were accompanied by a further increment in Ca^{45} entry with no significant change in tissue Ca. Thus, in many respects, the K-contracture in mammalian heart muscle resembled qualitatively that in the single skeletal muscle fiber.

A tentative explanation of the above data is that proposed by Hodgkin and Horowicz (2). They suggested that high-K, by depolarizing the cell membrance, released an activator (probably Ca or a compound of Ca) from a limited quantity of a precursor; the activator was then rapidly inactivated. Contraction would last until the precursor of the activator was nearly exhausted. They also suggested that the precursor might be stored in the sarcoplasmic reticulum. Such a hypothesis would account for the time course of the K-contracture in atria, and also for the finding that during tension development tissue Ca content did not change, but became more exchangeable.

In light of this hypothesis ouabain might produce its effects by promoting the rate of liberation of the activator from its precursor and possibly by reducing the rate at which the precursor is resynthesized. The observed action of ouabain on the time course of tension development in K-contracture as well as its effect on Ca^{45} uptake is in agreement with this hypothesis.

Summary. The K-contracture in isolated rabbit atria is transient in nature, resembling qualitatively that seen in single skeletal muscle fibers, but differing from that found in frog ventricle. Tension development is accompanied by an increase Ca^{45} entry with no detectable change in tissue Ca content. The rate of rise of tension, the level of peak tension and the rate of decline of tension is increased by ouabain. It was concluded that K releases an activator (probably Ca) from a precursor stored at a cellular site, and then is rapidly inactivated; the contraction lasting until the precursor is exhausted. Ouabain is believed to act by promoting the release of activator and possibly by reducing the rate at which the precursor is reformed at its storage site.

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Alteration in Lipid Content of the Liver in the Rat After Partial Hepatectomy.* (31349)

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Significant metabolic alterations occur in the liver within 24 hours after partial hepatectomy(1-4). Among these changes a remarkable rise in total lipid concentration, due mostly to accumulation of triglycerides, is apparent as early as 6 hours after partial hepatectomy(5).

As indicated by Johnson and Albert(6,7), the higher levels of lipids found in the liver after surgery appear to reflect the utilization of fatty acid originating from the peripheral adipose tissue and not by increased synthesis *in situ*. According to these authors, based on studies with ^{14}C-acetate, fatty acid synthesis is low during the 24-hour period after partial hepatectomy(7), during which time the accumulation of lipids in the liver is most pronounced.

The increased liberation of fatty acids (F.A.) from peripheral fat depots in euglycemic animals involves the participation of several hormones, such as ACTH and the

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TABLE I. Total Lipids per Gram of Liver 24 Hours After Partial Hepatectomy in Rats.

	mg of total lipid/g of liver (wet wt) ± standard error			
	Non-operated controls	Sham-operated	30% Hepatectomized	70% Hepatectomized
Fed *ad libitum*	46 ± 2.6 (33)*	53 ± 2.15 (7)	56 ± 3.1 (8)	96 ± 3.93 (10)
Fasted during 24-hr period	50 ± 1.5 (6)	47 ± 1.7 (5)	58 ± 2.3 (6)	94 ± 4.2 (5)

* Numbers within parentheses indicate number of rats in each group.

Lipid-Mobilizing Factor(8-11). Adrenaline also intervenes in this process, through a direct stimulation of tissue lipase(12,13).

On the other hand, when the mobilization of fatty acids from depot fat is depressed after either cordotomy or adrenalectomy, lipid accumulation in the liver does not occur(14-16).

The mobilization of lipids that occurs in partially hepatectomized animals also has been attributed to natural post-operative fast, to surgical trauma(17) and to specific alterations in regenerative processes(18).

In this work an investigation of the relationship between circulating free fatty acids and total liver lipids within 24 hours post surgery was made.

The participation of fasting, surgical stress, and partial hepatectomy (to the extent of either 30 or 70%), as factors possibly affecting the levels of total lipids 24 hours after surgery, also was investigated. The influence of pituitary hormones, corticosteroid hormones and catecholamines upon total lipid levels found in the remnant of the liver was studied in rats submitted to either adrenalectomy, hypophysectomy or treatment with either reserpine or guanethidine, prior to partial hepatectomy.

Material and methods. Male rats, of Wistar strain, with weights ranging between 180 to 230 g were used in all experiments. Partial hepatectomy was done according to the method of Higgins and Anderson(19), by removing either the medial and left lateral lobes, which correspond to approximately 70% of the liver by weight, or the left lateral lobe only, which corresponds to about 30% of the total liver. Surgery done on sham-operated (S.O.) rats consisted of laparotomy, handling of the liver and closure of the abdominal cavity. Ardenalectomy and hypophysectomy were performed at 2 days and 20 days, respectively, prior to partial hepatectomy. All adrenalectomized animals were kept on physiological saline solution *ad libitum* as a source of fluid. All surgery was carried out under ether anesthesia between 8:00 a.m. and noon.

Reserpine was given intraperitoneally in 2 doses, each of 7.5 mg/kg, at 24 hours and 12 hours, respectively, before partial hepatectomy. Guanethidine also was given by the intraperitoneal route in 2 doses, each of 15 mg/kg, at 1 hour before and 8 hours after partial hepatectomy, respectively.

All animals were kept on the regular diet (complete) *ad libitum,* except in the experiments in which the animals were allowed to fast for the 24 hours immediately after partial hepatectomy. Total lipid (T.L.) level in the liver was estimated after extraction according to the technique of Folch(20). Free fatty acids (F.F.A.) in the blood were assayed by Dole's technique in blood samples collected by heart puncture in rats anesthetized with ether(21).

Results and discussion. The roles of fasting, surgical stress and percentage of residual liver after partial hepatectomy, as factors possibly influencing the accumulation of lipids 24 hours after partial hepatectomy, were investigated by using sham-operated and 30% or 70% hepatectomized rats; a normal non-operated group afforded an over-all control. The results shown in Table I, obtained with partial hepatectomized animals fed *ad libitum,* indicate that the amount of residual liver is a critical factor in determining the extent of accumulation of lipids that occurs, since only the 70% hepatectomized animals had increased total lipids in the liver, 24 hours after surgery.

The effect of fasting was investigated in another experiment carried out in the same way as that described previously, except that all rats, including the non-operated controls,

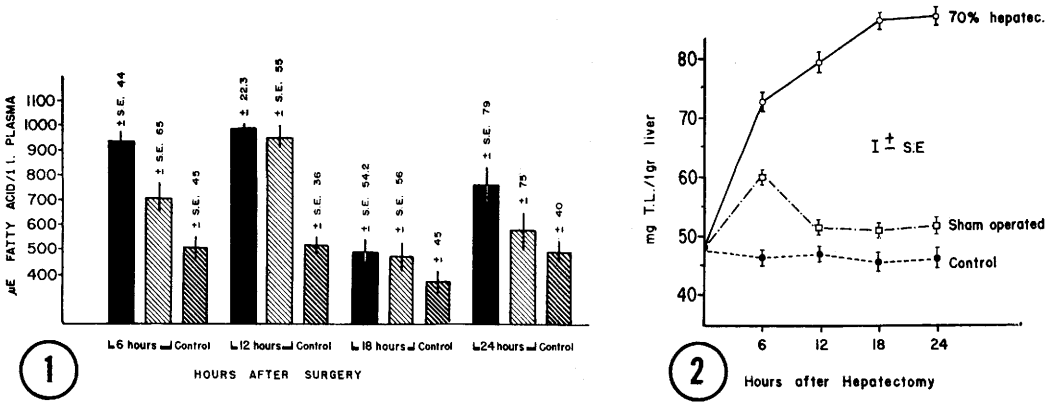

FIG. 1. Free fatty acids in plasma of rats during 24-hour period after partial hepatectomy. Values are expressed as micro-equivalents of fatty acids ± standard errors (S.E.) per liter of plasma, respectively, for the group 70% hepatectomized, solid area (5 rats); sham-operated, heavy lines (5 rats); and non-operated controls, light lines (4 rats).

FIG. 2. Total lipids per gram of liver during 24-hour period after partial hepatectomy. Results expressed as mg of total liver lipids per gram of wet weight liver.

were fasted for 24 hours after surgery.

The results presented in Table I indicate no difference between the corresponding fasted and fed groups.

The possible influence of either pituitary or suprarenal hormones, as well as that of catecholamines, on increased liberation of fatty acids from peripheral adipose tissue (8-16) and upon total lipid levels, as found 24 hours after 70% hepatectomy, were investigated. For this purpose the experimental groups of animals were divided into 4 groups: hypophysectomized, adrenalectomized, reserpine-treated and guanethidine-treated, respectively. Total lipid levels (mg/g of wet weight liver) found in the animals deprived of either pituitary or adrenal glands were 90 (±12.1)† and 93 (±6.7), respectively. In the animals submitted to treatment with either reserpine or guanethidine the results were 116 (±5.7) and 99 (±6.95), respectively.

These data indicate that the absence of either pituitary or adrenal hormones, as well as either the depletion of catecholamines or blocking of their liberation does prevent the post-hepatectomy fatty infiltration of the liver.

These experiments did not exclude the possibility that mobilization of F.F.A. occurred with different intensities in the sham-operated, 30% and 70% hepatectomized groups; hence additional experiments were carried out to investigate this aspect of the problem. In these experiments the levels of circulating F.F.A. were assayed in the blood at 6, 12, 18 and 24 hours, respectively, after partial hepatectomy.

In these experiments, the animals were divided into 3 groups: non-operated controls, sham-operated and 70% hepatectomized. Concomitant determination of total liver lipids was done in the remnant of the livers of all groups.

The results shown in Fig. 1 indicate no significant difference in the levels of F.F.A. found in the blood of the 70% hepatectomized, as compared to those found in the sham-operated group. On the other hand, a significantly higher level of F.F.A. was found in the operated groups, as compared to the non-operated controls, 6 and 12 hours, respectively, after partial hepatectomy.

These data confirm the hypothesis that the factor responsible for higher lipid accumulation in the 70% hepatectomized animals, lies within the liver itself and is not related to different degrees of fat mobilization from peripheral depots in the sham-operated and 30 or 70% hepatectomized animals.

The determination of total liver lipid levels in these animals showed an early and transient rise in the sham-operated group, but a

† Numbers within parentheses indicate standard errors of mean values.

progressive and marked rise in the 70% hepatectomized group (Fig. 2).

As the rise in circulating F.F.A. within the first 24 hours after surgery is not significantly different between the sham-operated and the 70% hepatectomized animals, and because the rise in total liver lipids in the sham-operated rats is significantly different only at 6 hours after surgery, as compared to the non-operated controls, the accumulation of lipids that is still present 24 hours after surgery in the 70% hepatectomized rats may be attributed most likely to influences within the liver that are initiated by the excision of such a large proportion of the parenchymatous tissue. Thus, the rise in liver fat per unit of weight found in the 70% hepatectomized rats seems to be directly related to the metabolic overload imposed by the circulating free fatty acids upon a liver significantly reduced in number of cells and therefore with relatively diminished over-all metabolic capacity.

Summary. A study of lipid levels in the liver of rats either 30% or 70% hepatectomized and in sham-operated animals was made 24 hours after surgery, as well as in non-operated controls. The results indicated that lipid infiltration of the remnant of the liver of the partially hepatectomized animals is dependent on the proportion of the liver removed from the animals and not on such additional factors as surgical stress, post-operative fasting, adrenalectomy or hypophysectomy. The treatment of the animals with either reserpine or guanethidine also did not influence the lipid levels, as indicated by those found 24 hours after partial hepatectomy. It was found that the levels of free fatty acids in the 70% hepatectomized rats and in the sham-operated animals were not significantly different during the first 24 hours after surgery.

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