Using these methods, Cohn and his colleagues have separated a β-lipoprotein having spherical particles 185 A. in diameter and molecular weight of about 1,300,000, and an α-lipoprotein with particles about 300 A. long and 50 A. wide and molecular weight about 200,000. Many important lipids, such as œstrogens and carotenoids, appear to be associated with the β-lipoprotein. The chylomicrons in the blood are stabilized by a lipoprotein—the protein being linked to the non-reactant triglyceride core by lecithin. One conception of membrane structure is of a basic lipoprotein framework to which further lipid sub-units can be added to provide a lipid/protein mosaic. Mitochondria and other intracellular structures are said to be lipoproteins. The effects of solvents and dehydration on nerve myelin have been studied by combining X-ray diffraction and micro-analysis. The observations suggest the existence of lipid/protein and lipid/lipid subunits as part of a larger lipoprotein complex. Lipoproteins provide a structural medium which can accommodate both lipids and water. Association of lipid with protein may prevent oxidation—after separation, the lipid can oxidize rapidly. Fat transport in the blood is mainly as glyceride rather than lipoprotein. In general, a lipoprotein consists of a lipid/protein subunit largely dependent on electrostatic forces and particularly sensitive to *p*H changes and dehydration, and a lipid/lipid subunit in which van der Waals forces and the formation of hydrogen bonds might be more important.

Mitochondria were discussed by Dr. G. H. Bourne, who described them as rods, filaments or granules seen best by dark-ground illumination and phase-contrast microscopy, and often occupying a particular orientation in the cell as if they were arranged by currents of diffusion linked with the sub-microscopic structure of the protoplasm. They can be separated by differential centrifugation and shown to consist mainly of protein, lipid and ribonucleic acid, but they may also contain small amounts of vitamins, some pigments and certain enzymes. Most of the succinoxidase of the cell is to be found in the mitochondria, which appear, therefore, to be intimately connected with the aerobic respiration of cells. Mitochondria are greatly reduced during starvation, but return on feeding. They are to be regarded not as semi-permanent self-reproducing cell organelles, but rather as temporary aggregates of complex composition and as a reserve store of metabolic substance for the cell.

Mr. M. M. Swann spoke of his researches with the polarizing microscope on cytoplasmic structure in the sea urchin egg, with particular reference to the changes occurring during the mitotic cycle. The highly oriented metaphase spindle and asters give way to a less oriented structure as mitosis progresses, and it appears that the agent controlling this change is liberated directly or indirectly by the chromosomes. This less oriented arrangement of protoplasmic material is normally so weakly birefringent as only to be visible with very refined methods. It consists apparently of form and intrinsic birefringences acting in opposition, and more or less cancelling out. This curious arrangement seems to obtain in rather different forms in both the fertilized and unfertilized eggs, and in other cells as well, and it is perhaps to be regarded as the 'cytoskeleton'. The asters and spindle are therefore not *de novo* structures, but modifications of a structure always present.

J. N. DAVIDSON

FOLIC ACID, VITAMIN B_{12} AND ANÆMIA

THE programme for Section I (Physiology) of the British Association at the meeting this year at Newcastle upon Tyne included a symposium on folic acid, vitamin B_{12} and anæmia. In a brief introduction, the chairman, Prof. R. A. Peters, mentioned the importance of the topic and the intense interest aroused by the synthesis of folic acid and the isolation of vitamin B_{12}.

The first paper, on the chemical aspects, was read by Dr. E. Lester Smith. This contribution centred round the methods of treatment of the macrocytic anæmias, especially pernicious anæmia. The first effective treatment was discovered by Minot and Murphy in 1926. Their use of raw or lightly cooked liver by mouth was quickly superseded by liver extracts given at first orally and, later, by injection, made possible by more extensive purification through fractional precipitation with alcohol and other means. Some progress towards the isolation of the active principle was made by American, Norwegian, Swiss and British biochemists; but the problem proved exceptionally difficult, mainly on account of the lack of a satisfactory assay method. The final isolation of vitamin B_{12} was announced almost simultaneously in 1948 in America by Rickes and co-workers at Merck and Co., Inc., Rahway, N.J., and by Lester Smith of Glaxo Laboratories, Ltd., Greenford, Middlesex. This culmination of twenty-two years of research aroused great interest, which was increased by the announcement that the red crystalline substance had an extraordinarily high biological activity and contained cobalt in its molecule.

Some years previously, several American teams prepared, from liver, yeast and spinach, concentrates that promoted the growth of *L. casei* and other micro-organisms; they also promoted normal growth and prevented anæmias in chicks or monkeys on deficient diets. This series of researches culminated in the isolation of a crystalline substance known as folic acid or pteroylglutamic acid, which was synthesized by a large group of workers at Lederle Laboratories, Pearl River, N.Y., within a very short time of its isolation from natural sources. The great confusion that had existed over an apparent multiplicity of related factors was cleared up by the isolation of two conjugates of folic acid with an additional two and six molecules respectively of the glutamic acid radical. They have different activities towards micro-organisms, but can be converted into folic acid by specific conjugases.

It was only after synthetic folic acid became available that its efficacy in macrocytic anæmias was announced. From the high doses required, however, it quickly became apparent that folic acid could not be the effective agent in purified liver extracts. A little later it was shown that it is somewhat less effective hæmatologically than liver extract (both given at adequate dose-levels), while it is entirely ineffective against the neurological complications of pernicious anæmia.

The war-time scarcity of feeding stuffs focused attention on the fact that chicks and other farm animals need animal protein in their diet. Concentrates of an 'animal protein factor' were prepared from fish solubles and from cow manure, and gradually accumulating evidence indicated that this factor might be identical with the anti-pernicious anæmia factor of liver. Finally, Stokstad and others showed that the animal protein factor could be elaborated by suitable micro-organisms and that the bacterial product was effective in pernicious anæmia. This discovery opened a way for production of vitamin B_{12} by fermentation methods similar to those used for making antibiotics. Indeed, it was announced at the end of 1948 by the Merck group that a strain of *Streptomyces griseus* (the organism used for streptomycin production) produced vitamin B_{12}.

The presence of cobalt in vitamin B_{12} seemed at first to link this substance with the known requirement of ruminants for traces of cobalt in their diet. Any direct connexion was disproved, however, by the discovery that vitamin B_{12} was ineffective for sheep on a cobalt-deficient diet. Nevertheless, a less direct connexion may be postulated. It seems that the cobalt is required not directly by the animal but by the rumen bacteria, which play a large part in ruminant digestion. It is likely that these bacteria utilize part of the cobalt to synthesize vitamin B_{12}, which then finds its way into the liver of the animal.

The second paper, on bacteriological aspects, was given by Dr. D. D. Woods, of the Department of Zoology and Comparative Anatomy, Oxford, who pointed out that micro-organisms have played a worthy part in this work. All the well-characterized members of the vitamin B group, including folic acid and vitamin B_{12}, are now known to be essential growth-factors for some micro-organism or other. By no means all bacteria require all these factors; broadly speaking, when a factor is not required, this means that the organism concerned is capable of synthesizing it. Thus it is true of both folic acid and vitamin B_{12} that certain micro-organisms require them and can therefore be used in their microbiological assay, whereas other organisms synthesize useful amounts of the factors and could be used for their production.

Microbiological assays have several advantages over the alternative animal assays for folic acid, or clinical assays for vitamin B_{12}. Thus the deficient media are relatively easy to prepare. The criterion—namely, growth of the organism or its absence—is simple in comparison with the assessment of symptoms in higher animals. Finally, there is usually a clear-cut relationship between dosage and response, and results are obtained quickly, often within twenty-four hours. On the other hand, it so happens that folic acid, and also vitamin B_{12} especially, are among the most difficult factors to assay microbiologically. The organisms usually employed for vitamin B_{12} assay are certain micro-aerophilic lactobacilli; since these do not require vitamin B_{12} at all for purely anaerobic growth, quantitative response depends on the degree of aeration of the medium and careful control of the concentration of reducing agents.

Factors in the vitamin B group are required not only by bacteria and animals, but also by fungi, protozoa, insects, birds and higher plants. One may therefore conclude that they are essential metabolites for all types of cell. It follows that in studying their function one may use any convenient organism, and in practice micro-organisms are often the most convenient. The picture is still far from complete, but there are indications that folic acid may have a function in the biosynthesis of pyrimidines, thymine (a constituent of desoxyribonucleic acid) and possibly purines, such as adenine. It is also probable that folic acid functions as part of the structure of the coenzyme involved in these syntheses. It is possible that folic acid, which contains a *para*-aminobenzoic acid residue, may function like the latter substance in the biosynthesis of certain amino-acids. For vitamin B_{12} the evidence is still less complete, but there are indications that it may be involved at some stage in the biosynthesis of desoxyribosides, possibly for the synthesis of the desoxyribose moiety or for its attachment to the purine or pyrimidine.

The concluding paper of the session, by Dr. C. C. Ungley, of the Royal Victoria Infirmary, Newcastle, was on clinical aspects. Dr. Ungley has assayed on some eighty patients the liver fractions that were used in the isolation of vitamin B_{12} in Great Britain. His paper, however, concerned the findings on some fifty patients treated with the pure crystalline compound at various dose-levels. Confirming previous findings with liver extracts, the reticulocyte response proved a somewhat unreliable index. The increase in red blood cells conveniently assessed at the fifteenth day was much more closely related with dose. The expected response is a function of the initial level of red cells, but a statistical method was evolved to adjust the responses to a 'theoretical' initial level of two million.

It was then found that on average a single dose of 10 μgm. would produce the 'expected response', according to the accepted formula, but that larger doses gave greater responses, which were roughly proportional to the logarithm of the dose in the range 5–80 μgm. For maintenance, doses of 10 μgm. every two weeks gave satisfactory results in nearly all patients. No fresh neurological symptoms developed in any of the patients maintained for periods up to fifteen months on vitamin B_{12}, while cases of already established subacute combined degeneration of the spinal cord improved after continued dosage with vitamin B_{12}, and to the same degree that would be expected from dosage with active liver extracts. Dr. Ungley also reported several cases of macrocytic anæmia of pregnancy that responded to folic acid after failing to respond to vitamin B_{12}.

E. LESTER SMITH

OBITUARIES

Dr. A. P. Laurie

IT is difficult nowadays to think back to the time when it was considered eccentric to apply the tools of the scientist to the problems of the artist—when there was no laboratory, no group of research physicists and chemists, at the National Gallery, the Louvre, the British Museum, the Courtauld Institute of Art, the Fogg Art Museum. These, and their counterparts elsewhere, owe much to one bold pioneer—Arthur Pillans Laurie, whose death on October 7 at the age of eighty-seven has deprived them of their doyen.

Born on November 6, 1861, near Edinburgh, the son of Prof. S. S. Laurie, he was educated at the Universities of Edinburgh and Cambridge. His early scientific interests lay in the field of electrochemistry; he worked on the E.M.F. of alloys in voltaic cells and kindred problems, and obtained a D.Sc. at Edinburgh. He had a keen appreciation of the fine arts; and an early contact with Holman Hunt directed his scientific interests towards the materials of the craftsman. Although he specialized in the materials employed in painting and the graphic arts, and