Growth Factors

A DISCUSSION meeting on "Growth Factors" took place at the Royal Society on Thursday, June 24. The discussion revealed the emergence of a line of biochemical application which hitherto has been obscured by the diversity of its interest.

For a number of years, sporadic reports have been published by workers in the fermentation industries and bacteriology that the growth of yeast and bacteria depends not only on the provision in the diet of gross sources of energy and nitrogen, but also upon illusive materials—'bios', 'accessory growth factors', akin to the 'vitamins', responsible for the functioning of special phases of animal metabolism or even for the growth of animals. More recently, these tentative findings have been reinforced by workers in other specialized fields, for example, in botany and protozoology, and, by the use of modern biochemical technique and knowledge, it would now appear that the case established in the nutrition of animals is equally established in the nutrition of the most diverse varieties of cells; namely, that all cells from the lowliest bacterium to the cells of the highest animals are enabled to carry out the series of reactions between the sources of energy and nitrogen, which result in the production of energy and growth, only by the agency of other substances mostly of a nature akin to those already described in animal metabolism—vitamins. The only notable difference between the various forms of life is that these accessory substances are normally synthesized by some cells but not by others, and thus in the former case these substances need not be supplied in the nutrient diet.

The proceedings were opened by Prof. F. Kögl, of Utrecht, with a review of the present state of knowledge of the plant hormones, auxin *-a* and *-b* and heteroauxin (β-indolylacetic acid). The auxins were first thought to exert their effect on cell elongation, but now it is recognized that they regulate plant growth in many ways. Auxin-*a*, for example, is thought to account for the phenomenon of phototropism. Auxin-*a* lactone loses its activity under the action of ultra-violet light, and thus the shaded side, containing a greater concentration of activity, would elongate and produce the effect of phototropism. The action of heteroauxin seems to be primarily associated with the formation of roots on stem cuttings. This action is, however, not dependent on chemical structure, since a number of unrelated substances have a similar effect, recalling the non-specificity of œstrogenic compounds described by Dodds and co-workers.

Prof. Kögl also gave an account of his 'biotin', a sulphur-containing substance of great potency which may be the chief component of 'bios', originally described by Wildiers as a necessary growth factor for yeast. Biotin has also been shown to have an effect on the growth of higher plants.

Dr. P. Fildes (London) reviewed the subject as it appears to the medical bacteriologist, tracing the evolution of the vitamin concept for bacteria from Twort and Ingram's growth factor for Johne's bacillus (1912) to the present time, when vitamin B_1 has been proved to be essential for *Staphylococcus* and propionic acid bacteria, and nicotinic acid or cozymase for *Staphylococcus* and the influenza bacillus. He laid stress on the facility with which bacteria can adapt themselves to altered nutritional conditions, and ascribed the fact that parasitic bacteria specially require growth factors to a loss of synthetic function which has resulted from long association with an environment in which these factors are preformed. These dependent bacteria can readily be trained back to their 'original' state, in which they can synthesize the factors and so do not require to be supplied with them. In a series of different species of bacteria, each ultimately requiring cozymase for growth, it was shown that the complexity of the nutrients from which cozymase can be synthesized depends upon the synthetic power of the bacteria at the time of examination.

M. André Lwoff (Institut Pasteur, Paris) pointed out that certain bacteria and Protozoa cannot grow without a supply of hæmin, because they are unable to synthesize it from iron compounds in the nutrients. The importance of hæmin is ascribed to its function as a stage in the synthesis of cytochrome in Keilin's system. Its effect is to increase greatly the oxygen consumption of organisms starved of it.

M. and Mme. Lwoff have demonstrated that the long-known 'vitamin factor' of the influenza bacillus is none other than Harden and Young's cozymase or Warburg's co-enzyme. Metabolic studies have shown that cozymase acts as a codehydrogenase for various substrates and much increases the oxygen uptake of influenza bacilli and anaerobic glycolysis. Both hæmin and cozymase function as bacterial growth factors as components of the dehydrogenase-cytochrome system of Keilin and Warburg.

Mr. B. C. J. C. Knight (London) gave an account of the *Staphylococcus* and *Sporogenes* factors referred to by Dr. Fildes. He showed that the former consists of nicotinic acid, a constituent of cozymase and of the two halves of the vitamin B_1 molecule—the pyrimidine and thiazole rings. The activity of each compound depends strictly on certain chemical configurations. The *Sporogenes* factor has not been finally determined, but there is evidence that it may have a much wider importance than merely the regulation of the metabolism of the obligate anaerobes.

Dr. G. M. Richardson (London) described uracil, a component of nucleic acid, as an essential factor in the anaerobic growth of *Staphylococcus*. Uracil is synthesized by the organism aerobically, and therefore under these conditions its effect on growth cannot be demonstrated. Anaerobically, however, the synthetic power of the organism is sufficiently depressed to make the demonstration possible. No metabolic function has hitherto been ascribed to uracil.

In the discussion which followed the more formal proceedings, there appeared to be complete agreement between the various speakers not only in detail but also in the wider implications of the discussion. Dr. E. R. Holiday (London) referred to the demonstration of nicotinic acid in Knight's crude *Staphylococcus* factor by means of absorption spectra. M. Lwoff recalled other factors which have been found by his colleagues in the Pasteur Institute, namely, the forms of sulphur necessary for the growth of certain fungi (Volkonsky) and the sterols found by Mlle. Cailleau to be necessary for flagellates.