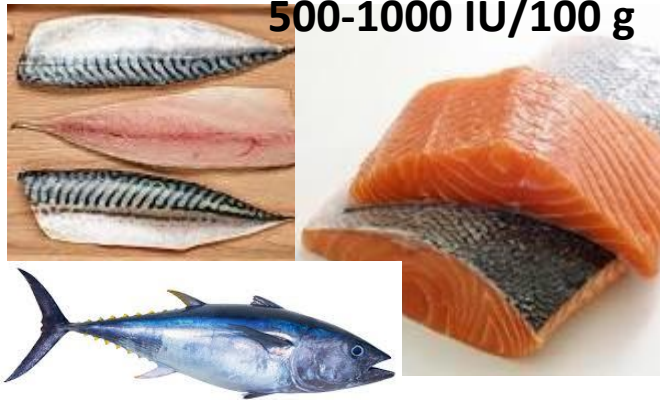
- Vitamin D deficiency /insufficiency is widely recognized as a global health problem that is likely to be involved in pathogenesis or progression of many acute and chronic health disorders
- *The available evidence does not meet the criteria for establishing cause-and-effect relationships*
 - limitations of observational studies
 - the causal relationship couldn't be established in a number of randomized studies or meta-analyses.
- This may reflect the fact that vitamin D level reduction is just a biomarker of ill health.
 - The inflammatory processes involved in the disease occurrence and the functional limitations of the diseases would have a role in reducing serum 25 (OH) D level, which would explain why low vitamin D is reported in a wide range of disorders.

NEW Vitamin D supplementation: randomized controlled intervention trials

- RCT meta-analysis:
 - Supplementation was **not associated with overall mortality** (Zhang Y et al. 2019)
 - Supplementation significantly **↓ cancer mortality** but **did not reduce the overall incidence** of cancer (Zhang Y et al. 2019, Keum N et al. 2019)
- RTC 25,871 participants, median follow-up of 5.3 years of supplementation **did not reduce the incidence of cancer or CVD** (Manson JE et al 2019)

Vitamin D: Food sources

Very few natural food sources

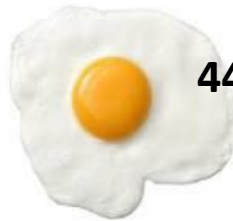


500-1000 IU/100 g

NEED EFSA: 600 IU/day USA: 800 IU

- D3 **Top sources:** The flesh of **fatty fish** (tuna, salmon, mackerel) fish liver oils
 - Study: Farmed salmon 75% less than ‘wild caught’
- D3 **Small amounts:** egg yolks, some cheese, meat
- D2: Some mushrooms
 - inconsistent quantities ;
↑ after exposure to UV
- **Fortified foods**

20-40 IU/100g



44 IU/1egg



20-45 IU/100g

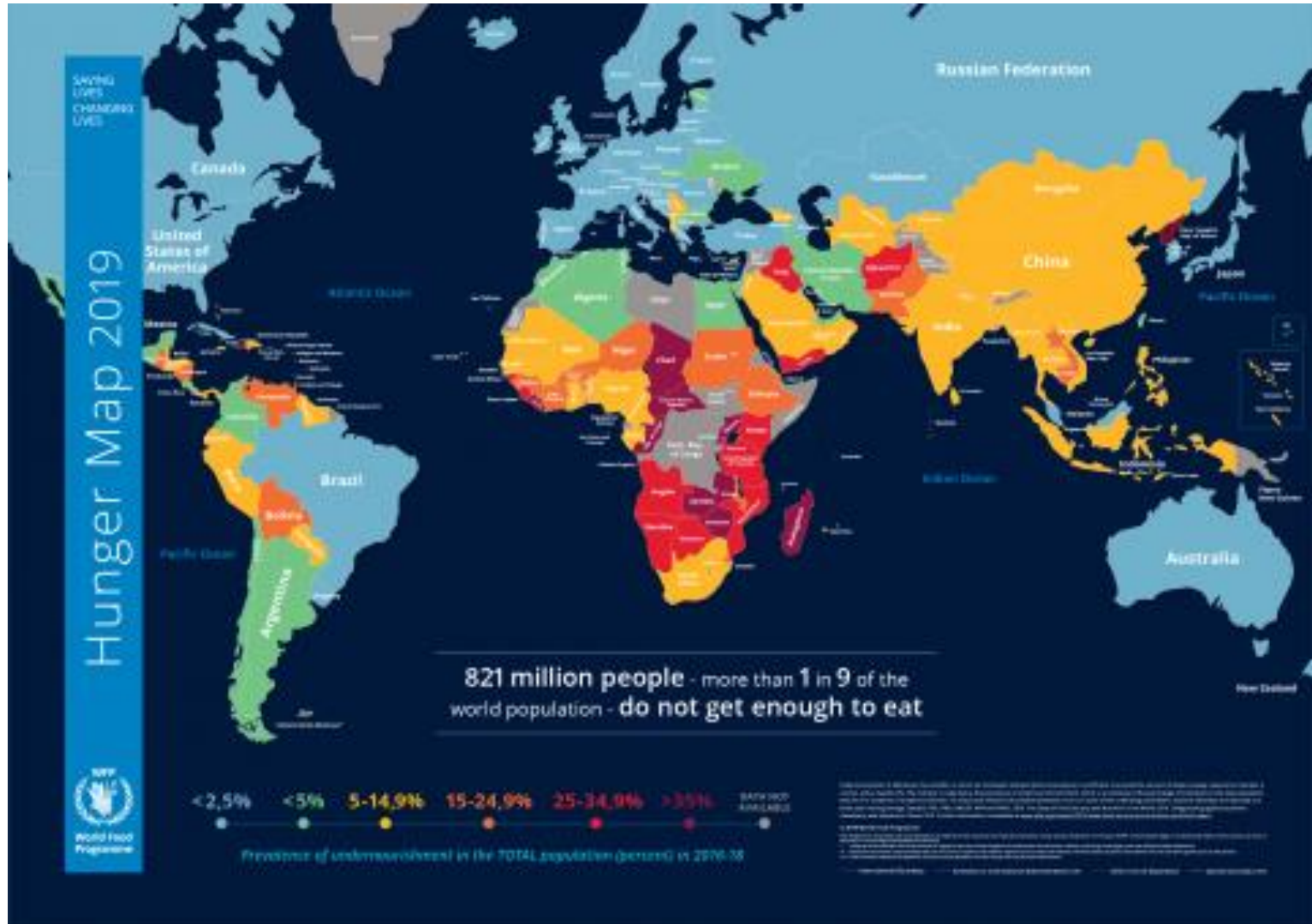


Values USDA database

Hunger Map 2019



(Protein energy malnutrition)



DO WE HAVE MALNOURISHED PEOPLE IN THE CZECH REPUBLIC?



Malnutrition in hospitalized patients

- 30-60 % at admission
- 30% develops during hospitalization
- 70 % deteriorates during hospitalization

Most at risk:

- Malignancies 85 %
- Bowel diseases 80%
- Seniors 50 %

Malnutrition

- Simple – hypometabolic state
- Stress – hypercatabolic state especially protein breakdown in a relatively short time

Stress malnutrition: consequences of hypercatabolism

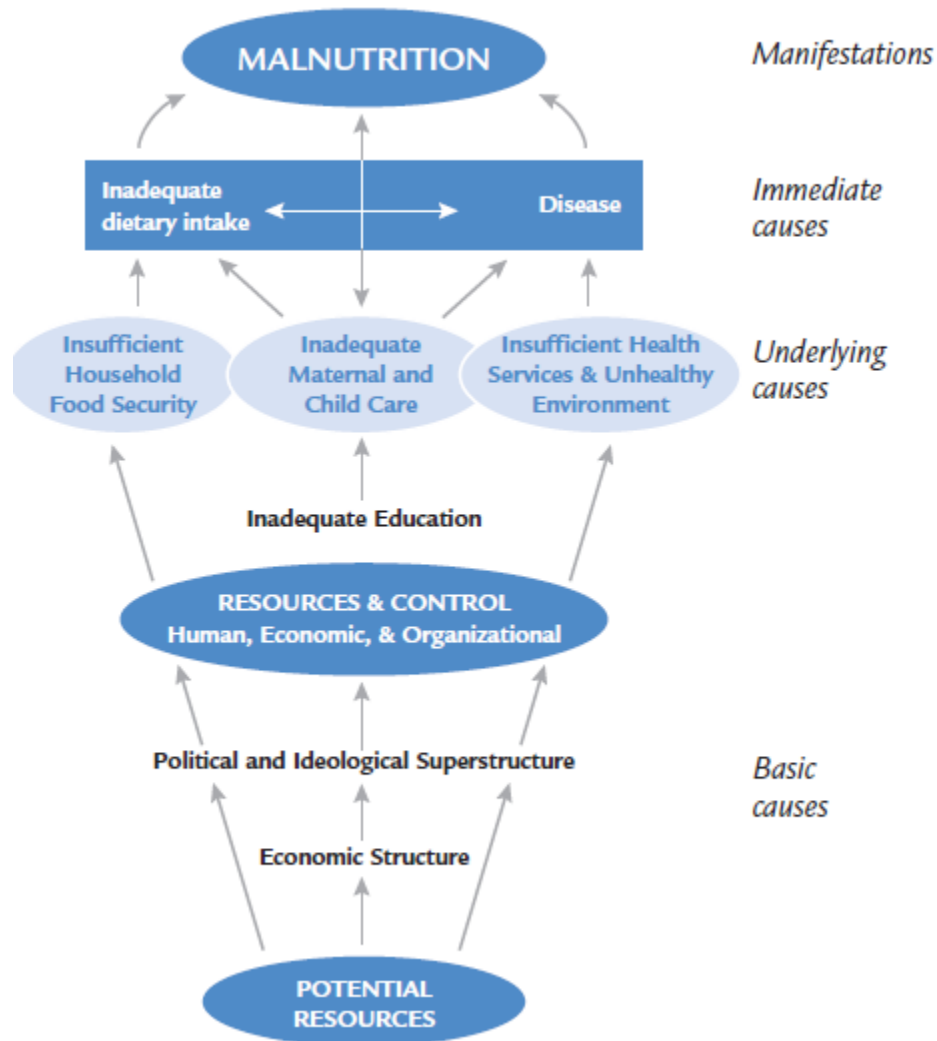
- Brain alteration: anxiety, depression
- Muscle mass loss
 - myocard function: contributes to shock development
 - decreased ventilation: contributes to respiratory insufficiency
- Impairment of intestine
 - Impaired barrier function: endogenous sepsis - multiorgan failure
 - Decreased absorption of nutrients
- Decreased immunity
- Impaired wound healing

Management of malnourished patients

- Active identification
- Energy & nutrient need assessment
- Ensuring adequate food administration
- Monitoring during nutrition intervention
- Home nutrition care

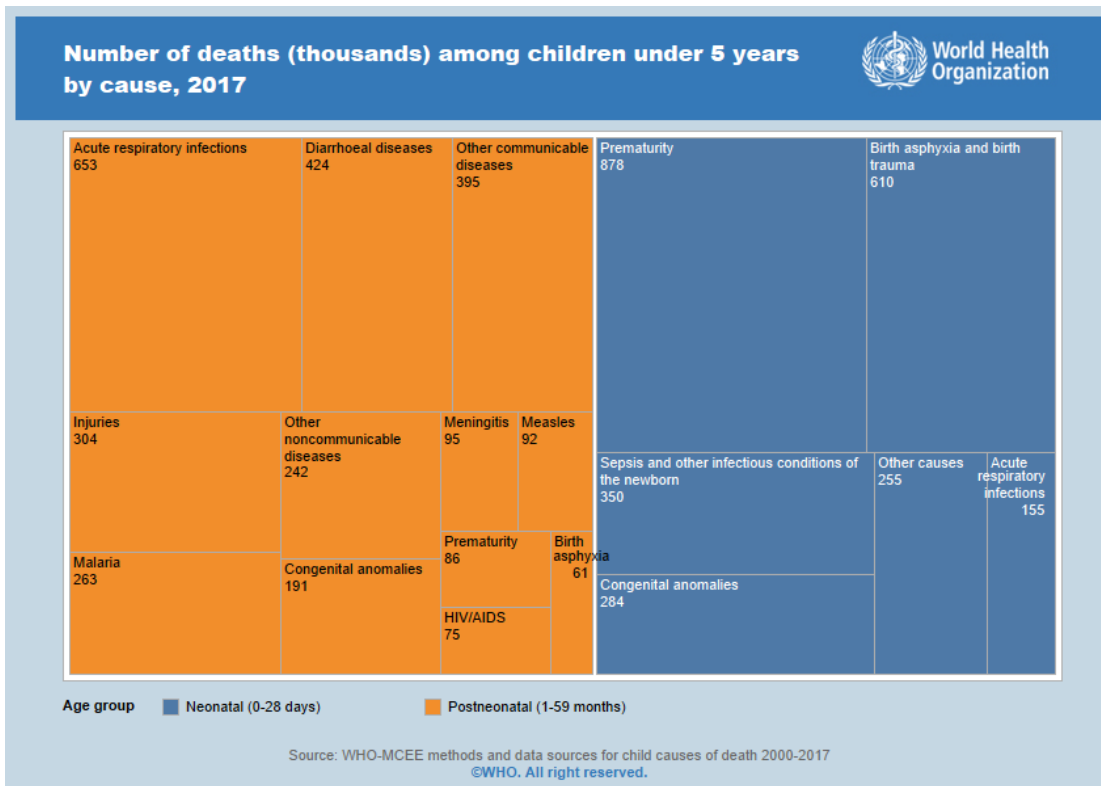
PROTEIN ENERGY MALNUTRITION IN THE WORLD

Causes of malnutrition



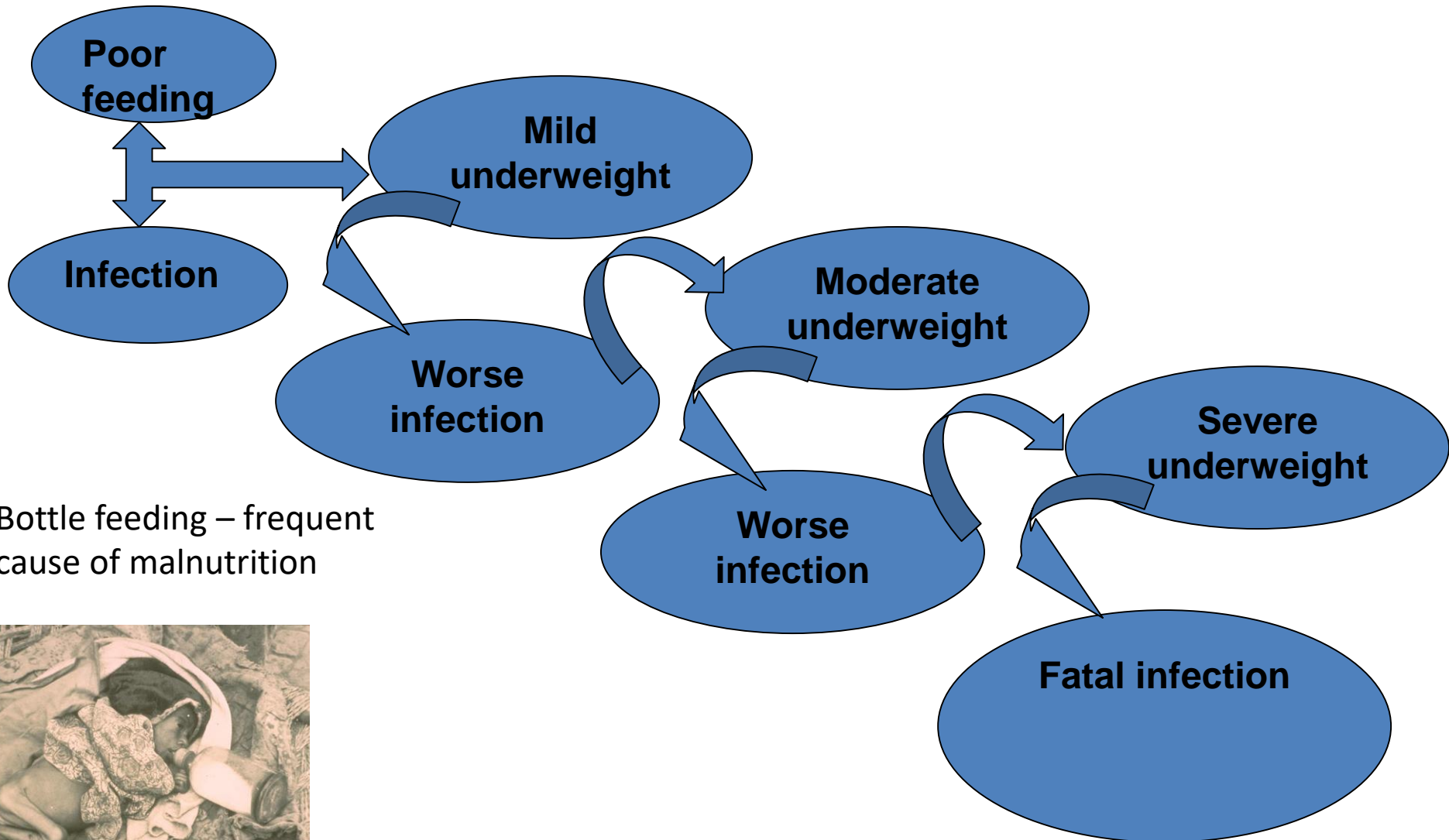
Causes of <5 child mortality, 2017, World

- At least 1/3 of all under-five deaths are due to the presence of undernutrition



https://www.who.int/gho/child_health/mortality/causes/en/

Spiral of malnutrition



Severe acute malnutrition (SAM)

- Acute malnutrition most frequently develops between 6 and 24 month of age
- Marasmus
 - Extreme wasting
 - WH/L < -3 z-scores



Kwashiorkor: sugar baby

- Growth stops
- Muscle loss
- Oedema
- Psychic changes
- ... may have other signs: liver steatosis, hair, skin
- Relatively abundant energy intake – fat present



Kwashiorkor



Aetiology of kwashiorkor

- Kwashiorkor, an enigmatic form of severe acute malnutrition, is the consequence of inadequate nutrient intake plus additional environmental insults.... **but WHAT insults?**

[Smith MI](#) et al. Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. [Science](#). 2013 Feb 1;339(6119):548-54. Center for Genome Sciences and Systems Biology, Washington University in St. Louis, St. Louis, MO 63110, USA

Aetiology of kwashiorkor

- Deficiency in protein intake, low levels of antioxidants in the diet are **NOT** considered primary causal factors of kwashiorkor:
 - Diet of children with marasmus have similar deficiencies
 - Dietary supplements of protein and antioxidants in children who are high risk for kwashiorkor have not been shown to reduce the risk of kwashiorkor (Ciliberto H, Ciliberto M, Briend A et al. Antioxidant supplementation for the prevention of kwashiorkor in Malawian children: randomised double blind, placebo controlled trial. *BMJ* 2005;330(7500):1095-6)
 - Oedema resolves on a restricted protein diet (Golden MH. Protein deficiency, energy deficiency, and the odema of malnutrition. *Lancet* 1982;1(8284):1261-5)
- Many hypotheses over the time....

Aetiology of kwashiorkor: New hypothesis

- **Changes in the gut microbiota** that favor the production of metabolites that
 - insult the human cell membrane integrity in an undernourished host, OR
 - disruption of the gut microbiota's protective function with respect to environmental toxins.
- MANARY, MJ, et al. Kwashiorkor: more hypothesis testing is needed to understand the aetiology of oedema. *Malawi Medical Journal*. 2009, vol. 21, no. 3, s. 106-107, ISSN 1019-1941.
- Smith MI et al. Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* **2013** Feb 1;339(6119):548-54. Center for Genome Sciences and Systems Biology, Washington University in St. Louis, St. Louis, MO 63110, USA.

Chronic PEM: stunting

