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VITAMIENE IN DIE SAMESTELLING VAN BLOED

Bloedkunde en voedingsleer is baie afhanklik van mekaar soos bv. blyk uit die probleem wat voedingsanemies oplewer. Heelwat navorsing is al gedoen, met oënskynlik weersprekende resultate in sommige gevalle, oor die rol en die onderlinge verhouding in metabolisme van sulke vitamienfaktore soos foliumsuur en cyanocobalamin (vitamien B_{12}). Die verskil in die resultate van die eksperimente en in die opvattings waartoe hul aanleiding gegee het kan toegeskryf word aan veranderings in oënskynlik nietige voedingsfaktore en aan die verskille in die diere wat gebruik was.

Williams[1] het onlangs die funksies van foliumsuur, cyanocobalamin en askorbiensuur bespreek. Hy beklemtoon die belangrikheid van die ontdekking van foliniese suur en die verband wat dit met foliumsuur besit. Dit is moontlik dat foliniese suur een van die ko-ensieme is wat van foliumsuur verkry word of dat dit 'n tussenproduk is in die vorming van 'n ko-ensiem. Die gebrek aan volledige kennis i.v.m. die samestelling van cyanocobalamin het navorsing i.v.m. die funksie van hierdie vitamien vertraag. Daar bestaan 'n verwantskap tussen askorbiensuur en foliumsuur; dit kan waargeneem word in skeurbuikdiere en ook in *in vitro* studies; dit is vir 'n toename in die omskepping van foliumsuur na foliniese suur verantwoordelik. Benewens ander bekende funksies skyn askorbiensuur ook geassosieer te wees met foliumsuurmetabolisme.

Foliumsuur en cyanocobalamin skyn ook betrokke te wees met die metabolisme van ander stowwe o.a. *thymine* en *thymidine*, *purines*, *glycine*, *methionine*, *tryptophane* en *haem*. Totdat die individuele reaksies op elke stadium bestudeer kan word, kan die fundamentele meganismes, wat by die metabolisme van hierdie vitamiene betrokke is, nie verduidelik word nie. Die chemiese, mikrobiologiese en dierestudies waarop ons huidige kennis van die onderlinge verhoudings van vitamien- en ander voedingsfaktore berus, word deur Williams[1] bespreek. Sommige kliniese eksperimente wat beplan is om hierdie verhoudings te toets en die resultate wat verkry is na 8 jaar van sulke studies, word deur Mueller en Will[2] voorgelê.

Dit is welbekend dat die vitamiene waarvan ons melding gemaak het, doeltreffende middels vir sekere

EDITORIAL

VITAMINS IN BLOOD FORMATION

The two fields of haematology and nutrition depend much on each other, as shown for example in the problem of the nutritional anaemias. There has been much research, some of the results apparently contradictory, on the role and the interrelationship of such vitamin factors as folic acid and cyanocobalamin (vitamin B_{12}) in metabolism. In experimental work changes in apparently unimportant nutritional factors and differences in the animals used and in their management could account for different results and concepts that have been put forward.

The way in which folic acid, cyanocobalamin and ascorbic acid function has been discussed recently by Williams.[1] He points out the significance of the discovery of folinic acid and its relationship to folic acid. It is possible that folinic acid is one coenzyme derived from folic acid, or perhaps an intermediate in the formation of a coenzyme. The lack of complete knowledge about the structure of cyanocobalamin has retarded research into the function of this vitamin. Ascorbic acid has some relationship to folic acid; this has been observed in scorbutic animals, and also in *in vitro* studies showing that it augments the conversion of folic acid to folinic acid. In addition to its other well-known functions ascorbic acid would appear to be associated in the metabolism of folic acid.

Among the substances in whose metabolism folic acid and cyanocobalamin appear to be involved are thymine and thymidine, purines, glycine, methionine, tryptophane, and haem. Until the individual step-by-step reactions can be studied the fundamental mechanisms involved in the metabolism of these vitamins will not be clearly elucidated. The chemical, microbiological and animal studies which have led to the present understanding of the interrelationships of vitamin and other nutritional factors are discussed by Williams.[1] Some clinical experiments devised to test these interrelationships, and the results obtained after 8 years of such study, are presented by Mueller and Will.[2]

anemies is maar, soos hierbo aangedui, is die meganismes wat dit bewerkstellig of hul onderlinge verhouding nie duidelik nie. Mueller en Will[2] bied 'n skema aan die hand i.v.m. die moontlike onderlinge verhoudings van baie van die voedingstowwe wat by erythropoiësis betrokke is; die metabolisme van foliumsuur en die gesuggereerde verwantskap van askorbiensuur blyk uit die abnormaliteite in die reaksie en dit mag die voorval van die megaloblastiese anemies verklaar. Hierdie werkers bied verder 'n uitvoerige skema aan wat 'n uiteensetting gee van die moontlike onderlinge verhoudings van die vitamiene by die kernsuurmetabolisme van pasiënte met megaloblastiese anemie. 'n Fundamentele stelling hier is dat cyanocobalamin en foliumsuur as katalisators ageer in 'n reaksie waarin kernsuur gevorm word, en askorbiensuur op foliumsuurmetabolisme 'n uitwerking het; oënskynlik is cyanocobalamin ook by foliumsuurmetabolisme betrokke. 'n Gebrek aan foliumsuur en cyanocobalamin word geassosieer met tekortkomings in die kernsuurmetabolisme wat tot biochemiese veranderings lei wat in verband gebring word met die hewigheid van die megaloblastiese verandering. Alhoewel foliumsuur aanvanklik die metabolisme van kwaadaardige anemie sal herstel, sal dit later 'n groter tekort aan cyanocobalamin in die hand werk en dit sal lei tot hematologiese en neurologiese manifestasies van die siekte. In kwaadaardige anemie van swangerskap is daar ook 'n defek in die kernproteïenmetabolisme wat te wyte is aan 'n tekort aan die foliniese suur ko-ensiem; die metabolisme-defek is ietwat anders as dié wat gevind word by kwaadaardige Addison-anemie, en foliumsuur word gegee.

Baie navorsing moet nog op biochemiese, hematologiese en kliniese gebied gedoen word ten einde die probleme op te los van die onderlinge verhoudings van foliumsuur, cyanocobalamin (vitamin B_{12}) en askorbiensuur by normale metabolisme (kernsuursintese) en by pasiënte met megaloblastiese anemie. Die navorsing wat nodig is, word aangedui in die aangehaalde publikasies, en diegene wat in hierdie onderwerp belangstel behoort hierdie publikasies te bestudeer.

1. Williams, J. N. (1955): Amer. J. Clin. Nutr., 3, 20.
2. Mueller, J. F. en Will, J. J. (1955): Amer. J. Clin. Nutr., 3, 30.

It is well known that the vitamins we have mentioned are effective agents in certain anaemias but, as pointed out above, the mechanisms by which they produce remissions or the manner in which they are interrelated is not clear. Mueller and Will[2] present a scheme of the possible interrelationships of many nutrients involved in erythropoiesis; the metabolism of folic acid and the suggested relationship of ascorbic acid are shown, with the abnormalities in the reaction which may explain the occurrence of the megaloblastic anaemias. These workers go further and present an elaborate scheme in which is shown the possible interrelationships of the vitamins in the nucleic-acid metabolism of patients with megaloblastic anaemia. A basic proposition in all this is that cyanocobalamin and folic acid are catalysts in a reaction in which nucleic acid is formed, and ascorbic acid has an effect on folic-acid metabolism; cyanocobalamin also is apparently concerned in folic acid metabolism. Deficiency of folic acid and cyanocobalamin is associated with defects in the metabolism of nucleoprotein, resulting in biochemical changes that can be related to the severity of megaloblastic change. While folic acid may initially correct the metabolism in pernicious anaemia, there will be later a greater deficiency of cyanocobalamin leading to haematological and neurological manifestations of the disease. In pernicious anaemia of pregnancy there is also a defect in nucleoprotein metabolism, arising from deficiency of folinic acid coenzyme; the metabolic defect is somewhat different from that occurring in Addisonian pernicious anaemia, and folic acid is administered in treatment.

Much work remains to be done in the biochemical, haematological and clinical fields towards solving the problems of the interrelationships of folic acid, cyanocobalamin (vitamin B_{12}) and ascorbic acid in normal metabolism (nucleic acid synthesis) and in patients with megaloblastic anaemia. The research required is indicated in the publications we cite, which should be studied by those interested in this field.

1. Williams, J. N. (1955): Amer. J. Clin. Nutr., 3, 20.
2. Mueller, J. F. and Will, J. J. (1955): Amer. J. Clin. Nutr., 3, 30.

IRON PREPARATIONS

The requirements of iron for the normal person are very small. The diet ordinarily provides more iron than is needed, for good supplies of iron are present in certain foods, particularly green vegetables, peas, beans, dried fruits, eggs and liver. Other foods, such as milk, white bread, fish and chicken are relatively poor sources of iron.

The amount of iron absorbed does not appear to depend on the level of haemoglobin but on the reserves of iron in the body. The amount absorbed appears to depend on the presence of an iron acceptor, named apoferritin, in the cells of the intestinal mucosa; the ferritin which is formed gives iron to the plasma whence, transported by plasma globulins (as siderophilin or transferrin), it is transferred to the tissue stores. The amount of iron absorbed is determined by the equilibrium between the iron levels in the tissues, the plasma, and the intestinal mucosal acceptor mechanism.

It has long been known that ferrous salts are better absorbed than ferric salts, and this has been confirmed by the use of radio-active iron salts. Moreover, the utilization of ferrous salts is much greater than that of ferric salts. There also appear to be some differences in the therapeutic value of ferrous salts. Ferrous sul-

phate is very widely used in the form of tablets; in this form it does not run the risk of being oxidized to the ferric state, it is convenient for administration to adults, and the disadvantages regarding taste or blackening of the teeth are avoided. Such tablets, sugar coated and sometimes attractively coloured, have been mistaken by young children for sweets; as a consequence of their ingestion in relatively large amounts severe gastric haemorrhage has occurred and sometimes death.

In a recent investigation on iron-deficiency anaemia in pregnancy Gatenby and Lillie[1] found that many women complained, usually on the grounds of nausea and vomiting, about the ferrous-sulphate tablets given to them. Other preparations were tested and the best results were obtained with ferrous gluconate. The haematological responses, in the absence of intolerance, showed little difference. These authors suggest that every pregnant woman should receive an efficient preparation of iron during the last trimester. Here, and for other iron-deficiency anaemias, ferrous gluconate (e.g. 'ferronicum', 'ferlucon') may prove more satisfactory than ferrous sulphate from the point of view of gastro-intestinal tolerance.

In recent years iron preparations have become available for parenteral administration. This method of therapy is relatively seldom required. It may be used for patients who cannot tolerate or who are refractory to iron preparations given by mouth, in cases with intestinal disease such as ulcerative colitis, and for patients who need iron quickly before an operation; or in late pregnancy when time is short and oral therapy causes gastro-intestinal disturbances; or where transfusions are contra-indicated because of myocardial defect. Saccharated iron oxide ('ferrivenin') may be given intravenously, but care is required because it is alkaline and sometimes causes unpleasant local reactions; also, the dark colour of the solution necessitates special technique with a large syringe and a fine needle to make sure of a truly intravenous injection. Iron-dextran solution is available for intramuscular injection, but here, too, care is required; the injection should be made deeply into the muscle in the gluteal region or the lateral aspect of the thigh with the skin first displaced an inch or two laterally before the needle is inserted. This technique is necessary to prevent leakage and staining of the skin, which may persist for several weeks.

Iron-deficiency anaemia is a common condition and fortunately therapy is effective in most patients receiving ferrous compounds by mouth.

1. Gatenby, P. B. B. and Lillie, E. W. (1955): Lancet, **1**, 740.