pears that about 60% of the acacia was retained by the liver, a smaller proportion by the spleen, and much smaller amounts by kidney and muscle.

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On the Fatty Acids Essential in Nutrition.*

GEORGE O. BURR AND WILLIAM R. BROWN.

From the Department of Botany, University of Minnesota.

Within the last few years a number of laboratories have published data in support of the view that diets quite low in fat are not complete. This is a reversal of the view held 10 years earlier. Working with diets extremely low in fats, Burr and Burr[1] showed that a disease supervened which could be cured by the addition of small amount of unsaturated fats or pure linolic acid. An examination of their data and that of other workers led to the postulation of essential fatty acids which could not be synthesized in adequate quantities by warm blooded animals. Their results have been repeated, partially or in full, by several workers. However, some workers [2, 3, 4, 5] have encountered scaly skin and necrotic tails in rats which were not curable by fat and this has led them to the view that we, too, are dealing not with a fat deficiency, but possibly with a vitamin B factor. There is no evidence that scaly skins and necrotic tails are specific for any single deficiency. Therefore, the production of these symptoms by one method does not preclude ready production by another.

Since all work in this laboratory strengthens the belief in beneficial effects of certain fats and fatty acids, it seems well at this

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[1] Burr, G. O., and Burr, M. M., *J. Biol. Chem.*, 1929, **82**, 345. The diet is made of purified casein, sucrose, salt mixture, supplemented by concentrates of vitamins A, D and E fed on whole dried yeast (ether extracted) of proven high quality (Northwestern).

[2] Hume, E. M., and Smith, H. H., *Biochem. J.*, 1931, **25**, 300.

[3] Gregory, E., and Drummond, J. C., *Z. f. Vitaminforschung*, 1932, **1**, 257.

[4] Funk, C., Caspe, S., and Caspe, H., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 816.

[5] Roche, A., and Roche, J., *Comp. Rend. Soc. Biol. Paris*, 1932, **109**, 463.

time to point out differences in technique which may readily account for the lack of agreement.

The diets used by the above workers indicate they were all deficient in growth factors. Funk, Caspe and Caspe did not add adequate vitamin B. Roche and Roche found their pathological skins on diets so deficient that the rats weighed only 80-100 gm. after 12 weeks. Those rats receiving whole yeast instead of yeast extract showed no skin lesions. Hume and Smith state "The growth of the animals is not considered in the results; the supply of vitamins B_1 and B_2 was insufficient for good growth over the major part of the experiment so that growth performances have no significance." The vitamin B source was marmite. It should be noted further that their animals did not always receive enough vitamin A so that bladder stones were encountered. They also used starch diets in place of sugar diets. Gregory and Drummond likewise use an extract of yeast which obviously is greatly deficient in one or more of the water soluble vitamins. Gregory and Drummond's growth curve for a "fat-free" diet is reproduced as accurately as possible in Fig. 1. For comparison is given the average growth curve of a group of 24 rats recently raised in this laboratory and still under observation. The end of the 8-week growth period commonly used for vitamin B tests is marked by X. While the Gregory and Drummond rats grew 28 gm. in the 56 day period our rats grew 86 gm., or over 3 times as fast. The average growth of these female rats on our fat-free diet in our colony is, therefore, about 1.6 gm. daily. During the 4 weeks of most rapid growth preceding the onset of fat deficiency, they gained 2.1 gm. daily, which is considered by many workers normal for stock females. Since growth is the quantitative measure of vitamins B and G, our diets would be considered very high in both factors (which is to be expected when 0.65 gm. of high grade dried yeast is consumed daily) while the Gregory and Drummond diet VIIb would be rated as decidedly deficient in at least one of the growth factors.

Although we had earlier found additional yeast ineffective in improving our rats after they had begun to decline on the fat-free diets, this experiment was repeated on the entire group of 20 rats (4 having died). Their daily dose of yeast was increased from 0.65 gm. to 0.90 gm. daily (39% increase). Growth was not resumed. The decline in weight was not even checked. (Fig. 1). At the end of a 5 week period of increased yeast dosage, there was no general improvement of the skin and during this period 5 cases of severe hematuria appeared, one of which died. For comparison,

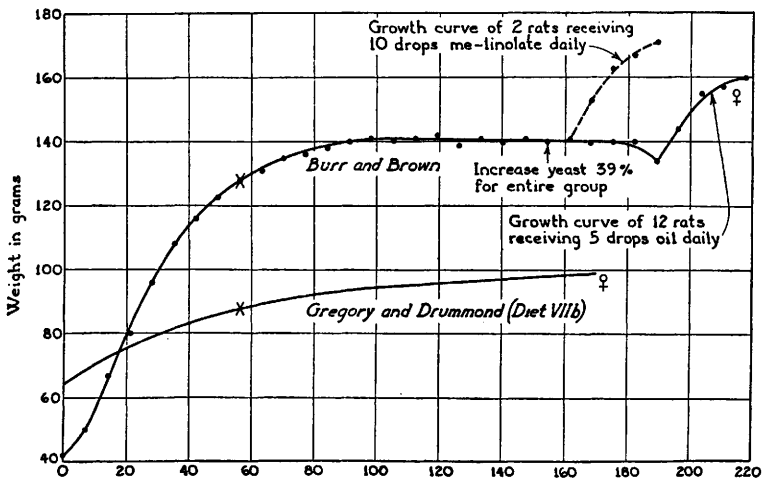

FIG. 1.

2 of the rats were fed 10 drops daily of pure methyl linolate at the same time. Their immediate growth response is shown as a branch of the main curve (Fig. 1).

As the animals were rapidly growing worse on the high yeast dose, fat supplements (5 drops daily) were now given to 12 of them (others used for analyses). The immediate growth response is seen in Fig. 1. At the end of 5 weeks a general improvement of the skin was evident. Hematuria disappeared from those rats which had shown it. No new cases appeared.

There is another important difference between the English work and ours. Hume and Smith find no scale or necrosis until the 180th day of experiment and Gregory and Drummond find it only after 90 days or more (2 cases out of 24 at 90 days). Rats on our diet show more or less severe scaliness throughout the groups within a few weeks. The scaliness appears during the period of rapid growth and could hardly be attributed to a lack of one of the growth factors.

It should be pointed out that fat deficiency is characterized by a late failure in growth (at 130-150 gm. weight) after an early period of rapid growth in the presence of excess growth factors. This failure is accompanied by a high percentage of kidney lesions,[6] abnormal gas exchange [7, 8] and abnormal water consumption.

[6] Borland, V. G., and Jackson, C. M., *Arch. Path.*, 1931, **11**, 687.

[7] Wesson, L. G., and Burr, G. O., *J. Biol. Chem.*, 1931, **91**, 525.

[8] Burr, G. O., and Beber, A. J., *J. Biol. Chem.*, 1932, **97**, 36.

Finally, death always ensues after 6-10 months on the diet. But when our diet is supplemented with 10 drops daily of a good fat, animals remain in good health for 18 months and scaliness of the skin has never been encountered.

From the point of view of the general metabolism of the rat, scaliness of the skin may be of secondary importance. It occurs in varying degrees of severity from group to group and is difficult to measure quantitatively. Time of year seems to affect its severity and we suspect humidity as an important factor. It has been found that scale tends to disappear from the feet of rats kept for long periods of time in humid metabolism chambers. We are now checking this theory.

As pointed out in our earlier papers, tail necrosis and scaly skin can result from numerous dietary conditions. Some good examples are general underfeeding,[9] deficiency of G (B_2)[10], diets rich in egg white,[11] rancid fat in the diet,[12] and deficiency of fatty acids. It is not necessary (nor even justifiable without further work) to assume that these diverse causes work through a common factor such as abnormal skin lipids which we now believe responsible for the scaliness of our rats.

Conclusion. The recently reported cases of skin lesions discussed here were produced under conditions which indicate a lack of some growth factor. In no case were conditions such that uncomplicated fat-deficiency could result. It would be impossible, therefore, for these rats to respond to small doses of unsaturated fats. An adequate supply of all water soluble growth factors must be fed if the typical fat deficiency results are to be obtained. Growth should approximate that given by the daily consumption of 0.65 gm. or more of high grade dried yeast.

[9] Smith, A. H., and Bogin, M., *Am. J. Path.*, 1927, **3**, 67.

[10] Goldberger, J., and Lilie, R. D., *Pub. Health Rep., U.S.P.H.S.*, 1926, **41**, 1025.

[11] Parsons, H. T., *J. Biol. Chem.*, 1931, **90**, 351.

[12] Whipple, D. V., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 319.