ABC of Nutrition

A STEWART TRUSWELL

OTHER NUTRITIONAL DEFICIENCIES IN AFFLUENT COMMUNITIES

Protein-energy malnutrition in Britain and other Western industrial countries is almost always secondary to disease—for example, it may be due to diseases of the gastrointestinal tract (persistent vomiting, dysphagia, upper intestinal obstruction, malabsorption) or wasting diseases (some cancers, metabolic disorders) or to radiotherapy. It is briefly described in “Enteral and parenteral nutrition,” where management to prevent or treat it in hospital is shown. How to assess the degree of malnutrition is dealt with in “Measuring nutrition.” For a background, famine and childhood protein malnutrition are described in “Malnutrition in the Third World—I.”

In Britain the vitamin deficiency that is still a public health problem is rickets. Its pathogenesis is discussed under vitamin D in “Vitamins—II.” Among hospital patients in countries like Britain, however, the most common vitamin deficiency is probably folate deficiency, of which there is an account in “Vitamins—II.”

The most serious nutritional deficiency in alcoholics is the complex of Wernicke’s encephalopathy and Korsakoff’s psychosis, which is summarised under thiamin in “Vitamins—I.”

The following nutritional problems have not been discussed anywhere else in this series.

Iron deficiency

Cumulative frequency of daily iron requirements in menstruating women.

Halberg L. *Human Nutrition: Clinical Nutrition* 1982;36C:259-78.

Iron deficiency is probably the commonest nutritional deficiency in the world: according to one estimate it affects over 500 million people globally. People in industrial countries are often affected as well as those in developing countries, especially women aged 15 to 50. Iron is the second most abundant metal in the earth’s crust but it is virtually insoluble in the usual complexes of ferric iron in foods at neutral pH, and absorption is difficult.

There is no physiological mechanism for secretion of iron so maintenance of iron homeostasis depends on its absorption. Normally in men, children, and postmenopausal women iron is lost only in desquamated surface cells at a rate of 1 mg/day or less.

Blood is by far the richest tissue in iron; 1 ml contains 0.5 mg so that a regular loss of only 2 ml/day—for example, from epistaxis or haemorrhoids—doubles the iron requirements. Women of reproductive age lose an average of 30 ml blood per period, corresponding to 0.5 mg iron per day, so they need more iron than men. An important minority lose considerably more. They, pregnant women, children growing fast, and anyone with chronic bleeding all need to absorb extra iron or use up what tissue stores they have.

Absorption of iron is inefficient. It averages roughly 10% from a mixed diet but is much less from many plant foods and from eggs and dairy foods. Haem iron is better absorbed than non-haem iron. Absorption of the latter is enhanced by animal flesh and by vitamin C and reduced by tannins (as in tea) and phytates. Iron absorption is being studied by extrinsic labelling of foods with radioiron. The different factors in foods combine algebraically to produce a high or low absorption from the meal. For example, iron absorption is reduced if the meal is taken with tea but enhanced if it is taken with orange juice.

Iron is essential for haemoglobin formation. It is also part of myoglobin, of some enzymes required for neurotransmitter synthesis, and of an important enzyme in DNA synthesis. In deficiency, sometimes before there is anaemia, reduced maximum muscular work capacity has been reported,

Sequential changes in the development of iron deficiency

	Normal	Iron depletion	Iron deficient erythropoiesis	Iron deficiency anaemia
Iron stores				
Erythron iron				
Reticuloendothelial marrow iron (0-6)	2-3	0-1	0	0
Transferrin iron binding capacity ($\mu\text{g/dl}$)	330 $\pm$ 30	360	390	410
Plasma ferritin ($\mu\text{g/l}$)	100 $\pm$ 60	20	10	<10
Iron absorption	normal			
Plasma iron ($\mu\text{g/dl}$)	115 $\pm$ 50	115	<60	<40
Transferrin saturation (%)	35 $\pm$ 15	30	<15	<10
Sideroblasts (%)	40-60	40-60	<10	<10
Red blood cell protoporphyrin ($\mu\text{g/dl/RBC}$)	30	30	100	200
Erythrocytes	Normal	Normal	Normal	Microcytic and hypochromic

From Bothwell TH, et al. *Iron Metabolism in Man*. Oxford: Blackwell, 1979.

and elsewhere reduced cognitive learning in children and impaired cell mediated immunity have been described.

In people at risk of iron deficiency the haemoglobin (at least) should be checked, in:

- Infants at the age of 1 year
- Children and adolescents during phases of rapid growth
- Through and after pregnancy
- After gastric surgery at least once a year
- Women with heavy periods (direct questions may need to be asked)
- Patients presenting with gastrointestinal symptoms or disease
- Anyone with a history of recurrent bleeding, with a positive occult blood test or a woman who is a frequent blood donor.

Ferrous sulphate tablets are standard therapy for iron deficiency anaemia, but it seems that patients often do not take all their tablets. Gastrointestinal side effects are related to the dose of elemental iron. Ferrous sulphate, three tablets a day (300 mg each), gives 180 mg of iron for the day. Compliance and hence response may be better with two ferrous sulphate or three ferrous gluconate (300 mg) tablets, which give only 100 mg of iron per day. Slow release tablets are less effective.

Prevention

A common cause of iron deficiency is that women, who require twice as much as men, consume only half as much. They often eat less liver, meat, and fish, the best sources of available iron. People who take no exercise or are on a weight reducing diet have such a low calorie intake that it is difficult for them to eat enough iron. (See Barber SA, Bull NL, Buss DH. Low iron intakes among young women in Britain. *Br Med J* 1985;290:743-4.) Iron absorption is increased in deficient individuals but this may not be enough to compensate for low intake or increased losses. Staple foods are fortified with iron in some countries (not in Britain) and old fashioned iron cooking pots add some iron to the food.

Calcium and the bones

Age related changes in total skeletal weight of whites and negroes.

Merz AL, Trotter M, Peterson RR. *American Journal of Physical Anthropology* 1956;14:589-610.

Calcium is the most obvious and persistent of the micro-nutrients, the fifth most abundant element (and the most abundant cation) in the body, yet it is more difficult to measure adequacy of intake for calcium than for other nutrients. There are two major questions about calcium.

- (1) Will a generous intake during childhood and adolescence contribute to taller adult height or heavier bones, or both? If so how much is needed?
- (2) Will a generous intake from about 45 years onwards delay the onset of osteoporosis, especially in women, who are more likely to be affected? If so how much is best and in what form?

Over 99% of body calcium is in the skeleton. Here it not only provides structural support but is a large reservoir for maintaining the plasma calcium concentration at very stable concentrations. Any reduction of absorbed calcium does not show in the plasma concentration, which is immediately reset by an increased parathyroid hormone concentration and the formation of 1,25 dihydroxyvitamin D. Ionised calcium in the plasma has many vital functions—muscle contractility, neuromuscular irritability, blood coagulation, etc—which would be disturbed if its concentration fell.

Estimated daily increment in skeletal calcium of children at various ages.

Leitch I, Aitken FC. *Nutrition Abstracts and Reviews* 1959;29:393-41.

In 1927 a series of tests was carried out in Scotland in which about 1500 children in the ordinary elementary schools in the seven largest towns were given additional milk at school for a period of seven months. Periodic measurements of the children showed that the rate of growth in those getting the additional milk was about 20% greater than in those not getting additional milk. The increased rate of growth was accompanied by a noticeable improvement in health and vigour. This experiment was twice repeated by different observers who obtained substantially the same results on numbers up to 20 000 children.

Orr JB (later Lord Boyd Orr). *Food Health and Income*, 1936.

Other dietary associations with osteoporosis

Obesity may protect but crash dieting increases urinary calcium loss.

Anorexia nervosa is associated.

Fluoridation of water supplies (1 ppm) appears to be protective.

High consumption of alcohol, coffee, meat, salt, and cola beverages tends to reduce available calcium.

Regular moderate weight bearing exercise may be protective.

By different modulators the ionised calcium inside cells is also tightly controlled. An inadequate dietary calcium will therefore not normally be allowed to lower plasma or intracellular calcium concentrations and their numerous important soft tissue functions; instead a little less will go into the bones in children or a little will be removed from the bones in adults.

Calcium in the bones amounts to 25 g at birth and builds up to about 1200 g in an adult. From the indices of growth and skeletal composition the amount of calcium which is being added to the bones each day in growing children can be calculated. It averages about 180 mg calcium per day but reaches 400 mg per day at the peak of adolescent growth. This amount is the required positive balance. Calcium absorption is inefficient—faecal calcium is often 70-80% of intake in adult calcium balances—and there is an obligatory loss of calcium in urine as well. The diet must therefore supply substantially more than the daily skeletal increment, and the recommended daily amount in Britain is 600 mg in children and 700 mg from 9-14 years. There is evidence that in some conditions a supplement of milk (the best source of calcium) has improved the growth rate of children. The great increase in the height of young Japanese adults from 1950 to 1970 coincided with a tripling of the national calcium intake from about the lowest in the world to 600 mg/day.

Yet it is hard to understand how poor children in the Third World on diets of cereals and vegetables and no milk obtain enough calcium to grow. Their final adult height is usually lower than in industrial countries, but osteoporosis in older people is less of a problem. There are four possibilities to explain the more economical handling of calcium in Third World people:

- More skin synthesis of vitamin D from sunshine in the tropics.
- Genetic adaptation.
- Lower intake of animal protein (which is known to increase the obligatory urinary calcium).
- Lower intake of salt (which also increases urinary calcium loss).

Population studies in America failed to show any correlation between metacarpal cortical width on radiographs and calcium intake. But calcium metabolism is complex and intake is not the same as net balance. Metacarpal bone width, though convenient, is clearly an unreliable way of measuring total body calcium.

Three trials of the effect of calcium supplements on postmenopausal bone loss have been reported recently. Two report some inhibition of bone loss, the third does not. There have been different interpretations: some calcium experts are encouraged, others unimpressed. It is generally accepted that oestrogens delay postmenopausal bone loss but convincing proof of the value of calcium supplements will require longer trials, preferably using high technology measurements that can give better estimates of bone thickness: photon absorptiometry of the forearm bones or computerised tomography of several bones or even whole body calcium by in vivo neutron activation analysis.

Dieting can be dangerous

Articles which show the dangers of some diets

Liquid protein and fasting—Isner JM, et al. *Circulation* 1979;60:1401-12.

Zen macrobiotic diets—AMA Council on Foods and Nutrition. *JAMA* 1971;218:397-8.

Dr Atkins's diet revolution—AMA Council on Foods and Nutrition. *JAMA* 1973;224:1415-9.

Vitamin B-12 deficiency in vegan infants—Wighton MC, et al. *Med J Aust* 1979;ii:1-3 (see next box).

Beverly Hills diet—Mirkin GB, Shore RN. *JAMA* 1981;246:2235-7.

Malnutrition can result from dietary regimens which happen to be very unbalanced nutritionally. Some of these were introduced by medical graduates, others are unscientific. The following are only a sample.

"Liquid protein" combined with fasting in the USA in the late 1970s led to at least 60 deaths from cardiac arrhythmias in people with no history of heart disease. The product "Prolinn," an extract from beef hides, lacked several essential amino acids. It was withdrawn, but prolonged fasting with or without protein supplements (even those of good biological value) carries the risk of sudden fatal arrhythmias and has been criticised authoritatively.

Zen macrobiotic diets consist of 10 levels. The highest level is 100% cereals and prescribes a very low fluid intake. They have led to scurvy and/or impaired renal function, anaemia, hypocalcaemia, and emaciation. In some cases these have been fatal. These diets have been condemned by the American Medical Association.

Dr Atkins's diet revolution—This weight reducing diet in a popular paperback written in 1972 prescribes a minimal carbohydrate intake. Ketosis is inevitable, and the diet raises plasma lipid concentrations. It was

An exclusively breast fed infant of a vegan mother

"Neurological deterioration commenced between 3 and 6 months of age and progressed to a comatose premoribund state by the age of 9 months. Investigations revealed a mild nutritional vitamin B-12 deficiency in the mother and a very severe nutritional B-12 deficiency in the infant with severe megaloblastic anaemia. Treatment of the infant with vitamin B-12 resulted in a rapid clinical and haematological improvement but neurological recovery was incomplete. . . ."

By 17 months of age his general level of motor, social, and intellectual development was that of a child of 11 months.

Wighton *et al*, 1979

Anorexia nervosa

Treatment in special anorexia unit

Supervised eating
Behavioural therapy
Supportive psychotherapy

condemned by the American Medical Association but can still be found on bookstalls, having sold millions of copies.

Strict vegan diets for infants—Plant foods contain no vitamins B-12 or D. The latter can be synthesised in the skin if a child is exposed to sunlight, but the most serious nutritional complication of strict vegetarian diets is vitamin B-12 deficiency in infants. The milk of vegan mothers contains insufficient vitamin B-12 unless she takes a supplement. This vitamin is required for normal myelin formation, and infants' nervous systems are specially susceptible to deficiency. They can show impaired mental development, involuntary movements, and even coma responsive to vitamin B-12 as well as megaloblastic anaemia.

The Beverly Hills diet—This weight reducing diet requires consumption of nothing but fruit (all in a certain order and only the designated fruits) for the first 10 days. Some bread, salad, and meat are added later. The theory behind this diet is unscientific, and it has been criticised in detail in the *Journal of the American Medical Association*.

Anorexia nervosa is an illness of our time, although it was first described and named in 1874. Many teenage girls and young women say they are dieting to stay or become slim but most are not very successful. They do not stick to their diets. The young woman with anorexia nervosa is unusual: without talking about dieting she succeeds in losing a lot of the weight that the others say they would like to. But then she cannot stop. By rigid control of her eating she avoids foods that she understands to be fattening. She has a phobia of being fat and often a distorted body image, seeing herself fatter than she really is. Amenorrhoea is characteristic.

Up to one in 100 middle class women from 15 to 25 may be affected. Before this loss of weight the young woman with anorexia nervosa was often a model of good behaviour, conformism, and achievement though this probably concealed a sense of ineffectiveness and self doubt.

Some women not only abstain: they have learnt to induce vomiting or purging and may have eating binges between. When habitual this behaviour is bulimia nervosa.

The physical effects of a young woman starving herself to 45 kg and below are similar to those described for famine in the article on "Malnutrition in the Third World—I." But there are differences. The anorectic patient (appetite is there but being suppressed) usually eats adequate protein and micronutrients and is restless and overactive. There is skinniness or emaciation, cold extremities, lanugo hair, bradycardia, low blood pressure, and normal pubic and axillary hair. Plasma potassium concentrations may be low if there has been vomiting or purging, and plasma cholesterol or carotene values are sometimes raised.

The amenorrhoea is similar to that which occurs in starvation.

Early diagnosis is important because a long illness, severe weight loss, and bulimia (which tends to occur in older cases) are all bad prognostic features. The young woman denies she is too thin or that she is dieting. Amenorrhoea may appear to have preceded the weight loss. Other organic diseases that can lead to emaciation and amenorrhoea have to be excluded—for example, thyrotoxicosis, malabsorption, and hypopituitarism. But the bigger challenge for the family doctor is to detect the characteristic features of anorexia nervosa and to convince the young woman that she needs treatment.

Treatment is usually best done by a specialised team, most often a psychiatrist with special experience in anorexia working with a dietitian. A patient with anorexia nervosa of average severity should preferably be admitted to a special anorexia unit. The first aim is to persuade her to increase food intake and get her weight up to a target figure (usually a compromise). Eating is tactfully supervised by nurses, and behavioural principles can be effective: more privileges for each step of weight gain, previously agreed by the patient. As she is refed and becomes physically stronger it becomes easier for the patient to tackle the changes needed so that she can adapt to society and develop a healthier body image. Supportive psychotherapy starts in the unit and has to be continued as an outpatient.

Nutrients, foods, and drugs can interact in several ways

- *Foods can affect drugs*, for example, by affecting absorption, an acute effect of single meals.
- *Nutrition can affect drugs*. Either the nutritional state or particular foods regularly eaten can affect drug metabolism and hence dosage and toxicity.
- *Particular drugs can affect the nutritional state*. Appetite, absorption, metabolism, and concentration of nutrients can be affected, positively or negatively, by different drugs.
- *Drugs can cause unpleasant reactions to minor components in some foods* whose metabolism we normally take for granted—for example, hypertension from tyramine in cheese in patients taking monoamine oxidase inhibitors.
- *A few drugs are used as foods*, as part of the usual diet: alcoholic drinks, coffee, tea, and carbonated cola beverages.
- *Nutrients are used as drugs*. The nutrients are all obtainable in pure form. They may, in doses above the nutrient requirement, sometimes have a useful pharmacological action—for example, nicotinic acid for hyperlipidaemia.

Should I take the medicine before or after meals, doctor?

Most drugs are best taken *with or just after meals*, because this is the easiest way to remember to take any drug and some are gastric irritants. Absorption of several drugs is a little delayed but this is unimportant and a few are better absorbed when taken with meals—for example, griseofulvin, alprenolol, metoprolol, and labetalol.

Plenty of water should be taken with uricosurics (to prevent renal precipitation) and with cholestyramine and bulk formers like methyl cellulose.

A few drugs should be taken *half an hour before meals*: antibiotics which are labile in acid—ampicillin, benzylpenicillin, cloxacillin, erythromycin, lincomycin, tetracycline, rifampicin, and isoniazid. So should two antidiabetic agents—glibenclamide and glipizide—and, of course, appetite suppressant drugs.

Drugs affecting nutritional state

Particular drugs can affect the nutritional state, changing the results of biochemical tests or even leading on occasions to clinical undernutrition, overnutrition, or malnutrition.

Appetite may be decreased by anorectic drugs, bulking agents, dexamphetamine, phenformin, cardiac glycosides, glucagon, morphine, phenylbutazone, indomethacin, cyclophosphamide, fluorouracil, methylphenidate, salbutamol, levodopa, etc, and by drugs that alter taste (griseofulvin, penicillamine, and lincomycin).

Appetite may be increased by sulphonylureas, oral contraceptives, cyproheptidine, chlorpromazine, androgens, anabolic steroids, corticosteroids, insulin, lithium, amitriptyline, pizotifen, clomipramine, benzodiazepines, and metoclopramide.

Malabsorption for more than one nutrient may be induced by neomycin, kanamycin, paromomycin, colchicine, phenindione, para-aminosalicylic acid, chlortetracycline, cholestyramine, colestipol, cyclophosphamide, indomethacin, liquid paraffin (fat soluble vitamins), methotrexate, and methylidopa.

Energy metabolism may be stimulated by caffeine, smoking, and some sympathomimetic drugs.

Carbohydrates—Increased blood glucose concentrations may be produced by corticosteroids, thiazide diuretics, diazoxide, oral contraceptives, and phenytoin. Hypoglycaemia may be produced by propranolol and by alcohol (as well as by sulphonylureas, biguanides, and insulin).

Lipids—*Plasma total cholesterol* may be raised by chlorpromazine and some oral contraceptives. As well as specific cholesterol lowering drugs, aspirin, para-aminosalicylic acid, colchicine, trifluoperidol, phenformin, and sulphinpyrazone may lower total cholesterol. *Plasma high density lipoprotein cholesterol* may be raised by phenytoin, ethanol, cimetidine, terbutaline, and prazosin. It may be lowered by danazol, propranolol, and oxprenolol.

Plasma triglycerides may be raised by propranolol, ethanol, and (oestrogenic) oral contraceptives. They may be lowered by norethisterone.

Protein—*Nitrogen balance* may be made negative by corticosteroids, vaccines, and tetracyclines. It may be made positive by insulin or anabolic steroids. *Plasma aminoacids* may be increased by tranilcyproline and lowered by oral contraceptives. Plasma phenylalanine may be raised by trimethoprim and methotrexate.

Thiamin absorption can be reduced by ethanol or by antacids.

Riboflavin status may be lowered by oral contraceptives and by chlorpromazine.

Niacin may be antagonised by isoniazid.

Vitamin B-6 may be antagonised by isoniazid, hydralazine, cycloserine, ethionamide, penicillamine, oral contraceptives, oestrogens, hydrocortisone, imipramine, levodopa, piperazine, and pyrazinamide.

Folate may be antagonised by ethanol, phenytoin, oral contraceptives (uncommonly), cycloserine, triamterene, and cholestyramine. In addition

several drugs owe their antibacterial action to antagonism of folate metabolism—more in microbial than mammalian cells—pyrimethamine, trimethoprim, and pentamidine. Methotrexate, aminopterin, and methotrexate are potent folate antagonists which have more effect on rapidly dividing cells—for example, cancer cells.

Vitamin B-12 absorption may be impaired by slow K, para-aminosalicylic acid, metformin, colchicine, trifluoperazine, and by high doses of vitamin C, cholestyramine, and methotrexate. Prolonged nitrous oxide anaesthesia oxidises vitamin B-12 in vivo. Smoking and oral contraceptives reduce the plasma concentration.

Vitamin C—Plasma concentrations are lowered by oral contraceptives, smoking, aspirin, and tetracycline. Ascorbate excretion is increased by corticosteroids, phenylbutazone, sulphinpyrazone, and chlorcyclizine.

Vitamin A plasma concentration is increased by oral contraceptives. Absorption may be reduced by liquid paraffin and cholestyramine.

Vitamin D status is lowered by anticonvulsants—for example, phenytoin, phenobarbitone, glutethimide, and when these are taken in high dose for long periods rickets can occur.

Vitamin E is antagonised by iron in premature newborns.

Vitamin K—Coumarin drugs—for example, warfarin—are antimetabolites. Purgatives and intestinal antibiotics, such as neomycin, tetracyclines, and sulphonamides, may remove the contribution from colonic bacteria. Salicylates and cholestyramine may reduce absorption, and cefoperazone antagonises the vitamin K-epoxide cycle.

Potassium—Drugs are important causes of potassium depletion: purgatives and laxatives increase faecal loss; thiazide diuretics and frusemide and ethacrynic acid increase renal loss. Other drugs that may increase urinary potassium are carbenicillin, penicillin, glucocorticoids, liquorice, outdated tetracycline, gentamicin, and alcohol.

Calcium—Absorption may be increased by aluminium hydroxide or by cholestyramine and decreased by phosphates and corticosteroids. Thiazide diuretics decrease urinary calcium excretion. Gentamicin, mithramycin, actinomycin D, and ethacrynic acid increase it.

Iron—Allopurinol, fructose, and ascorbic acid increase absorption. Antacids, phosphates, and tetracycline decrease it. Oral contraceptives tend to increase serum iron.

Iodine—Sulphonylureas, phenylbutazone, para-aminosalicylic acid, cobalt, and lithium can cause goitre; they interfere with iodine uptake in the gland. Serum protein bound iodine is increased by oral contraceptives, x ray contrast media, and potassium iodide, and decreased by phenytoin.

Phosphate absorption is decreased by aluminium and calcium compounds.

Zinc depletion from increased urinary excretion may be produced by thiazide diuretics and frusemide, by cisplatin, penicillamine, and alcohol.

Magnesium depletion from increased urinary loss may be produced by thiazides and frusemide, cisplatin, alcohol, aminoglycosides, amphotericin, cyclosporin, and gentamicin.

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