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 (*3*); 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.

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A Qualitative Chemical Change in Carcinogenesis[1]

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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.

with a protein, occurs in the process of epidermal carcinogenesis in mice.

The procedures for shaving the mice, applying the carcinogen, methylcholanthrene, and removing the epidermis from dermis have been described (*2*). The epidermis or other tissues were extracted by refluxing on a steam bath with mixtures of peroxide-free ether and ethyl alcohol prepared by shaking occasionally with powdered calcium oxide for a period of 1–2 days and then distilling from a small fractionating column. After the tissues were extracted twice for a period of ½ hr, the solvents were filtered into 150-ml beakers and evaporated to near dryness on a steam bath. The last traces of solvents were removed *in vacuo* in a desiccator over $CaCl_2$. The total lipid was then re-extracted with anhydrous peroxide-free ether, and the latter filtered through Munk-

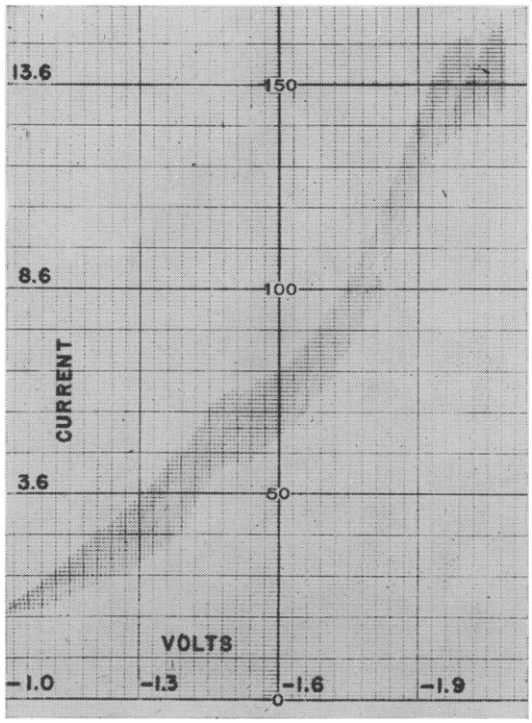

FIG. 1. Polarogram of the lipids from hyperplastic mouse epidermis in 75% dioxane.

tell's OB paper into a weighed, glass-stoppered, 50-ml Erlenmeyer flask. The ether was then driven off on a steam bath, the last traces being removed with a stream of nitrogen, and the samples were stored in an atmosphere of nitrogen in a refrigerator until ready for use.

Since the polarograph was found to be very useful for the quantitative determination of cytochrome C and for following the purification of the latter from tissues (*1*), the possibility of using this instrument for a study of the electrolysis of the lipids extracted from mouse tissues was investigated. After tests with various organic solvents it was found that mixtures of dioxane and water were most suitable for the polarography of lipid substances. Tetra-*n*-butylammonium iodide (hereafter denoted by R_4NI) was used as a supporting electrolyte. Dioxane was purified and R_4NI prepared by the procedure of Laitinen[2] and Wauzonek (*5*). Dioxane was added to the lipid in the Erlenmeyer flask, and the solution was completed by warming on a steam bath. Redistilled water was then added to attain the desired concentration and sufficient R_4NI to make a final concentration of 0.1 M, the latter concentration being used in all the experiments. The mixture was then warmed on a steam bath to facilitate solution. The electrolysis with a Sargent, Model XXI, Polarograph was carried out with a mercury pool anode in an Heyrovsky vessel of suitable size which was provided with side arms for anode connection, introduction of nitrogen, removal of oxygen, and admittance of a slow stream of nitrogen over the solution during electrolysis. The nitrogen was passed through dioxane prior to its entrance into the vessel. All measurements were made at 25° C. The anode potential was measured against a saturated calomel electrode (S.C.E.) with a salt bridge in the usual manner (*4*).

A polarogram of the lipid of methylcholanthrene-treated mouse epidermis extracted with a mixture containing 50% alcohol and 50% ether is shown in Fig. 1.

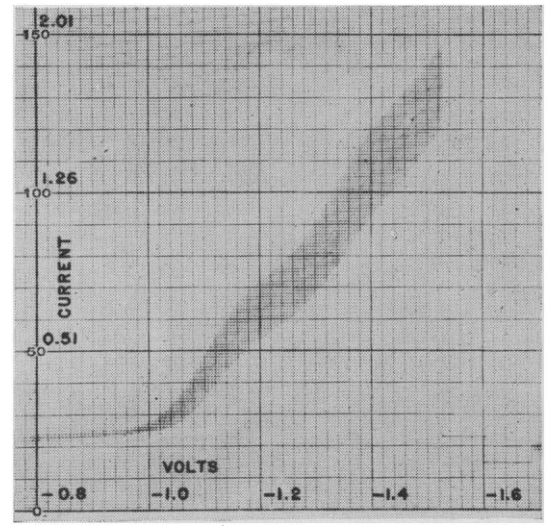

FIG. 2. Polarogram of the lipids from hyperplastic mouse epidermis in 50% dioxane.

In all the figures the current is expressed as microamperes against the applied potential in volts. The half-wave potential of the first wave is −1.76 v and that of the second, −2.10 v vs. the S.C.E. The concentration of the lipid was 9.8 mg/ml; of water, 25%; and of dioxane, 75% (anode potential, −0.430 v). Two distinct waves were present, and for further resolution the water concentration was increased to "water out" the more insoluble lipids. This effect is demonstrated in Fig. 2.

[2] The authors are indebted to H. A. Laitinen for samples of pure and crude tetra-*n*-butylammonium iodide used in the preliminary phase of this work. A good grade of this quaternary ammonium salt can be obtained from the Rhoads Chemical Company, 417 Cleveland Avenue, Plainfield, New Jersey.

The lipid concentration was 6.5 mg/ml and that of dioxane, 50% (anode potential, – 0.390 v). The nature of the lipids in solution is so altered that a double wave has now appeared where the first wave appeared in Fig. 1. The half-wave potential of the first wave is – 1.47 v and that of the second, – 1.66 v vs. the S.C.E. The third wave, corresponding to the second wave of Fig. 1, is not shown since it was not altered appreciably during carcinogenesis. Even when the lipid concentration is reduced to 3.25 mg/ml and that of the dioxane to 37.5%, the double wave, the same as that in Fig. 2, is well defined. The half-wave potentials of the two waves are the same throughout carcinogenesis (Table 2).

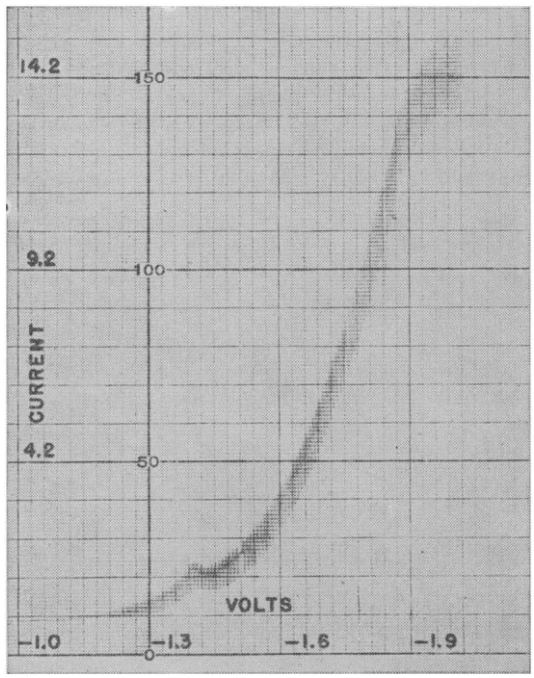

FIG. 3. Polarogram of the lipids from a methylcholanthrene-induced tumor in 75% dioxane.

When methylcholanthrene-induced carcinomas and transplantable carcinomas (Nos. I[3], II[3], and III[3]) were extracted with a mixture containing 50% alcohol and the lipid polarographed as above, a great difference was noted. A polarogram of the lipid from an induced tumor is shown in Fig. 3. The lipid content was 13 mg/ml in 75% dioxane. The half-wave potential of the first wave is – 1.79 v, and of the second, – 2.13 v vs. the S.C.E. When Fig. 3 is compared with Fig. 1, it can be seen that the first wave of the latter has a different curvature and appearance than that of Fig. 3.

When the lipid of this carcinoma sample was reduced

[3] Transplantable tumors Nos. I and II are well-differentiated squamous cell carcinomas with many mitoses. The nuclei of tumor No. II are larger than those of No. I. Tumor No. III is very well differentiated, slow growing, and contains less mitosis than tumors I and II.

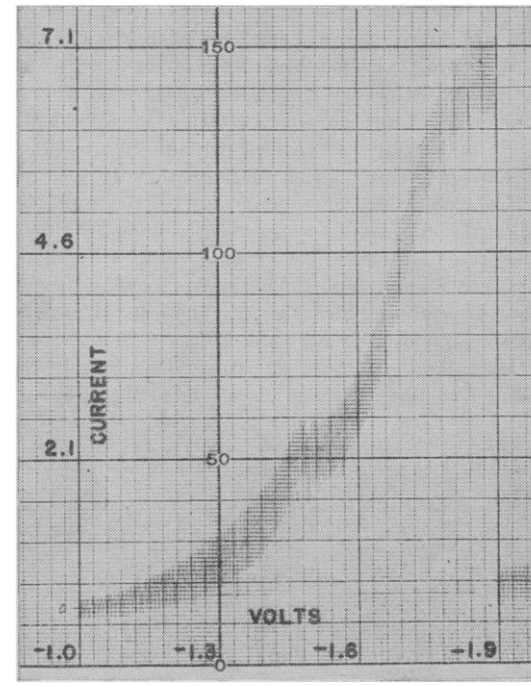

FIG. 4. Polarogram of the lipids from transplantable tumor No. III in 75% dioxane.

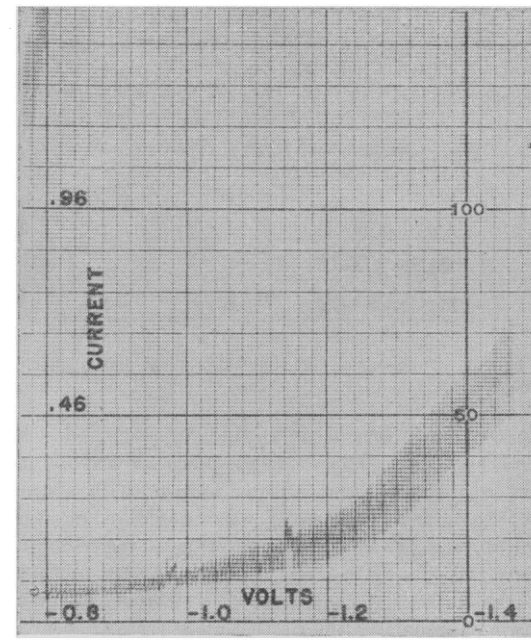

FIG. 5. Polarogram of the lipids from tumor No. III in 50% dioxane.

to 6.5 mg/ml in a mixture of 50% dioxane, no waves appeared comparable to the double wave of Fig. 2. However, some of the methylcholanthrene-induced tumors ex-

tracted in a 50% alcohol mixture did give a single wave similar to that of Fig. 5. The reason for this lack of consistency with induced tumors will become apparent later. On the other hand, transplantable tumors, with the exception of 2 of 5 samples of tumor No. II, did not give the single wave when extracted with a mixture containing 50% alcohol.

TABLE 1

HALF-WAVE POTENTIALS OF THE REDUCIBLE MATERIAL IN CARCINOMAS

Type of carcinoma	Percentage of alcohol in alcohol-ether mixture	Half-wave potential in volts vs. the S. C. E.
Induced	25	−1.62
"	25	−1.72
"	40	−1.72
Induced*	50	−1.65
Tumor No. I	25	−1.70
" " "	25	−1.66
" " "	75	No wave
Tumor No. I†	40	"
" " "†	10	"
Tumor No. II	75	"
" " "	50	−1.64
Tumor No. II‡	50	−1.64
Tumor No. III	25	−1.68
" " "†	25	No wave

* Average of 6 samples. About 50% of induced tumors had the wave.

† Tumor in 95% alcohol overnight, then ether added.

‡ Two of 5 tumors No. II gave the wave in a mixture of 50% ether, 50% alcohol, but none of tumors Nos. I and II.

mixture of 50% dioxane, there was a single wave with half-wave potential of −1.68 v vs. the S.C.E. (Fig. 5). The half-wave potentials for other tumor samples are shown in Table 1.

An examination of Table 1 reveals that the half-wave potential of the single wave found in the carcinomas is nearly the same as that of the second wave of the double wave (Fig. 2) found in normal and hyperplastic epidermis (Table 2). In other words, the component responsible for the first wave of the lipid of normal and hyperplastic epidermis has been altered and is no longer reducible at the dropping mercury electrode. Therefore, a qualitative chemical change in a lipid has occurred during carcinogenesis, and experiments were devised to ascertain whether the material in normal and hyperplastic epidermis having the double wave consisted of a single compound or of two compounds, one of which had been altered in the carcinomas so that it was no longer reducible.

When normal or hyperplastic epidermis is extracted with mixtures containing 40, 50, 60, or 75% ether, the double wave is obtained, and a nearly constant difference in voltage (average, 0.21 v) exists between the second and first wave (Table 2). Furthermore, the half-wave potential of the waves is independent of the concentration of the lipid (approximately 3–12 mg/ml) and of the dioxane concentration between 62.5 and 37.5%. These observations indicate that we are dealing with a single compound. On the other hand, the single wave of the carcinoma (Fig. 5) is always obtained in material extracted by mixtures containing 60 and 75% ether. It

TABLE 2

HALF-WAVE POTENTIALS OF THE REDUCIBLE MATERIAL IN NORMAL AND HYPERPLASTIC EPIDERMIS

Epidermis	Percentage of alcohol in alcohol-ether mixture	Half-wave potentials in volts vs. S. C. E.					
		First wave			Second wave		
		A	B	C	A	B	C
Normal	50		−1.48	−1.48		−1.69	−1.65
"	40		−1.49	−1.40		−1.74	−1.70
"	25		−1.46	−1.49		−1.68	−1.65
"	60		−1.48	−1.40		−1.73	−1.60
Hyperplastic 3 paintings with MC*	60		−1.47			−1.66	
3 "	25	−1.46	−1.49	−1.42	−1.69	−1.68	−1.63
10 "	25	−1.48			−1.73		
24 "	50	−1.48	−1.47	−1.42	−1.69	−1.68	−1.65

A—in 62.5% dioxane at ½ original concentration.
B—" 50.0% " " ½ " "
C—" 37.5% " " ¼ " "
* Methylcholanthrene.

When induced and transplantable tumors were extracted with mixtures of 75–60% ether, the single wave always appeared. A polarogram of the lipid of tumor No. III (10.7 mg/ml) in 75% dioxane is shown in Fig. 4. The half-wave potential of the first wave is −1.79 v and that of the second, −2.01 v vs. the S.C.E. When the concentration of the lipid was reduced to 5.35 mg/ml in a

was found only occasionally in the induced, and never in the transplantable tumors Nos. I and III if the alcohol content of the extractant was 50% or more. The half-wave potential of this single wave is nearly the same as that of the second part of the double wave of epidermis. If normal or hyperplastic epidermis is allowed to stand in 95% alcohol for 1–10 days in a refrigerator

and then sufficient ether is added to make a 50% mixture, the material showing the double wave can be extracted. In contrast, if the carcinomas are treated in a similar fashion, the single wave shown by these tissues never appears, and even adjusting the ether concentrations in the extracting solution to 60 and 75%, after fixation in 95% alcohol, concentrations which are most effective in obtaining the wave from fresh tissue give only small amounts, if any, of this reducible material. Ethyl alcohol probably fixes the lipoprotein *in situ* and renders the lipid practically nonextractable under our conditions. It is thus apparent that the lipid in the carcinoma differs from that in the tissue of origin with respect to solubility in ether and to extractability from the tissue after fixation in 95% alcohol. The half-wave potentials of the double wave in the lipid of normal and hyperplastic epidermis are the same over a wide range of concentrations of alcohol and ether in the mixture used for extraction. The half-wave potentials are also independent, within the limits studied, of the amount of lipid, water, and dioxane in the solution which is polarographed, and the diffusion current of the double wave/100 mg of lipid is approximately constant under these conditions. In addition, the double wave is unaltered after fixation in 95% ethyl alcohol and subsequent extraction. These data indicate that the reducible material is probably a single compound. In the carcinomas the solubility of the altered lipid is so changed as to require more ether for solution and, moreover, is fixed in large part *in situ* by the addition of alcohol and this becomes almost ether insoluble. The single wave has a half-wave potential almost the same as that of the second wave of the two found in epidermis.

The differences described above that were found in the behavior of the material from mouse epidermis and from the tumors at the dropping mercury electrode demonstrate that an alteration in the structure of a lipid occurs during the process of epidermal carcinogenesis in mice. The difference in the lipid of the carcinomas is due to a quantitative alteration of a part of the lipid material of normal and hyperplastic epidermis, but the net result is a qualitative change resulting in altered physical and chemical properties of the lipid material.

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Book Reviews

An outline of social psychology. Muzafer Sherif. (Ed. by Gardner Murphy.) New York: Harper, 1948. Pp. xv + 479. (Illustrated.) $4.00.

The time was, and not very many years ago, when a certain text in social psychology contained little but the views of a single psychologist regarding a few of the phenomena of our social order. Another text of this period served as a vehicle in which the ideologies of Freud, Lewin, and Marx were made to appear somewhat compatible. In contrast, the texts of today are far more alike. They adopt rather similar eclectic positions regarding the theoretical structure of their science and are careful not to ignore its more important experimental data. Yet there still would appear to be uncertainty as to just what areas make up the field of social psychology.

And, of course, there is the well-known tendency for each textbook writer to ride his own hobby. Thus, the basic research interests of M. Sherif being what they are, it should come as no surprise that approximately 60% of the space of his *An outline of social psychology* should be allocated to "Groups and Norms (Values)." Another portion is devoted to "Motives" and the rest to "Individual Differences in Social Reactions."

Sherif's text is noteworthy for its judiciously chosen references to contemporary lay source materials, the writings of Ernie Pyle being featured most often. Newcomb has written a section on his important Bennington College researches. Also noteworthy are two chapters, "The Effects of Deprivation at the Human Level (Individual and Social)" and "The Effects of Technology." The latter is particularly interesting in that it presents a brief account of the worth-while work Sherif did some years ago with many villagers in the more remote parts of Turkey.

In the "Editor's Introduction" Gardner Murphy says of Sherif: "To him, more than to any other single person, is attributable the whole manner of approaching social psychology which characterizes the present period." Whether this is a valid statement or merely the outpourings of a too enthusiastic editor, it is clear that Sherif, the author of *Psychology of social norms,* is eminently well qualified to write this more general book in social psychology. The reader need have no fear that the author's foreign background has biased his writing. Indeed, Sherif seems thoroughly familiar with Western European ways. His Turkish background serves largely to give him an added supply of interesting illustrative materials. Here, then, is a worth-while book. It should, in the reviewer's opinion, be read by every social and clinical psychologist.

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