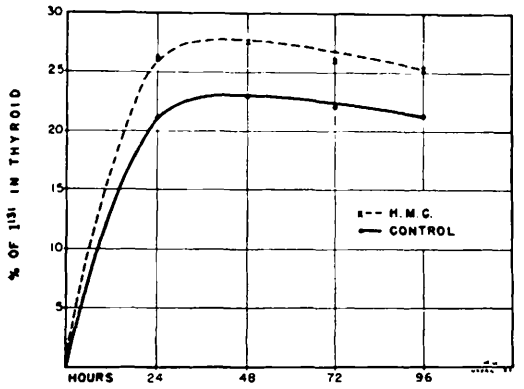

FIG. 1. Average thyroid uptakes on 19 patients before and after hesperidine methylchalcone (H.M.C.) administration using I^{131} as a tracer.

summarized in Table I show that the oral administration of one gram of H.M.C. significantly increases the thyroidal accumulation of I^{131}. This increase averaged between 20.7 and 26.1% at all observed time periods. H.M.C. was more effective in increasing thyroid uptake in some patients than in others. In this study the range was from 6.3% to 55% greater than pre-H.M.C. period when the uptakes for the four time periods were averaged. The shape of the composite uptake curves when H.M.C. was administered is similar to that obtained before the administration of H.M.C. (Fig. 1). Although it was not possible to obtain hourly or 24-hour urine samples on all patients, they were not significantly different when H.M.C. was administered.

Discussion. These data suggest that the bioflavone derivative, H.M.C., is capable of increasing the thyroidal accumulation of I^{131} in man. These results are consistent with those obtained in rats. In all of the subjects studied, an increase in thyroid uptake was observed. If this drug is used in conjunction with I^{131}, smaller doses might be required to obtain comparable results in thyroid therapy. Such possible usefulness should be evaluated.

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Participation of Adrenal Cortex in Alterations in Carbohydrate Metabolism Produced by Epinephrine.* (19986)

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The subcutaneous injection of epinephrine (0.02 mg per 100 g body weight) into fasted normal rats is followed in a period of 4 hours by a depletion of muscle glycogen and an accumulation of glycogen in the liver(1). Since similar injections of epinephrine also cause a release of adrenal cortical steroids by reason of their capacity to cause ACTH secretion(2), the question arises as to the possible participation of the adrenal steroids in the alterations in carbohydrate metabolism that follow epinephrine injection.

This has been tested by comparing the effects of epinephrine injection in fasted normal and adrenalectomized rats. In addition, since marked differences in the response of these animals was observed, the influence of adrenal cortical hormones in correcting this difference was also estimated.

Methods. Male Wistar rats weighing 180-280 g were used. All animals were kept in a constant temperature room and on a uniform and constant diet. All were fasted for 24 hours before the experiment. Adrenalectomized animals received 1% NaCl as drinking fluid after operation and were used 7-14 days later. Glycogen in liver and muscle was determined by the usual methods, and blood glucose and lactate on samples obtained from

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TABLE I.

	No. rats	Liver glycogen*	Muscle glycogen	Glucose in body fluids	Net change
Normal	6	5 ± 2	288 ± 10	30 ± 1	
" + epinephrine	6	48 ± 5	200 ± 19	54 ± 3	
Change		+43	—88	+24	— 21
Adrex.	6	2 ± 5	278 ± 6	22 ± 1	
" + epinephrine	8	8 ± 2	112 ± 11	50 ± 2	
Change		+6	—166	+28	—132
Adrex. + cortisone pellet	2	2	303	30	
" + " " + epinephrine	4	32 ± 5	111 ± 11	47 ± 2	
Change		+30	—192	+17	—145
Adrex. + A.C.E.	5	42 ± 6	286 ± 16	30 ± 2	
" + " + epinephrine	7	92 ± 4	187 ± 9	59 ± 3	
Change		+50	—99	+21	— 28

* All values expressed as mg/100 g body wt.

the tail veins. The carbohydrate levels are expressed in mg/100 g of body weight and for this purpose the muscles were assumed to be 50% of the body weight, and the glucose and lactate to be distributed in 50% of the body weight. All animals received either a subcutaneous injection of 0.02 mg/100 g of a freshly diluted solution of epinephrine (Adrin. Sharpe and Dohme) or a similar volume of normal saline. They were sacrificed 4 hours later under nembutal anesthesia.

Results. (Table I) In normal animals 4 hours after epinephrine injection the loss of muscle glycogen is almost balanced by the accumulation of glycogen in the liver and of glucose in the body fluids. On the other hand, similar injections into adrenalectomized rats caused practically no increase in liver glycogen although the fall of muscle glycogen was approximately twice that found in intact animals. Consequently, the net loss of carbohydrate was some sixfold greater. This was not accounted for by an excessive accumulation of either glucose or lactate in the body fluids since analysis indicated that at the end of the four hour period the levels of both these substances were the same in intact and adrenalectomized animals.

It would appear that in the absence of the adrenal cortical hormones a much larger proportion of the products released by the accelerated rate of glycogenolysis in muscle and liver are utilized by pathways other than those detectable by this technic. These might include an accelerated rate of oxidation, or an increased rate of fatty acid synthesis. Welt and Wilhelmi(3) have brought forward some evidence which indicates that the rate of fatty acid synthesis is increased in adrenalectomized rats.

In this regard the recent experiments of Kerppola(4) are of interest. This investigator has found that large doses of cortisone given to rabbits greatly reduce the phosphorylase activity of liver and muscle, leading in his view to an accumulation of glycogen in consequence of the inhibition of glycogenolysis. If this is correct then in the absence of cortical hormone there would presumably occur an increased rate of glycogenolysis which would be further enhanced by the known stimulation of phosphorylase activity by epinephrine(5).

Since it is known that epinephrine injections of this kind provoke a secretion of adrenal cortical hormones, the effect of maintenance and excess amounts of these steroids on the response of adrenalectomized rats to epinephrine was also studied. Table I indicates that while the previous implantation of cortisone pellets (10 mg) into adrenalectomized rats was followed by a more normal accumulation of liver glycogen, it did not prevent the excessive loss of muscle glycogen and in consequence there is a large deficit in the carbohydrate balance sheet following epinephrine injection. On the other hand, the injection of 1 cc of water extract of the adrenal cortex (Upjohn) every 2 hours for 8 hours before epinephrine injection and for every 2 hours during the period

of epinephrine action led not only to a normal accumulation of liver glycogen, but to a decreased net loss of muscle glycogen. As a result the overall carbohydrate balance sheet was of normal proportions. These results suggest that at least a part of the normal response of the carbohydrate metabolism of fasted rats to the injection of epinephrine is a consequence of the concomitant effect of this hormone in stimulating the release of ACTH from the anterior lobe of the pituitary.

Summary. 1. The subcutaneous injection of epinephrine (0.02 mg/100 g body weight) into fasted adrenalectomized rats is followed by a twofold greater loss of muscle glycogen than in intact rats, and by little or no increase in liver glycogen. Consequently, there is a sixfold greater disappearance of carbohydrate from the body that is not accounted for by the accumulation of glucose or lactic acid in the body fluids. 2. The injection of large quantities of adrenal cortical extract, prior to and during the period of epinephrine action, brings about a restoration of the carbohydrate balance to that found in intact rats.

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Experimental Porphyria. III. Hepatic Type Produced by Sedormid.* (19987)

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An experimental porphyria in rabbits treated with phenylhydrazine, lead, and light has been described in previous reports(1,2). This porphyria was shown to have many features characteristic of the rare erythropoietic (congenital or photosensitive) type of porphyria seen in humans(3). More recently, attempts have been made to find compounds which would produce an experimental porphyria similar to the human hepatic type(3). Ellinger and Riesser(4) described the occurrence of ether-insoluble (uro-type) porphyrins in the urine of patients with trional intoxication, and Fischer and Duesberg(5) later reported the finding of trace amounts of a similar porphyrin in the urine of rabbits treated with sulfonal. Conflicting, and generally negative results have been reported from other laboratories investigating these and similar substances in animals(6,7).

Duesberg(8) reported the presence of porphyria in a patient treated with large amounts of Sedormid (allylisopropylacetylcarbamid). It has now been found that this compound markedly increases the excretion of porphyrins and porphobilinogen in normal rabbits. These and other findings which demonstrate the hepatic nature of this new type of experimental porphyria, form the basis of the present report.

Methods. Rabbits of either sex weighing from 1500 to 3000 g were used, though best results were generally obtained in rabbits weighing less than 2 kg. Sedormid‡ was given orally at the rate of approximately 200 mg per kilo body weight per day in a single dose

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