Reproduction, Lactation, and Vitamin E.

AS the dietary requirements for growth have become more clearly defined with the introduction of purified nutrients, it was soon observed that diets adequate for growth might not suffice for reproduction or lactation, either quantitatively or qualitatively. Quantitative deficiencies are easily remedied: investigation of the qualitative has led to a better appreciation of the part played by protein, salts, and vitamins in nutrition, and to the discovery of a new type of sterility. The young are dependent for their supplies upon the mother until they are weaned: inadequate diets during pregnancy are reflected in the condition of the young when born or later: during lactation such diets result in failure to rear the offspring. The growing organism requires different ratios between the various elements of the food as compared with the adult and the qualitative dietary requirements of the nursing mother depend chiefly on the necessity of satisfying these needs. Thus a relatively greater intake of certain salts and growth-promoting vitamins is required by a nursing mother than by an adult of the same weight who is not being subjected to a similar strain.

Failure of reproduction is a characteristic effect of many deficient diets and is usually shown by failure to breed or by failure to rear the young born. A special type of sterility has been described by H. M. Evans and his co-workers and shown to be associated with a dietary deficiency: the substance lacking is apparently an organic compound of unknown composition; it has been labelled vitamin E. Our knowledge of this vitamin has recently been collected by H. M. Evans, G. O. Burr, and T. L. Althausen ("The Antisterility Vitamine Fat Soluble E," *Memoirs of the University of California*, vol. 8). The sterility is unique in that implantation of the embryos in the uterus occurs normally, but later they are resorbed and no young are ever born. The sexual cycle in female rats suffering from vitamin E deficiency occurs normally: in other types of sterility, either the sexual cycle is disordered or implantation fails to occur. In the male, vitamin E sterility is accompanied by degeneration of the testicular glands.

To determine whether a given rat is suffering from vitamin E sterility it is essential to carry out fertility tests. The occurrence of œstrus or pro-œstrus must be observed, from the change in type of cell found in a vaginal smear, and must be followed by the signs of successful copulation with a fertile male, the presence of a vaginal plug and spermatozoa in the female passages. If implantation is successful the vaginal smear shows red-blood cells about the 13–15th day of gestation. In the authors' stock of animals, 5-18 per cent of successful matings are not followed by implantation: the animals used for testing for the presence of vitamin E should not show a higher percentage of failures, otherwise they are unsuitable for the test and are presumably suffering from some other type of deficiency. Resorption of the young occurs about the 20–25th day and is shown by a gradual fall in weight of the animal, in contrast to the abrupt fall seen when a litter of living young is born. The suitability of the animal for the test can be controlled by supplying a source of vitamin E at the next gestation and obtaining a healthy litter.

Histological examination of the uterus of these animals at different stages of gestation shows that the development of the young is definitely retarded after the 8th day: about the 13th day many of the fœtuses die and the placentæ start to degenerate about the 16th day. Death is ascribed to changes in the yolksacs, especially interference with hæmatopoiesis and failure of development of the fœtal capillaries in the placenta. The fewness of the red-blood corpuscles as compared with the numbers seen in normal embryos is noticeable about the 11th day.

In contrast to the normal sex-life of the sterile female, the sterile male shows marked testicular degeneration. For a short period a male may be sterile and show normal testes histologically: that some change has already occurred in the organs, however, is shown by the fact that even prolonged administration of vitamin E will result in the cure of only 25 per cent of sterile males, and even in these most of the tubules will be degenerated. In the next stage the spermatozoa fail to show normal movements, and finally disappear: the animal becomes incapable of forming the vaginal plug on copulation with the female and in the last stage loses all sex interest.

The diet used to produce these effects contains alcohol-extracted casein, cooked corn starch, cod-liver oil, salts, lard, and yeast: it is thus adequate so far as the other dietary constituents are concerned. Sterile females supplied with a sufficiency of vitamin E will have a normal gestation and produce living young: by using such animals as test objects it has been possible to determine the distribution of the vitamin in Nature and to prepare extracts containing it in concentrated form. In general it may be stated that animal foods are not good sources of the vitamin: it is not stored in the testes and the viscera contain little: it is chiefly present in muscle and fat, though even here it is not in a concentrated form: milk contains little. Vegetable foods provide the most potent sources, especially lettuce and wheat-germ: the oil extracted from the latter has proved a convenient source. Fertility can be ensured by a dose of 0·55 gm. of the oil on the first day of gestation or by a daily dose of 25 mgm. during gestation. Experiments have shown that for any given gestation to be successful the vitamin must be present in adequate concentration in the body from the 5th to the 20th day of this gestation. Twenty times the minimum dose will suffice for two but not for three gestations: the vitamin is used up in the ordinary metabolic processes of the body, and although it is essential for gestation it does not appear to be utilised more rapidly during it. Sterile animals

contain less of the vitamin in their tissues than those on an adequate diet: it can be detected also in new-born young. It exerts its action on intraperitoneal injection as well as following oral administration. In excess it will not increase the fertility of the animals above the normal for the particular stock.

Preliminary experiments appear to show that vitamin E is also essential for normal lactation.

As regards its chemical properties, vitamin E shows close relationships to the group in which vitamins A and D are placed: it is found in the unsaponifiable fraction of wheat-germ oil, but is unstable to a hot saponification in this oil, although stable when in a purer condition. It is stable to aeration and hydrogenation but not to bromination: it is not destroyed by drying lettuce nor by cooking plant or animal tissues. By fractionation of wheat-germ oil a sterol-free fraction can be obtained, distilling at 225-230° C. at 0·01 mm. pressure, containing all the activity: no nitrogen, sulphur, or halogen is present in the active fraction, 5 mgm. of which fed on the day of mating will suffice to ensure a normal gestation. Its behaviour on fractionation thus resembles closely that of the growth-promoting fat soluble vitamin A.

Failure of reproduction on similar synthetic diets has been noted by other observers, especially by B. Sure, but Evans and his co-workers have made the most complete analysis of this particular type. U. Suzuki, W. Nakahara, and N. Hashimoto (*Proc. Imp. Academy*, Tokyo, vol. 3, p. 619; 1927: *Scientif. Papers, Instit. Phys. and Chem. Research*, vol. 7, p. 143; 1927), have obtained failure of reproduction with degeneration of the testes in the males, but without demonstrable changes in the ovaries in the females, when white rats were maintained on diets free from, or relatively low, in fat, vitamins A and B being supplied in the form of concentrates. Their diets, however, failed to secure absolutely normal growth. Evidence of resorption of embryos was obtained in a few of the females. It is probable that the results were due to vitamin E deficiency. W. P. Kennedy (*Quart. J. Exp. Physiol.*, vol. 16, p. 281; 1926) has also confirmed some of the details of Evans' work.

It may be pointed out in connexion with the examination of food materials as sources of certain of the vitamins, that there is some evidence that erroneous conclusions may be drawn when the substance under test is mixed in with the other constituents of the diet, owing to an interaction between it and some of these constituents resulting in a destruction, partial or complete, of the vitamin. Thus H. A. Mattill (*J. Am. Med. Ass.*, vol. 89, p. 1505; 1927) has adduced evidence that vitamins A and E may be oxidised in the presence of certain fats or salts in the diet: and H. M. Evans and G. O. Burr (*ibid.*, vol. 88, p. 1462, and vol. 89, p. 1587), have obtained similar results in the case of vitamin E. Lard among the fats and ferrous sulphate among the salts appear to be among the destructive agents: a definite relationship between the lard and the amount of wheat-germ necessary to cure sterility has been demonstrated: hydrogenated lard appears to be without this effect: a ferric salt has not the same action as a ferrous salt.

Although so much attention has been recently directed towards the part played by the vitamins in reproduction and lactation, it is essential that the influence of the other constituents of the diet and the proper balance of all the constituents should not be omitted from consideration. Gladys A. Hartwell (*Biochem. J.*, vol. 21, p. 1076; 1927), using a diet of caseinogen, potato starch, butter, cod-liver oil, salts, and marmite, found that 16 per cent butter or 12 per cent with 4 per cent cod-liver oil and 16 per cent caseinogen produced nearly normal growth in rats: with 14 per cent cod-liver oil growth was less good, and no litters were produced: the uteri and mammary glands were abnormal and the testes in the male were frequently small and the animals sterile. With 16 per cent butter and 4 per cent cod-liver oil, reproduction was poor, the does dying or failing to rear their young: the males were fertile. Increasing the protein content or adding lactalbumin gave slightly better results, but the best were obtained with 12 per cent butter alone in the diet, although still not so satisfactory as among the animals of the stock colony. She suggests that excess of vitamins A and D may upset growth, or that vitamin E is necessary for growth as well as for fertility: it is possible that interaction between the constituents of the diet in the diet itself may be a factor in the results obtained: thus the cod-liver oil may inactivate the vitamin E of the butter. The same author has also shown that potato protein is inadequate for growth, reproduction, and lactation, probably due to the difficulty of feeding sufficient protein on a simple potato diet (*ibid.*, p. 282), and that an oatmeal diet, although it allows of fairly good growth, is not adequate for reproduction or lactation (*ibid.*, vol. 20, p. 750; 1926). In this case also the total protein in the diet was low. W. P. Kennedy (loc. cit.) has found that fertility is impaired by a high protein diet and also by one low in calcium, and that the movements of the isolated uterus of these animals in a bath of Ringer's solution may not be absolutely normal, as well as the response to variations in the calcium content of the surrounding fluid (*Quart. J. Exp. Physiol.*, vol. 16, p. 333; 1926).

U. Suzuki and N. Hashimoto (*Scientif. Papers, Instit. Phys. and Chem. Research*, vol. 4, p. 236; 1926) found that on a diet of condensed milk supplemented with salts and a vitamin B concentrate, growth was normal but reproduction rare: fertility was improved by the addition of 0·1-0·5 per cent cholesterol. These authors also report that a higher proportion of cholesterol in the diet was toxic, leading to cessation of growth and even death: there appeared to be a relationship between this toxic effect and the vitamin A content of the diet.

Apart from the reflection of the adequateness of a diet in the number and condition of the young

born—if the diet is so far adequate for reproduction—the condition, and especially the weight of the mother, form an index of its suitability. Miss Hartwell (*Biochem. J.*, vol. 21, p. 572; 1927) has found that on a variety of diets the mother rat gains about 20 gm. in weight during gestation, whether the diet is good or poor: in the latter case there are fewer young in the litter and many are born dead. On the other hand, during lactation the mother may lose up to one-third of her weight in supplying the needs of her young, if the diet is inadequate. Thus it appears that the mother only sacrifices her own tissues during lactation and not during gestation. S. Bartlett has found that cows also continue to grow during gestation and lactation provided that their diet is satisfactory (*J. Agricult. Sci.*, vol. 16, p. 392; 1926). The necessity of proper diets is further shown by some figures published by Forbes and his co-workers (E. B. Forbes, J. A. Fries, W. W. Braman, and M. Kriss: *J. Agricult. Research*, vol. 33, p. 483; 1926). From metabolism experiments on cows it is concluded that the percentage utilisation of the metabolisable energy of the ration for maintenance reaches 75-80, for production 70-75, but for growth only about 60. Similar studies, which include milk analysis, can scarcely be carried out on rats owing to their small size, so that it is of interest to bring together the results obtained in the case of these two species of animals, and to note the similarity of their behaviour during gestation and lactation.

News and Views.

THE scientific and economic problems of the textile industry, to the importance of which considerable attention was paid at the Leeds meeting last year of the British Association, form the theme of several recent publications. Two noteworthy communications are "A Survey of Textile Industries" by Sir Arthur Balfour's Committee on Industry and Trade, and "A Survey of the Production and Utilisation of Wool," published by the British Research Association for the Woollen and Worsted Industries. The latter report is of a very general character. It summarises the extensive nature of the problems of the industry, and attempts to indicate lines of investigation for the improvement of the world's wool production for the particular purposes of textile manufacturers. Some of the observations made in the report are not very specific. The importance of the study of the "growth of wool on the living sheep, how it originates, how it develops, and how it attains its final form, and, above all, why fibres differ, why fleeces differ, why breeds differ," is of course obvious. But this matter seems to involve just those difficulties which make the answer to some of the fundamental biological problems a matter of the greatest interest and complexity. The report clearly emphasises the urgent necessity for a real systematisation and definition of certain properties of the wool fibre. It suggests a possible classification of wools from the point of view of their utility to the spinner and manufacturer, in accordance, first of all, with their milling properties, and, secondly, with their spinning powers.

THE real difficulty of progress in these matters depends on the fact that the fundamental properties of wool from the viewpoint of the spinner and manufacturer, if they are actually definable, are certainly not yet defined. The spinning power of a wool, it is true, is related to its quality, yet, as was pointed out in NATURE of Nov. 19, 1927 (p. 730), the quality number or count to which a particular wool will spin has at present no definite measure. Exact information upon the important processes of milling and felting is also not available. It is not surprising that one finds in these circumstances that "the blanket manufacturer knows exactly [the type of raw wool] which he requires, though not always is he able to express it in words." As the report states, unless the fundamental properties of a raw wool are known in its relation to the purposes for which it will ultimately be used, experiments for developing new types of wool are bound to be of doubtful value. The wool textile technologist has conditions to meet, however, in connexion with the raw material, which scarcely exist in connexion with the supply of the raw material for other industries. For example, supplies and qualities of fleeces can under certain conditions be controlled, but, as Sir Arthur Balfour's committee points out, "the expansion of wool supplies [and presumably the quality] seems likely to be largely dependent on the price of wool (conjoined with the price of mutton) in relation to the price of other agricultural produce, notably, wheat and cereals." This aspect of the raw material supply for the textile industry, while it does not of course form directly a part of the problem of the standardisation of wool by scientific means, is bound to receive considerable attention by the economist and agriculturalist. Its relation with the technological points enumerated in the report of the British Research Association for the Woollen and Worsted Industries has doubtless already taken an important place in the considerations of that body.

SCIENTIFIC workers generally will welcome the statement made in the House of Commons on July 23 by Mr. A. M. Samuel, Financial Secretary to the Treasury, that the Government is prepared to exempt from Customs duty scientific cinematograph films brought into Great Britain solely for exhibition to scientific bodies. As was stated in our issue of July 21 (p. 103), the subject was raised early this month as a direct consequence of the difficulties experienced by Mr. W. H. Wright, the distinguished American astronomer who delivered the George Darwin lecture before the Royal Astronomical Society on June 8, in introducing his cinematograph film of Jupiter. On the report stage of the Finance Bill in the House of Commons on July 23, Capt. Ian Fraser moved a new clause providing that the Customs duties imposed by the Finance Act, 1925, on negative and positive cinematograph films should cease to be payable in the case of a film certified by the Royal Society to be