assume particular shapes when spinning through the air after being shot out by the gaseous explosion from the meteorite crater. The craters, supposed to be meteoric, on the Island of Oesel in Estonia are in dolomite, while the rocks in the region of the Siberian fall are basaltic. In neither of these places could silica-glass and tektites be formed.

Silica-glass is very resistant to chemical action and it will withstand weathering processes longer than many other materials. Also, with its very low coefficient of thermal expansion, it will not be affected by changes in temperature—a very potent agent of rock disintegration in desert regions. For this reason tektites are preserved in recent deposits, such as the glacial deposits of Tasmania, the alluvial deposits of Bohemia, Indo-China, and the Philippine Islands, and in the tin-gravels of Billiton, where by slow chemical corrosion they have acquired a peculiar sculptured surface. The australites found on the surface of the Australian deserts do not show this surface sculpturing and are more perfect in form. They are therefore of more recent origin. An aerial survey of the districts where australites are found would probably reveal the presence of meteorite craters with associated large masses of meteoric iron. In the other districts, all traces of the craters would probably have been obliterated by denudation, and the meteoric iron rusted away.

[1] "Les Tectites de l'Indochine." By Prof. A. Lacroix. *Arch. Mus. Nat. Hist., Paris*, **8**, 139, 1932.
[2] NATURE, **129**, 932, June 25, 1932.
[3] NATURE, **129**, 781, May 28, 1932.

## Recent Research on the Vitamins

ADVANCES in our knowledge of the chemistry of the vitamins have recently been so rapid that a review of the position at any moment may require correction or amplification almost as soon as it is published. A useful summary of our knowledge of the nature and function of vitamins was provided in April and May of 1932 by Prof. J. C. Drummond in his Cantor lectures.[1] Some of the points made by the author may be briefly referred to here, and opportunity taken at the same time to review work which has been published since the delivery of the lectures.

Prof. Drummond summarises some of our knowledge in tabular form: the charts showing the minimum effective doses of the different vitamins in test animals, the functions and properties of the six B vitamins, and the distribution of the vitamins in foods are specially useful. He considers first the water-soluble vitamins C and B. The work of O. and A. Rygh and P. Laland[2] on the antiscorbutic potency of narcotine derivatives has not been confirmed by S. Smith and S. S. Zilva[3]. Daily doses of 1·37, 2·75 and 5·5 mgm. of dimethyl and methyl*nor*narcotine had no protective effect in guinea pigs kept on a scorbutic diet. It is possible that the doses were incorrectly chosen as Rygh *et al.* state that only optimal doses prevent the onset of scurvy in guinea pigs on a scorbutic diet. On the other hand, the fact that all Rygh's animals given narcotine derivatives died like the controls indicates that these supplements are not acting in the same way as a daily dose of lemon juice.

Negative results have been described also by other observers, including L. J. Harris and I. Mills, who found that irradiated narcotine and methyl*nor*narcotine were not antiscorbutic in doses ranging from 10 mgm. to 0·001 mgm. daily.[4] Zilva[5] and his colleagues have recently published full details of their work. No narcotine could be isolated from unripe orange juice by ethereal extraction, nor was a concentrate of vitamin C obtained from lemon juice by such means. Methyl*nor*narcotine in daily doses ranging from 10 γ to 2·7 mgm. had no antiscorbutic effect at all in guinea pigs maintained on a scorbutic diet, the experimental animals dying in 30–35 days with all the signs of severe scurvy.

Reference has already been made in these columns to the claim that vitamin C is a hexuronic acid[6]. The experiments on which the claim is based have now been published in detail.[7] Svirbely and Szent-Györgyi found that 1 mgm. of their product daily completely protected guinea pigs on a scorbutic diet from scurvy for 90 days: the animals also showed normal growth during this period. The minimum protective dose of lemon juice is usually regarded as 1·5 c.c. and this quantity contains approximately 0·5 mgm. of the acid. Since the substance contains a molecule of water less than is required for a hexuronic acid, Szent-Györgyi and W. N. Haworth have now suggested the name "ascorbic acid" for it (NATURE, **131**, 24; 1933). Waugh and King have also isolated a crystalline solid from lemon juice which was protective in a daily dose of 0·5 mgm. The possible objection that the material isolated from lemon juice was merely contaminated with a more potent antiscorbutic substance is not valid in the case of the work of the former authors, since the acid used was prepared from ox suprarenal glands. If the antiscorbutic factor is ascorbic acid, it is necessary to explain Zilva's observation that it is possible to oxidise the reducing factor in lemon juice without destroying the antiscorbutic potency, although the vitamin is now very labile: Svirbely and Szent-Györgyi suggest that in these conditions the acid may be present in a reversibly oxidised state. The antiscorbutic potency of this acid has been confirmed by Harris and Mills (*loc. cit.*), who also found raw suprarenal cortex potent, the activity running parallel to the acid content.

Turning to vitamin B, Prof. Drummond reviews the work of Jansen and Donath, Odake, and Windaus and his co-workers on the chemistry of vitamin $B_1$.[8] All observers now agree that the crystalline vitamin contains sulphur in its molecule, as well as carbon, hydrogen, oxygen and nitrogen.

H. W. Kinnersley, J. R. O'Brien and R. A. Peters, in a recent communication,[9] also confirm this observation: their crystals were obtained from bakers' yeast, and the hydrochloride is active in a pigeon day dose of 2–4 γ (a pigeon day dose is approximately equal to 1·5 vitamin $B_1$ international units). Windaus's preparation is active on pigeons in doses of 1·4–3·3 γ: both are more active than Jansen and Donath's original preparation, which contained also vitamin $B_4$.

Vitamin $B_1$ is usually considered to be a base. Examination of a number of bases for antineuritic or growth promoting powers has, however, so far given negative results. B. C. Guha and P. N. Chakravorty have recently announced in these columns[10] that irradiation of adenine sulphate with ultra-violet light confers vitamin $B_1$ properties upon it. In this connexion work on the absorption spectrum of vitamin $B_1$ concentrates has some interest: a band at 2600 A. was found by Guha[11], Windaus (*loc. cit.*) and others. F. F. Heyroth and J. R. Loofbourow have recently reviewed the question and reported some experiments of their own.[12] The absorption spectrum of yeast nucleic acid shows a band of maximum absorption near 2600 A., suggesting that vitamin $B_1$ concentrates contain purine or pyrimidine compounds. Irradiation of uracil or thymus nucleic acid increased the absorption between 2300 and 2550 A. No decrease in the absorption at 2600 A. was observed when only wave-lengths longer than 2960 A. were used for the irradiation. After irradiation, uracil and adenine develop a blue colour with arsenophosphotungstic acid, similar to that given by vitamin $B_1$ concentrates. Heyroth and Loofbourow found a fairly close correlation between potency and absorption at 2600 A. in the purest concentrates examined. Compounds which are likely to absorb in this region are those containing a pyrimidine-ring or those closely related to ergothioneine (betaine of thiolhistidine). This suggestion is of interest in view of the fact that vitamin $B_1$ is now held to be a sulphur compound.

It appears likely that pure crystalline vitamin $B_1$, prepared synthetically, will be available in the near future, as pure crystalline vitamin D is available to-day. Meanwhile, the animal test must be the final criterion. To ensure comparable results in different laboratories, the Permanent Commission on Biological Standardisation of the League of Nations has recommended the issue and use of a fuller's earth adsorbate from rice polishings as a standard for vitamin $B_1$, 10 mgm. of which is defined as containing one unit. H. Chick and H. M. Jackson[13] report on the use of this preparation. It has been found stable for a year, its vitamin $B_2$ content is only 1/25–1/50 of the vitamin $B_1$ present and it also contains vitamin $B_4$.

Prof. Drummond referred briefly to the recent work on the physiology of vitamin $B_1$ and emphasised the importance of distinguishing between the changes due to inanition and those caused by a deficient intake of vitamin $B_1$ *per se*. N. Gavrilescu and R. A. Peters[14] have found that the oxygen uptake of parts of the brain in pigeons suffering from polyneuritis is definitely below normal. Administration of vitamin $B_1$ to the birds or its addition to the minced brain tissue *in vitro* resulted in an increase in its consumption.

Prof. Drummond also summarised our knowledge concerning vitamin $B_2$. He considers that it is a neutral and not a basic substance, with a molecular weight greater than that of vitamin $B_1$.

Some recent work on vitamin $B_4$ may also be mentioned here. Absence of this vitamin from the rat's diet produces redness and swelling of the paws, a spastic gait and loss of co-ordination. Convulsions and paralysis are the characteristic signs of vitamin $B_1$ deficiency.[15] H. Barnes, J. R. O'Brien and V. B. Reader[16] describe the preparation of a crystalline compound with vitamin $B_4$ activity, having the empirical formula $C_4N_4H_5Cl$. It was obtained from yeast extract by adsorption on charcoal at *p*H 1. The charcoal was extracted with 50 per cent acid alcohol, the alcohol removed *in vacuo* and the extract subjected to successive treatments with mercuric sulphate, baryta, sulphuretted hydrogen and sodium phosphotungstate. A crystalline phosphotungstate was precipitated at *p*H 2 and recrystallised from 50 per cent alcohol. It was then dissolved in 50 per cent acetone, and the phosphotungstic acid removed with baryta; the acetone was removed from the filtrate, which was hydrolysed with 5 per cent hydrochloric acid: the solution was concentrated and alcohol and ether added. Crystals were deposited, with melting point 248° (with charring).

Although highly potent preparations of vitamin A have recently been obtained, it has not been found possible to crystallise them. Prof. Drummond refers to the recent work of Karrer, Morf and Schopp, suggesting that vitamin A is an unsaturated alcohol, having the empirical formula $C_{20}H_{30}O$ or $C_{22}H_{32}O$, its structure being related to half the carotene molecule.[17] I. M. Heilbron, R. A. Morton and E. T. Webster[18] have confirmed this suggestion. A concentrate was heated with finely powdered selenium at 300°–330° for 48 hours, and the product extracted with ether. After removal of the solvent, the oil was distilled over metallic sodium; the fraction distilling at 120°–200°/20 mm. was treated with picric acid, when the orange crystals of 1 : 6–dimethyl naphthalene picrate were obtained.

I. M. Heilbron, R. N. Heslop, R. A. Morton, E. T. Webster, J. L. Rea and J. C. Drummond[19] have described the properties of the most concentrated preparations of vitamin A, which they have recently obtained from halibut liver oil. The unsaponifiable fraction was obtained, freed from sterols and fractionally distilled at a pressure below 0·00001 mm. The main fraction distils at 137°–138°, with increase in potency. It is a pale yellow viscous oil which becomes mobile on warming, and is readily soluble in organic solvents; at 3280 A. $E^{1\ \text{per cent}}_{1\ \text{cm.}}$ = 1,350 and the Carr-Price

blue value is about 65,000. The analytical figures agree fairly well with those required for the formula $C_{20}H_{30}O$. Similar concentrates were prepared from sturgeon liver oil and mammalian liver fat, but the best material obtained from cod liver oil was only about half as pure. Biological tests on rats showed that daily doses of 0·025–0·1 γ cured xerophthalmia and promoted growth.

The antimony trichloride test indicates that these concentrates still contain variable quantities of a substance which is chromogenic but is different from vitamin A itself. The blue colours obtained with sturgeon and halibut liver oil concentrates show an absorption band at 6930 A. the intensity of which is usually a quarter of that of the band at 6170 A. but in halibut concentrates may be only one-tenth ; moreover, no selective absorption was observed at 6930 A. in mammalian concentrates. Morton[20] has found that the addition of 7-methylindole to the concentrate inhibits the development of the band at 6170 A. before that at 5830 A. is appreciably affected. In the richest concentrates the intensity of the band at 6170 A. is almost twice that of the band at 5830 A. If 7-methylindole is added to the concentrate in the ratio 4 : 1 (or 10 mol. to 1 mol.) the two bands appear of roughly equal intensity. The band at 6930 A. is not readily inhibited by this reagent. The independence of the two bands at 6170 A. and 5830 A. indicates either that two chromogens are present or that vitamin A reacts with antimony trichloride in two stages.

Reference has already been made in our columns to the possible correlation between the biological test and certain of the chemical and physical characteristics of oils containing vitamin A.[21] Another series of cod liver oils has now been examined and further tests have been performed on some of the previous series.[22] The variations between the different methods were greater than in the earlier series of tests, but it still appears that the intensity of the band at 3280 A. in the oil itself forms the best measure of its biological activity. The antimony trichloride test was not so satisfactory, although in the case of certain oils, when it was carried out on the unsaponifiable fraction of the oil, a correlation was found between the blue value and the biological activity. The biological tests had a large margin of error. It was found advisable to compare a sample with the standard oil in simultaneous tests rather than to rely exclusively on the curve relating growth to dose given obtained with the standard oil at some earlier date.

R. J. Norris[23] has also noted marked discrepancies between the biological and colorimetric methods of assay. The course of the inactivation of vitamin A by irradiation with ultra-violet rays was also followed. An initial latent period was found by biological test but not colorimetrically ; after four hours' irradiation, all the vitamin had been destroyed, but the colour test indicated that the potency had only been reduced about 25 per cent. The destruction of the chromogen follows the course of a bimolecular reaction.

The discrepancies may be explained in part by the error of the biological test and by the presence in oils containing vitamin A of substances which interfere with the development of the blue colour in the Carr-Price test or with its determination. R. S. Morgan[24] has found that the presence of any red in the colour estimated reduces the value of the blue.

The details of the conversion of carotene to vitamin A in the animal body are as yet unknown. The absorption of carotene from the intestine is a slow and incomplete process ; it is apparently related to the fat content of the diet. Small amounts may be found in the liver, but it appears that the bulk of the absorbed material is stored in that organ in the form of vitamin A.[25] The conversion presumably occurs in the liver, but Ahmad was unable to confirm the observation of Olcott and McCann that this organ contains an enzyme which converts carotene into vitamin A *in vitro*. When the diet is rich in carotene, the vitamin A stores in the liver are high. The stores are utilised when the diet is deficient in carotene or the vitamin, but the exact function of the latter in metabolism is unknown. W. J. Dann has shown that it is only with difficulty passed into the mother's milk, so that to build up a store in young animals it is necessary to give it directly to the latter[26] ; also in the rat, at least, very little reaches the young via the placenta. The failure of growth on a vitamin A deficient diet is not entirely due to loss of appetite. Rats on this diet may consume as much food as their litter mate controls given a supplement of vitamin A, but the amount of nitrogen deposited in the body is less and the amount excreted in the urine greater than in the latter, indicating an increase in the nitrogen metabolism. The increase of body-weight per gm. of food eaten is less when the animal has not available an adequate amount of vitamin A.[27] Vitamin A is apparently necessary for the deposition of body tissue. It is well known that certain epithelial surfaces cannot maintain their proper structure when the animal's stores are depleted, with the result that infectious processes develop in different regions of the body. Thus both the growth-promoting and the anti-infective properties of vitamin A appear to depend fundamentally upon its ability to maintain a normal structure in the different tissues of the organism.

The story of the isolation of crystalline vitamin D is now well known and has been referred to previously in these columns.[28] Prof. Drummond reviews the different investigations leading to its isolation in his third Cantor lecture and also refers in considerable detail to Mrs. Mellanby's work on dental caries, which has also been described in NATURE[29]. With the preparation of the pure vitamin, biological tests have become of less importance ; the earlier production of highly active compounds and their use in clinical practice led, however, to a great increase in the number

of such tests required, with the result that methods were standardised and their accuracy increased. We have already referred to the analysis of the curative radiographic method given by Bourdillon and his colleagues.[30] Working with Miss Bruce, he has recently completed a comparison of the prophylactic radiographic method with that based on bone analysis.[31] A radiographic scale was prepared showing eight stages from full rickets to normal bone. The relation between scale reading and logarithm of the dose was not linear. With bone analysis, on the other hand, the relation between percentage of bone ash and logarithm of dose was linear between doses of 0·03 and 0·32 unit vitamin D. An analysis of the errors of the different methods leads the authors to the following conclusions: the accuracy attainable is greater with bone analysis than with the use of a radiographic scale, using the prophylactic method, and the range of doses possible is greater; but the method of bone analysis has about the same degree of accuracy as the radiographic when the curative method of dosing is used in the latter instead of the prophylactic. The radiographic method is, of course, much the quicker and more animals can be used for each test. The authors also consider that the chief variations in the sensitivity of a stock fed on a supposedly constant diet are due to some factor other than vitamin D.

The method of bone analysis (with prophylactic dosing) is considered in greater detail by E. M. Hume, M. Pickersgill and M. M. Gaffikin.[32] The linear relationship between percentage of ash in the bones and the logarithm of the dose is only observed when eight or more animals are used on each dose. The exact position of the line depends on the severity of the rickets developed by the animals. The increments for percentage ash are smaller in the less rachitic series of rats, so that the straight lines of the graphs tend to converge to the point 54 per cent ash and 5 units dose.

Analyses of the 'line' test have been carried out by K. M. Key, B. G. E. Morgan and R. S. Morgan,[33] whilst the former authors and K. H. Coward have examined the possibility of using the growth-promoting property of vitamin D in its quantitative determination.[34] Key and Morgan constructed curves relating degree of healing to dose given, using Dyer's scale to assess the degree of healing. This scale is similar to the radiographic scales but has only six stages. Different curves were obtained in accordance with the different degrees of rickets which may be developed by the animals of different experiments. It is recommended that three reference curves be constructed, for slight, moderate and severe rickets respectively, for use in the assay of preparations for their vitamin D potency. The curves were used in an examination of the effects of changing the ratio of calcium to phosphorus in Steenbock's rachitogenic diet: changing the ratio from 4 : 1 to 2 : 1 was equal in effect to a daily dose of 0·7 unit of vitamin D. A knowledge of the effects of changing this ratio may be required when it is necessary to test food materials containing these elements for their content of vitamin D. R. S. Morgan measured the area of calcification in the 'line' test with the planimeter and found that the degree of healing was strictly proportional to the logarithm of the dose between 0·125 and 1·0 unit. Doubling the dose increased the area of calcification by 59 sq. mm. using a magnification from line to drawing of 11 diameters. With 10 pairs of rats, the probable error of a test is ± 7 per cent: this is less than with the radiographic method since the error in the diagnosis of healing is eliminated. The chief source of error is the variable response of litter mates to a given dose.

It is of interest to note that Coward, Key and Morgan found that there is also a linear relationship between the growth response of rats and the logarithm of the dose given. The animals were kept on the standard vitamin A-free diet without vitamin D. Vitamin A was supplied in the form of carotene. The growth method gives the same results as the line test, but is more laborious and probably less accurate. The growth response to vitamin D is less than that to vitamin A on the same diet.

In conclusion, it may be mentioned that Prof. Drummond considered some of the illnesses which may result from a deficient intake of the different vitamins. It is difficult to estimate how far minor disorders may be due to this cause in Great Britain to-day. It would be of great interest to carry out a dietary survey, on the lines of previous surveys dealing with the protein, fat and carbohydrate intake, but investigating the consumption of vitamin-containing foods, so that the vitamin requirements of the population might be more accurately estimated.


[1] *J. Roy. Soc. Arts*, **80**, 949, 959, 974 and 983; 1932.
[2] See also NATURE, **129**, 283; 1932.
[3] *Chem and Ind.*, **51**, 166; 1932.
[4] *Lancet*, (2), 235; 1932.
[5] R. L. Grant, S. Smith and S. S. Zilva: *Biochem J.*, **26**, 1628; 1932.
[6] NATURE, **129**, 576, 690, and 943; 1932.
[7] J. L. Svirbely and A. Szent-Györgyi; *Biochem. J.*, **26**, 865; 1932: W. A. Waugh and C. G. King; *J. Biol. Chem.*, **97**, 325; 1932.
[8] See also NATURE, **129**, 161; 1932.
[9] *J. Physiol.*, **76**, 17*P*; 1932.
[10] NATURE, **130**, 741; 1932.
[11] *Biochem. J.*, **25**, 931; 1931.
[12] *Bull. Basic Sci. Res.*, **3**, 237; 1931: **4**, 35; 1932.
[13] *Biochem. J.*, **26**, 1223; 1932.
[14] *Biochem. J.*, **25**, 1397 and 2150; 1931.
[15] V. Reader: *Biochem. J.*, **24**, 1827; 1930.
[16] *J. Physiol.*, **75**, 8*P*; 1932.
[17] See also NATURE, **129**, 88; 1932.
[18] *Biochem. J.*, **26**, 1194; 1932.
[19] *Biochem. J.*, **26**, 1178; 1932.
[20] *Ibid.*, 1197.
[21] NATURE, **129**, 514; 1932.
[22] K. H. Coward, F. J. Dyer, and R. A. Morton: *Biochem. J.*, **26**, 1593; 1932.
[23] *Bull. Basic Sci. Res.*, **3**, 89 and 249; 1931.
[24] *Biochem. J.*, **26**, 377; 1932.
[25] T. Moore: *Biochem. J.*, **25**, 275; 1931: B. Ahmad, *Ibid.*, p. 1195.
[26] *Ibid.*, **26**, 1072; 1932.
[27] M. M. Sampson, M. Dennison, and V. Korenchevsky: *Biochem. J.*, **26**, 1315; 1932.
[28] NATURE, **129**, 178; 1932.
[29] NATURE, **129**, 83; 1932.
[30] NATURE, **129**, 514; 1932.
[31] R. B. Bourdillon and H. M. Bruce: *Biochem. J.*, **26**, 506; 1932.
[32] *Ibid.*, 488.
[33] *Biochem. J.*, **26**, 196; 1932: and R. S. Morgan: *Ibid.*, 1144.
[34] *Ibid.*, 1585.