Selkurt and Johnson(12) and Meyer(13), which occurs during obstructive elevation of pressure in the portal vein. An arteriolar constriction occurs which may lower intestinal capillary pressure despite the elevation in venous pressure. Intestinal blood flow rates fall on the average about 40 per cent (14) and the venules and veins dilate, indicating that the capillary to large vein pressure drop will necessarily be considerably reduced. The capillary pressure may actually be elevated more after endotoxin than during mechanical portal obstruction, thus allowing for the possibility of a mechanical hydrostatic pressure mechanism for accumulation of tissue fluid seen after endotoxin by Aust *et al.* (3). This may be particularly important during the later stages of endotoxin shock when the localized areas of venous constriction become more numerous and more severe and are associated with a marked submucosal arteriolar dilatation(10). Haddy(15) has pointed out that the arteriolar dilatation and venous constriction in the dog forelimb, which was produced by the intraarterial infusion of histamine, may elevate the capillary hydrostatic pressure, and that this mechanism can account for histamine edema.

Summary. 1) The tissue pressure in the intestinal submucosa of the dog is significantly increased during the portal hypertensive phase and during the later stages following administration of a 1 mg/kg dose of *E. coli* endotoxin. 2) The change in submucosal tissue pressure is less for an equal or greater rise in portal vein pressure due to obstructive elevation of this pressure than during the portal hypertensive period of endotoxin shock.

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Action of l-Leucine on Plasma Insulin Effect and Glucose Uptake of the Diaphragm and Adipose Tissue. (27141)

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The mechanism by which l-leucine produces hypoglycemia in children(1) and in patients with pancreatic islet cell tumors(2) is not quite clear. Cochrane *et al.*(3) have very recently found peripheral effects to which the hypoglycemic action could be attributed and Grumbach and Kaplan(4) and Johnson, Herring and Field(5) impute the hypoglycemia to stimulant action on the Langerhans islet cells. We have studied the action of l-leucine, after intravenous injection, on the plasma insulin effect and glucose uptake by the diaphragm and epididymal fat of the same animal, as well as the effect of leucine added *in vitro* on glucose uptake by both tissues.

Methods. Animals. Male rats from our colony, weighing 120-130 g, were used; females with the same characteristics to estimate the plasma insulin effect with the iso-

TABLE I.

		Mean	σ	t	P	No. of animals
A	l-leucine inj. rats	.283	.133	2.26986	$.02 < P < .05$	16
	controls	.146	.153			12
B	l-leucine inj. rats	.581	.133	2.34575	$P < .01$	20
	controls	.475	.132			20
C	l-leucine inj. rats	.322	.077	2.09524	$P < .02$	38
	controls	.278	.106			38

A = Plasma insulin activity 10 min. after inj. of l-leucine. There is a rise in the effect.
B = Glucose uptake of diaphragm 10 min. after inj. of l-leucine.
C = Glucose uptake of the epididymal fat 10 min. after inj. of l-leucine.

TABLE II.

		Mean	σ	t	P	No. of animals
D	l-leucine *in vitro* (20 γ/ml)	.483	.086	2.098	$.02 < P < .05$	12
	controls	.407	.087			12
E	l-leucine *in vitro* (20 γ/ml)	.440	.093	4.38056	$P < .01$	24
	controls	.305	.100			24
F	l-leucine *in vitro* (20 γ/ml)	.011	.004	2.55102	$.01 < P < .02$	13
	controls	.007	.004			13

D = Effect of l-leucine on glucose uptake of rat diaphragm.
E = Effect of l-leucine on glucose uptake of rat epididymal fat.
F = Effect of l-leucine on glycogen synthesis of rat epididymal fat.

lated diaphragm. The rats had free access to water but were kept without food in a noiseless dark room, at 20°C, 16-18 hours before experiment.

Procedure. Intravenous injection (tail vein) of l-leucine 11 mg/100 g weight of rat, dissolved in 0.2 ml of Krebs buffer (final pH 8.6). Blow on head before decapitation 10 minutes after the injection. Glucose uptake of the diaphragm determined by incubating quarters of diaphragm, one from each side, with a total approximate weight of 150 mg, in Warburg flasks containing 2 ml Krebs-Henseleit buffer and 3 mg/ml glucose. Temperature 37.5°C. Oscillations 80-100 per minute. Amplitude 2 cm gaseous air phase. Time 90 minutes. Glucose measured by the Somogyi-Nelson method. 200 mg samples were used to estimate glucose uptake of the epididymal fat; these were incubated in the same way as the diaphragm but for 5 hours. In the experiments where l-leucine was used *in vitro* the quantity added to the buffer was 20 μg/ml. The insulin effect was estimated the following day, keeping the plasma at 4°C overnight by the method described previously for the isolated diaphragm(6). All results are expressed in mg of glucose which has disappeared from the medium per 100 mg of wet diaphragm. The statistical calculation was made by Students method "t".*

Results and discussion. As can be seen in Table I, intravenous injection of l-leucine produces a rise in plasma insulin effect and an increase also in the glucose uptake by the diaphragm and epididymal fat. This action is somewhat similar to that obtained when a hyperglycemia is produced by intravenous injection of glucose which stimulates insulin secretion, according to demonstrations of Candela and Candela(7), Whitney and Young(8) and others. The results, however, are not identical since glucose injection causes a decrease in glucose uptake of the epididymal fat(9). Table II shows the effect of l-leucine *in vitro* on the glucose uptake of the diaphragm and epididymal fat. l-Leucine causes an increase of glucose uptake in these tissues.

In view of these results we conclude that

* We are grateful to M. R-Candela for study of these data.

l-leucine has an effect very similar to that of the stimuli producing insulin secretion but that it also has a peripheral effect. It cannot be excluded that the rise in plasma insulin effect observed is due to an action of leucine on insulin or on the antagonists, and not on its secretion.

Summary. 1. Intravenous injection of l-leucine produces an increase in insulin activity of the plasma and in glucose uptake by the diaphragm and adipose tissue. This effect is attributed to stimulation of the islets and to greater insulin secretion, or to action on this hormone. 2. l-Leucine added to the incubation buffer increases glucose uptake by the diaphragm and adipose tissue.

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Clarification of the Diverse Actions of Iodide on Antithyroid Effect of Sulfonamides and Thionamides.* (27142)

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Since the early reports of MacKenzie(1,2) that the goitrogenic action of the sulfonamides was enhanced by addition of iodide, whereas iodide decreased the goitrogenicity of the thionamides, little has been done to explore this phenomenon further. The thionamides have been studied extensively and considerable knowledge of their effect on thyroidal biosynthetic processes has been acquired. Recent investigations have revealed that increasing doses of propylthiouracil (PTU) inhibit first the formation of iodothyronines (T_3 + T_4), then diiodotyrosine (DIT), and eventually monoiodotyrosine (MIT)(3,4,5). This last step is much more resistant and even relatively huge doses of PTU fail to block completely all MIT formation(5). However, a similar detailed study of the effect of sulfonamides on the thyroid gland has not been made.

The reports that iodide had a converse effect on the goitrogenic action of the sulfonamides and thionamides suggested to us that iodide administration might clarify differences in the mode of action of the two groups. We selected sulfadiazine (SD) and PTU as representatives of each.

Methods and materials. Male Sprague-Dawley rats weighing 100 g were fed a low iodine diet (LID) (≅ 70 μg I/kg) for 14 days containing SD and PTU in the specified amounts. Each group contained 3 rats. Half the animals were injected daily with 1 mg KI intraperitoneally during the course of the experiment. On the 14th day, 100 μC of I^{131} were given intraperitoneally to all animals receiving KI and to those receiving the largest doses of SD and PTU. The others received 20 μC. The animals were sacrificed 24 hours later and weight and I^{131} content of the thyroids determined. The glands from each group were then pooled and homogenized in 4 ml pH 8.6 phosphate buffer containing 1% pancreatin (Viokase 4×) and 1 mg thiouracil. Two drops of toluene were added to prevent putrefaction, and the thyroids were incubated 24 hours at 37°. Aliquots containing 0.025 μC were subjected to

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