TO-DAY'S DRUGS

Vitamins (2)

Vitamins may be divided into two main groups, the fat soluble and the water soluble. The fat-soluble vitamins were dealt with in our "To-day's Drugs" article last week.

WATER-SOLUBLE VITAMINS

The members of this group are (1) the substances collected together under the heading of the vitamin-B complex, and (2) vitamin C.

Vitamin-B Complex

The members of this complex are thiamine, riboflavin, nicotinic acid and nicotinamide, pyridoxine, pantothenic acid, biotin, vitamin B_{12} (cobalamin), and folic acid.

Thiamine (Vitamin B_1)

Thiamine hydrochloride is widely distributed throughout the tissues of the body and plays an important part in carbohydrate metabolism. The richest sources of thiamine are yeast, whole cereals, liver, peas, beans, and fresh green vegetables, though small amounts are present in almost all natural foods.

Requirements

The usual adult requirements are 1–2 mg. per day, and this amount is present in a normal mixed diet. Many factors influence individual needs in health, but it can be said that for practical purposes the vitamin-B_1 requirements are in proportion to the caloric or carbohydrate content of the diet.

Deficiency

Primary deficiency of thiamine may occur as a result of an unsatisfactory diet, especially if the carbohydrate intake is high. Such a state is most common in countries where polished rice is the main constituent of the diet, but may occur occasionally in this country as a result of neglect or unusual food habits. Secondary deficiency may result from (1) increased requirements, as in thyrotoxicosis or heavy manual work, (2) poor absorption, as in diarrhoea and vomiting, or (3) defective utilization, as in severe liver disease.

Deficiency of thiamine leads eventually to elevated levels of lactate and pyruvate in the blood, though clinical symptoms may occur in the presence of normal fasting levels; in such cases the ingestion of glucose or participation in physical exercise may cause a demonstrable rise in blood pyruvic acid.[1] The first symptoms of thiamine deficiency are usually loss of appetite and mental changes. In infantile beriberi there follow attacks of vomiting, abdominal pain, and screaming; later there is oedema and cardiac failure, and ultimately coma and death. In adults thiamine deficiency tends insidiously to produce a more chronic state of ill-health. Initially there are usually general and vague symptoms, but later involvement of cardiovascular and central nervous systems leads to specific changes. With cardiovascular involvement there develop peripheral vasodilatation and high output cardiac failure with marked oedema (wet beriberi); in this condition death may ensue suddenly. In other patients oedema is minimal or absent and the general picture is more of widespread polyneuropathy often with ocular involvement (dry beriberi); this condition is slowly progressive and may terminate with intercurrent infection. The clinical picture is, however, usually complicated by the presence of malnutrition and other vitamin deficiency. Wernicke's encephalopathy occurs most commonly in association with chronic alcoholism and malnutrition and is characterized by ophthalmoplegia, polyneuritis, ataxia, and mental deterioration.

Therapeutic Uses

Uncomplicated vitamin-B_1 deficiency is usually corrected rapidly by the oral administration of 20–30 mg. thiamine daily, but if the patient's life is in danger from cardiac failure parenteral administration may be advised. Wernicke's encephalopathy, oedema, and heart failure usually respond quickly and completely, though chronic neurological defects are slower to clear and may not recover completely.[2] The correction can usually be maintained merely by the institution of a balanced mixed diet. Thiamine has been used in the treatment of a multitude of conditions, including thalidomide neuropathy,[3] but there is no sound evidence that it is of clinical value in anything but thiamine deficiency.

Toxic Effects

Thiamine by mouth produces no toxic effects and any excess is excreted rapidly in the urine. Parenteral administration is seldom required and carries with it the occasional risk of a severe anaphylactoid reaction.

Riboflavin

Riboflavin is well absorbed from the bowel and forms coenzymes which take part in many reactions concerning tissue respiration and energy transfer. Riboflavin is found in many plant and animal tissues, and the richest sources are liver, milk, yeast, and green vegetables. It is also synthesized in the large intestine, but whether it is absorbed from this site is a matter of speculation.[4]

Requirements

No precise daily requirement is known. A well-balanced diet provides 1–2 mg. per day,[5] and this amount is usually considered satisfactory.

Deficiency

The principal signs of riboflavin deficiency are scrotal dermatitis, angular stomatitis, cheilosis, and corneal vascularization. These features have been variably produced in experimental studies of low dietary intakes,[6] but occur also in other conditions.

Therapeutic Uses

Riboflavin is often used in the treatment of the manifestations noted above using oral doses of up to 5 mg. three times per day. It has been tried also in many other conditions without striking results, but its use has been advocated in the treatment of keratomalacia to support the metabolism of interstitial cells.[1]

Toxic Effects

There are no known toxic effects in man.

Nicotinic Acid and Nicotinamide

Nicotinic acid is a pyridine derivative which is converted in the body to nicotinamide, the physiologically active form. Nicotinamide, like riboflavin, appears to be concerned mainly with tissue respiration and energy transfer. The richest sources of nicotinic acid are meat, whole grains, and yeast.

Requirements

It is likely that the human requirement is about 5–20 mg. daily, and this amount is present in a good mixed diet. No exact requirement can be stated, however, as it has been shown that nicotinic acid can be formed from tryptophan in the presence of thiamine, riboflavin, and pyridoxine ; about 60 mg. tryptophan is required to replace 1 mg. of nicotinic acid.[7]

Deficiency

Deficiency of nicotinic acid produces the clinical picture of pellagra, which is characterized by loss of appetite, lethargy, weakness, diarrhoea, dermatitis, and mental changes. Primary dietary deficiency is rare except in areas where maize, which has a very low content of tryptophan, is the main constituent of the diet. Secondary deficiency may be caused by an inadequate intake as a result of oropharyngeal lesions or gastrointestinal disorders ; it may also occur rarely in association with carcinoid tumours,[8] isoniazid therapy,[9] or Hartnup disease,[10] an inborn error of metabolism.

Therapeutic Uses

In the treatment of pellagra, nicotinamide is usually used in oral doses of 500 mg. daily, but it is important to institute an adequate mixed diet as early as possible. Nicotinic acid is better avoided in the treatment of pellagra because of its vasodilator effect. This effect has, however, led to its use in peripheral vascular disorders.

Toxic Effects

The vasodilator effect of nicotinic acid has been referred to above and otherwise no significant toxic effects are known.

Pyridoxine (Vitamin B_6)

The vitamin-B_6 group is composed of several closely related clinical compounds: pyridoxine, pyridoxal, and pyridoxamine. All three appear to have similar physiological actions. While pyridoxine has many functions in the body, the principal action is probably as pyridoxal phosphate, the coenzyme for transamination. Good sources of pyridoxine are liver, yeast, and whole cereals.

Requirements

Adults probably require 1–2 mg. daily, and this amount is present in most normal diets.

Deficiency

Deficiency of pyridoxine has occurred in adults given a pyridoxine antagonist[11] and has led to skin lesions, cheilosis, glossitis, general weakness, and liability to infection. Peripheral neuritis has occurred also, and the neuritis associated with isoniazid therapy is thought to be due to pyridoxine deficiency. Naturally occurring pyridoxine deficiency is very rare, but has been described in infants presenting with irritability and convulsions. In adults with ample iron stores a hypochromic anaemia responsive to pyridoxine has rarely been described.[12] [13] It seems likely that these occurrences are due to metabolic defects.

Therapeutic Uses

Pyridoxine is of value in the treatment of deficient states as described above ; infants and patients on isoniazid therapy respond rapidly. The administration of pyridoxine to anaemic patients should cause a reticulocytosis if the anaemia is due to pyridoxine deficiency.

Pyridoxine has been advocated for many conditions, including agranulocytosis, vomiting of pregnancy, irradiation sickness, acute alcoholism, and infantile skin conditions ; there is no conclusive evidence of its value except possibly in irradiation sickness[14] when given in doses of the order of 100 mg. Pyridoxine-deficient states usually respond rapidly to 10–50 mg. daily.

Toxic Effects

No toxic effects have been reported in man.

Pantothenic Acid

Pantothenic acid is a component of coenzyme A, which is concerned in many metabolic reactions. It is widely distributed in animal and vegetable foodstuffs. Although lack of this component in animals has produced signs of deficiency, no such state has yet been definitely described in man.

The " burning-foot " syndrome has been treated with pantothenic acid, but it is doubtful if this condition is due to deficiency of pantothenic acid alone. Pantothenic acid is said to have been used with some success in the treatment of streptomycin neurotoxicity[15] but is of no proved value in the treatment of other conditions such as diabetic neuropathy, postoperative ileus, skin conditions, and psychiatric states.[9] Recent results have suggested a possible use in the treatment of rheumatoid arthritis,[16] but this requires much more investigation before it can be recommended.

Biotin

Biotin is another member of the B group of vitamins and is of great biochemical and physiological interest. Experimental deficiency has been produced,[17] with resultant lethargy, anorexia, nausea, muscular pains, and paraesthesiae ; however, only one case of spontaneous deficiency has been recorded, and that was in a man living on the extraordinary diet of wine and raw eggs.[18]

Vitamin B_{12} (Cobalamin) and Folic Acid (Pteroylglutamic Acid)

These vitamins have been discussed fully earlier in this series in relation to megaloblastic anaemias.[19]

Vitamin C

Vitamin C is ascorbic acid, and is present in good quantity in most fresh fruits and vegetables, though foods of animal origin contain little. Vegetables which are stored lose much of their ascorbic-acid content, but fruits retain it well. Ascorbic acid is well absorbed from the bowel, widely distributed in the body, and takes part in many oxidation-reduction reactions in cellular metabolism. It is present in greatest concentration in the most metabolically active tissues—such as glandular tissue, the retinae, liver, and kidneys—and is excreted in the urine when the plasma concentration rises above the renal threshold of 1.4 mg./100 ml.

Requirements

The amount of vitamin C recommended for normal health in the adult varies considerably according to whether or not saturation is considered desirable. It seems likely that 20–30 mg. daily is adequate for maintenance of health in the adult, but more is required in adolescence, pregnancy and lactation, infections, thyrotoxicosis, and post-operative states. On the other hand, up to 75 mg. daily is recommended by some authorities for the normal adult.

Deficiency

Deficiency of vitamin C leads to the development of clinical scurvy, a condition which is now relatively uncommon in this country; young babies on artificial foods and old people existing on meagre rations are the groups most likely to be affected. Ascorbic acid is virtually absent from the plasma for about a hundred days before the first clinical signs of scurvy develop.[20] Lack of ascorbic acid leads to defective ground substance and prevents proper formation of connective and fibrous tissue. For this reason the tissues predominantly affected in scurvy are those of mesodermal origin.

The earliest features are usually weakness and lack of energy, which are soon followed by skeletal pain and enlargement and keratosis of the hair follicles. Later, perifollicular haemorrhages appear, purpura develops, and deep haemorrhages may occur. Anaemia develops, and appears to be due primarily to haemolysis.[21] The gums become swollen, spongy, and friable, the teeth loosen in their sockets, new wounds fail to heal, and old scars may break down. Should the disease progress further, convulsions may occur followed by coma and death.

Therapeutic Uses

The principal use of ascorbic acid is in the prevention and treatment of scurvy. The disease usually responds to small amounts, but it is customary to give 500–1,000 mg. daily in divided doses. Ascorbic acid is also used for its reducing properties and has proved effective in the treatment of methaemoglobinaemia and in increasing the absorption of orally administered iron. It has been recommended for many other conditions which, however, have not been established as indications for its use.

Toxic Effects

No toxic effects have, as yet, been shown to occur in man even with 1,000 mg. given daily for three months.

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Correction.—It has been pointed out to us by Crookes Laboratories Ltd. that the approved name for 6-dehydro-9β,10α-progesterone (4 January, p. 40) is now dydrogesterone.

Any Questions?

We publish below a selection of questions and answers of general interest.

Urticaria in Late Pregnancy

Q.—*At term or during the first few days of the puerperium an urticarial type of rash often appears. As a rule it is in the striae gravidarum, but may also be on the limbs and head and neck. It seems to occur with or without the exhibition of surface antiseptics or any oral or parenteral drugs. Is there a known cause for this?*

A.—A rash of the distribution described in the question is not unusual in the latter part of pregnancy. In its extreme form it is associated with blistering and presents a classical picture of herpes gestationis. This, fortunately, is rare. In its less severe form the condition is usually transitory and clears rapidly after delivery. An interesting feature is that some women develop this type of rash when the baby is of one sex but not when it is of the other. For example, a woman who has four children, of whom two are boys and two are girls, may develop the urticarial manifestation with each of the pregnancies in which the baby is a male. This would suggest that the responsible factor is associated with the infant itself. In other words, the mother is allergic to her own unborn child.

The erythematous type of rash of the distribution mentioned in the question occurring after delivery is probably a toxic manifestation associated either with trauma in the genital tract or with the use of an antiseptic or a reaction to one of the drugs administered during delivery.

Cancer from Other People's Smoke

Q.—*Is there any evidence to show that inhalation of smoke from other peoples' cigarettes predisposes to the development of pulmonary neoplasm?*

A.—It is reasonable to suppose that the inhalation of smoke from other people's cigarettes might carry with it some risk of inducing bronchial carcinoma, in view of the extent of the risk associated with direct smoking. The existence of a risk can be tested effectively only in non-smokers, among whom it might be examined by comparing the