fumarate > succinate. Pyruvate oxidation was largely abolished, and analysis of flask contents at the end of the experiment showed accumulations of pyruvate from other substrates that were proportional to the inhibition of O_2 uptake. The addition of fluoromalate to cultures at a concentration of 10^{-4} *M* during a growth period of 18 h caused pyruvate to accumulate from various sources of carbon. The concentrations of pyruvate produced were about the same as those reported[3] for growth in the presence of 10^{-4} *M*-fluoropyruvate, namely 1–2 μmoles pyruvate/ml for cells utilizing C_4 acids and parahydroxybenzoate, with negligible amounts accumulating from acetate. Citrate accumulation did not result from any of the carbon sources by the action of either drug, but citrate accumulation after addition of fluoroacetate to cultures was confirmed[3].

The action of malate synthetase is similar to that of the condensing enzyme which forms citrate, because the methyl group of acetyl CoA condenses with a –CO–COOH group in both cases. The presence of malate synthetase in this vibrio has been demonstrated[8] and accordingly the synthesis of fluoromalate from fluoroacetate is feasible. The present work shows that fluoromalate, if formed, could be expected to block pyruvate metabolism and there is no reason to postulate another route by which fluoropyruvate could be synthesized instead. No conversion of synthetic fluoromalate to fluoropyruvate could be demonstrated for an active malate decarboxylase preparation from *Lactobacillus arabinosus*[9].

One of us (A.G.C.) is indebted to the Agricultural Research Council for a research studentship.

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Received December 15th, 1958

Effect of neoplasia and fasting on phospholipid turnover rate in rat liver

Previous studies have shown that the phospholipid content of the Novikoff hepatoma was markedly lower than that of the normal rat liver[1,2]. It was also demonstrated that this change was specific to the neoplastic liver because there was no such alteration present in the rapidly growing regenerating liver. Studies on the physiological behavior of liver phospholipids showed that even after 6-days fasting 50 % of the phospholipids were present in the average liver cell. On the other hand, the average hepatoma cell

contained only 30 % of the normal liver phospholipid content. Therefore, it appears unlikely that anorexia and the resulting decreased food intake are responsible for the depletion of the phospholipid content of the Novikoff hepatoma[1].

To obtain information on the mechanism of the decrease in the phospholipid content of the hepatoma and in the liver of fasted rats, the turnover rate of this compound was studied by following the ^{32}P incorporation.

Male, adult Wistar rats of 150–220 g were kept in separate cages on Purina Fox Chow and water *ad libitum*. The fasted animals received only water. Rats bearing intraperitoneally transplanted 7-day old Novikoff hepatoma and normal rats were injected subcutaneously with ^{32}P (1 μC/g body weight). The animals were killed 1 h later and liver and hepatoma phospholipids were extracted according to the method of HOKIN AND HOKIN[3]. The phospholipid content is expressed per unit wet weight for comparison with other data in literature. The results are also expressed per average cell which is a more adequate basis for expression since it takes into account the fact that there are twice as many cells in the hepatoma as in the liver[4]. This is also an important consideration in fasting studies since cellularity of the liver increases steadily during a 6-day fasting period[5].

Table I compares the amount and ^{32}P incorporation of phospholipids in normal-fed and neoplastic rat liver. The marked decrease in the phospholipid content of the Novikoff tumor is in line with previous data[1,2]. This table shows that the specific activity and relative specific activity of the phospholipid phosphorus of the hepatoma were 35 % and 33 % respectively of the normal liver values. It may be concluded that the turnover rate of the phosphoryl radical of the phospholipid molecule is markedly depressed in this liver tumor.

Fig. 1 shows that the phospholipid content of the average liver cell gradually decreased during a period of 6-day fasting. This confirms previous data[1]. It is of interest to note that the specific activity, as measured by ^{32}P incorporation, gradually increased during the long-term fasting process.

The comparison of the data on phospholipid content and ^{32}P incorporation in hepatoma and in normal liver in fasting draws attention to the fact that the amount and turnover rate of phospholipids may not go parallel under physiological and pathological conditions. The results presented demonstrate that the difference between the depletion in the phospholipid content in the hepatoma and in the liver of fasted

TABLE I

INCORPORATION OF ^{32}P IN PHOSPHOLIPIDS OF LIVER AND HEPATOMA

(The means and standard deviations of 8 or more samples are given.)

Tissues	*Phospholipid content*		*Specific activity** ($^{32}P/^{31}P$)	*Relative specific activity***
	wet weight (μg P)	*per cell* ($\mu g\ P \cdot 10^{-6}$)		
Liver	1352 ± 119	6.8 ± 1.3	62.8 ± 31.4	226.3 ± 86.5
Hepatoma	582 ± 163	1.4 ± 0.4	22.0 ± 16.5	73.7 ± 42.5
Hepatoma/liver (%)	43	21	35	33

* ^{32}P = counts/min/g; ^{31}P = μg phospholipid P/g.

** Specific activity/injected dose/body wt.

rats is not simply quantitative. In fasting, the liver phospholipid content decreased, but it appears that the phosphoryl radical turns over very rapidly. This may be taken as an indication of an increased metabolic activity of the liver phospholipids during fasting condition. In the light of the isotope data it appears that the decreased amount of phospholipid in the Novikoff hepatoma may be due to a decrease in the synthesis *de novo* of the phospholipid molecules. The markedly decreased ^{32}P incorporation in phospholipids seems to be specific to liver neoplasia since *increased* incorporation was reported in the regenerating liver[6].

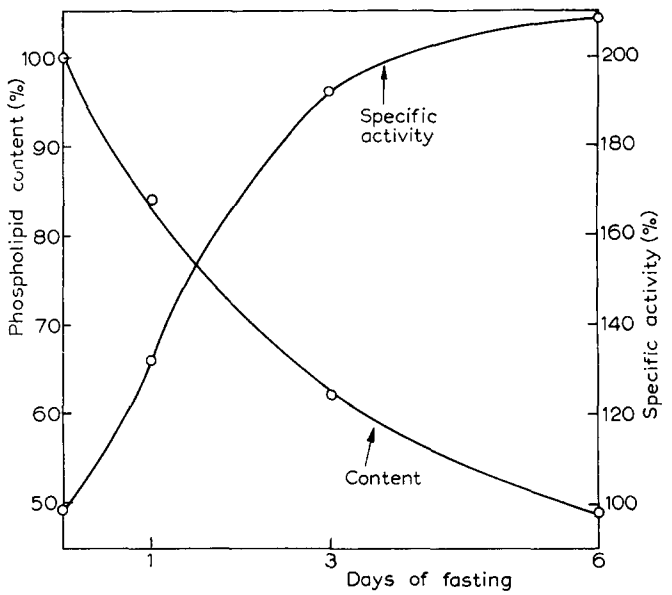

Fig. 1. The effect of 6-day fasting on liver phospholipid content and turnover rate. The phospholipid content is expressed per average cell; the turnover rate is given as specific activity. These terms are defined in Table I. The results are plotted as % of the value of normal-fed rats.

The excellent technical assistance of COLETTE AYOTTE and FRANÇOISE LUPIEN is gratefully acknowledged. This work was supported by a grant from the Cancer Research Society, Montreal, and by the National Cancer Institute of Canada.

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Received December 29th, 1958