was the presence of much protein in the nephrons. It was most abundant and deeply stained in the distal convoluted and collecting tubules but was also present in the proximal convoluted tubules and subcapsular spaces of glomeruli. The cells of the proximal convoluted tubules were usually swollen and granular and often showed hyaline droplet degeneration. The cells of the distal convoluted tubules showed similar but less striking changes. Special stains demonstrated fatty degeneration, notably of the convoluted tubules, and lipemia was noted in many cases. Slight degrees of chronic and subacute interstitial inflammation were present in 5 cases. There were no glomerular lesions except in 3 cases. These rats were killed, or died, 4, 5, and 8 days after onset. The capillaries were dilated with blood and with a hyaline coagulum. The tufts were comparatively acellular. Basement membranes were irregularly thickened in places but normal and even attenuated in others. In one instance a few neutrophilic polymorphonuclear leucocytes were present in the tufts and in the proximal convoluted tubules.

References

1. Freund, J., and McDermott, K. *Proc. Soc. exp. Biol. Med.*, 1942, **49**, 548.
2. Kersten, H., Brosene, W. C., Ablondi, P., and SubbaRow, Y. *J. lab. clin. Med.*, 1947, **32**, 1090.
3. Lindemann, W. *Ann. Inst. Pasteur*, 1900, **14**, 49.
4. Masugi, M. *Beitr. path. Anat. U.Z. Allg. Path.*, 1933, **91**, 82; 1933, **92**, 429.
5. Smadel, J. E., and Swift, H. F. *J. clin. Invest.*, 1939, **18**, 757.
6. Smadel, J. E., and Swift, H. F. *J. exp. Med.*, 1941, **74**, 345.
7. Smadel, J. E., Swift, H. F., and Farr, L. E. *J. exp. Med.*, 1936, **64**, 921; 1937, **65**, 527; 1939, **70**, 615.

Effect of Galactose on the Utilization of Fat[1]

Curt P. Richter

Psychobiological Laboratory,
Johns Hopkins Medical School, Baltimore

Schantz, Elvehjem, and Hart (*10*) reported that fat plays an important part in the utilization of galactose. They offered as evidence the observations that rats kept on a diet consisting only of skim milk excreted large amounts of galactose, and that the addition of butter fat (roughly in an amount equal to that of the lactose in the skim milk) reduced the excretion of galactose. Geyer, Boutwell, Elvehjem, and Hart (7) offered further similar evidence to prove this point.

With an entirely different technique, evidence was found in this laboratory that a reverse relationship exists between fat and galactose, namely, that galactose plays an important part in the utilization of fat.

For these experiments the so-called "single-food-choice technique" was used. Previous papers give full details (*8, 9*). It will suffice here to state that in the simplest form of this method rats of a standard weight and under standard conditions are placed on a diet that consists of only one foodstuff and water. The length of time the rats survive is taken as a measure of the nutritive value of the foodstuff. For example, it was found that without any food rats survived, on the average, only 4 days, whereas on galactose they survived 6 days and on glucose, 37 days. The significance of the results obtained with this technique depends on the observation that under these conditions rats seem to eat just as much of a purified foodstuff as they are able to utilize. This method has also been used, in a slightly more complicated form, to study the effects produced by various supporting substances. It was used, for example, to study the effect of thiamine on the utilization of glucose. To do this, the rats on a diet consisting exclusively of glucose were offered as a supplement 0.02% solution of thiamine hydrochloride. These rats survived, on the average, 76 days, or twice as long as on glucose alone, thus demonstrating beyond any doubt the remarkable effect that thiamine has on the utilization of glucose. In another form of this technique the interaction of foodstuffs on their mutual utilization can be studied by offering two foodstuffs at one time, as was done in the present experiments.

For these experiments domestic Norway rats were kept separately in cages that contained one or two nonspillable food cups and a graduated inverted bottle for water. The cages were made of wire cloth and were equipped with a large-meshed, wire-screen bottom to eliminate coprophagy.

Rats were started in the cages at ages of 38–47 days and kept on the stock diet until they were changed to the single-food diet. This occurred when they reached weights of between 120 and 150 gm.

In one series the rats had access only to galactose; in a second, only to oleo[2]; and in a third, to oleo and galactose (in separate containers). In a control series the rats had no food at all. On no food at all 15 rats survived from 3 to 6 days, with an average of 4.3 days. On galactose alone 13 rats survived from 4 to 8 days, with an average of 6.2 days; on oleo 10 rats survived from 19 to 38 days, with an average of 32.4 days; and on oleo and galactose 13 rats survived from 47 to 92 days, with an average of 69.3 days. This was over twice as long as on oleo alone, and over 11 times as long as on galactose alone.

Clearly, either the oleo must have had a great effect on the utilization of the galactose or the galactose must have had a great effect on the utilization of the oleo.

A comparison of the amounts of oleo and galactose eaten by the rats when they had simultaneous access to these two foodstuffs throws light on this relationship. The total caloric intake (average for the first 40 days) was 261.2 cal/kg/day, with the galactose contributing an average of 39.9 cal/kg, or only 15.3% of the total. For some of the rats the average daily galactose intake

[1] This study was carried out under a grant from the Sugar Research Foundation, New York City.

[2] Mrs. Filbert's, Baltimore, Maryland—vegetable oil, 80%; moisture, 15%; salt, 3.1%; skim milk, 1.5%; derivative of glycerine, 0.2%; sodium benzoate, 0.1%; vitamins from fish livers, 0.1%.

fell below 5% of the total. One rat that survived 71 days ate galactose only at irregular intervals and then in small amounts, while it ate constantly large amounts of oleo; at one stage it ate no galactose for 15 days. These results indicate that the calories received from galactose could not have contributed substantially to the length of time that the rats survived.

Of special interest is the fact that the rats with access to galactose ate more oleo than did those having access only to oleo, and much less galactose than did the rats that had access only to galactose.

The role played by galactose in relation to fat may be similar to that played in single-food-choice experiments by thiamine in relation to glucose (*8*); both increased amounts of the respective foodstuffs that the rats were able to utilize and thus increased the survival times.

In further experiments it was found that the ingestion of a mixture of oleo and galactose (9 or 19 parts of oleo to 1 part of galactose) had a similar effect on the survival time. In contrast, the ingestion of a mixture of oleo and glucose in the same proportions failed to increase the survival times above those of rats on oleo alone. This result indicates that galactose may have a specific effect on the utilization of fat.

In the reverse experiment a small amount of oleo was added to galactose (1 part to 9 parts of galactose). On this mixture the rats did not live significantly longer than they did on galactose alone.

These self-selection experiments in which the rats had access to galactose and oleo brought out a relationship between these substances which, on the basis of present biochemical knowledge, might not have been suspected. With their selections the rats showed that only very small amounts of galactose suffice to bring about a great increase in the utilization of the fat, oleo, and that large amounts are detrimental. Ershoff (*5*) produced cataracts on single-food mixtures of dextrose and galactose (50: 50) and on butter fat and galactose (30: 70); and Ershoff and Deuel (*6*) failed to find this marked effect of galactose on the utilization of fat, apparently because of the high proportion of the galactose in the single-food mixtures of galactose and oleo (70: 30).

These experiments with oleo were started during the war, when butter was not available in adequate amounts. Butter would have been a better fat with which to start; still better would have been a fat that does not contain even the very small amounts of protein, milk solids, and vitamins that are present in oleo.

Preliminary experiments with corn oil and galactose have thus far given essentially the same results.

The results show that fat apparently does not have any effect on the utilization of galactose. They do not agree with the conclusions of Schantz, *et al.* (*10*), but do agree with those of Zialcita and Mitchell (*11*). The latter workers repeated the experiments of Schantz, *et al.*, but with a purified diet rather than with skim milk powder, and found that the addition of fat did not alter the excretion of galactose. They concluded that fat, as such, has no influence on the metabolism of galactose.

In single-food-choice experiments in which fat constitutes the entire diet it is possible that ketosis prevents the rats from living longer. The observations of Deuel and Chambers (*3*), of Deuel, Gulick, and Butts (*4*), and of Butts (*1*) and Clark and Murlin (*2*) have shown that galactose has a strong antiketogenic effect, stronger than that of either glucose or fructose. This antiketogenic action might help to increase the survival time.

Deuel, Gulick and Butts (*4*) have reported that the ingestion of galactose has a pronounced nitrogen-sparing action. This action may also have helped to increase the survival times of the rats in the present experiments.

In the absence of more definite biochemical data, however, it would seem likely that these results depend on some specific and unknown metabolic effect of galactose.

Should the results of further experiments on rats disclose that galactose in such small amounts has the same effect on other fats as it does on oleo, and that galactose has a superior action to all other sugars in this respect, fortification of common fats and oils with small amounts of lactose, galactose, or skim milk powder might be considered for the diet of man.

References

1. Butts, J. S. *J. biol. Chem.*, 1934, **105**, 87.
2. Clark, D. E., and Murlin, J. R. *J. Nutrition*, 1936, **12**, 469.
3. Deuel, H. J., Jr., and Chambers, W. H. *J. biol. Chem.*, 1925, **65**, 7.
4. Deuel, H. J., Jr., Gulik, M., and Butts, J. S. *J. biol. Chem.*, 1932, **98**, 333.
5. Ershoff, B. H. *Amer. J. Physiol.*, 1946, **147**, 13.
6. Ershoff, B. H., and Deuel, H. J., Jr. *Amer. J. Physiol.*, 1947, **148**, 45.
7. Geyer, R. P., Boutwell, R. K., Elvehjem, C. A., and Hart, E. B. *J. biol. Chem.*, 1946, **162**, 251.
8. Richter, C. P., and Rice, K. K. *Amer. J. Physiol.*, 1942, **137**, 573.
9. Richter, C. P., and Rice, K. K. *Amer. J. Physiol.*, 1945, **143**, 336.
10. Schantz, E. J., Elvehjem, C. A., and Hart, E. B. *J. biol. Chem.*, 1938, **122**, 381.
11. Zialcita, L. P., Jr., and Mitchell, H. H. *J. Nutrition*, 1945, **30**, 147.

A Qualitative Chemical Change in Carcinogenesis[1]

Christopher Carruthers and V. Suntzeff

Barnard Free Skin and Cancer Hospital and *Department of Anatomy, Washington University School of Medicine, St. Louis*

In a review article on the "Properties of Cancer Cells" by Cowdry (*3*) the statement by Voegtlin is reiterated in that "no conclusive evidence exists at present which reveals any qualitative differences in chemical composition between normal and malignant cells. Whatever differences do exist are of a quantitative nature, the biological significance of which is difficult to evaluate."

In this paper evidence is presented to show that an alteration in the nature of a lipid, probably associated

[1] This investigation was aided by grants from the National Cancer Institute, the Charles F. Kettering Foundation, and the American Cancer Society.