port of potassium by human erythrocytes as do the cardiac glycosides. At low concentrations both groups of compounds slightly increase K transfer from plasma to cells; higher concentrations inhibit the process. These effects probably reflect activation and inhibition of a membrane ATPase which others have implicated in the active movements of cations in erythrocytes. Erythrophleum alkaloids and cardiac glycosides also share similar effects on mammalian hearts. In view of the structural differences between the 2 classes of compounds, and their biological similarities in 2 kinds of tissue, it is suggested that previous views on minimal structural requirements for digitalis-like activity in hearts and erythrocytes be revised.

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Lesser Effects of Endotoxin on Intestinal Weight in Young *versus* Older Dogs.* (27534)

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Response to intravenous administration of *E. coli* endotoxin in adult dogs has been characterized, in part, by an initial drop in systemic pressure, and an increase in portal venous pressure and intestinal weight(1). Weil and Spink(2) observed that shock could not be uniformly produced in immature animals. Zahl *et al.*(3) suggested that younger mice were more resistant to a lethal dose of endotoxin. Young rabbits were capable of withstanding a 50 times greater dose of endotoxin than adults as judged by 18 hours survival (4). In rabbits the vascular effects of endotoxin have been investigated in reference to the Schwartzman reaction(5). Others(6) have found an increased susceptibility of rabbits to the Schwartzman phenomenon with age.

Alterations in intestinal weight in adult dogs during the first 10 minutes following endotoxin administration have been compared with similar changes following mechanical increase in portal pressure for 10 minutes(7). The purpose of this investigation is to compare intestinal weight responses of mature and immature dogs during the period of portal hypertension and later stages of endotoxin shock.

Methods. Experiments were preformed on 5 adult and 6 young dogs. The teeth were used as criteria for establishing age. All

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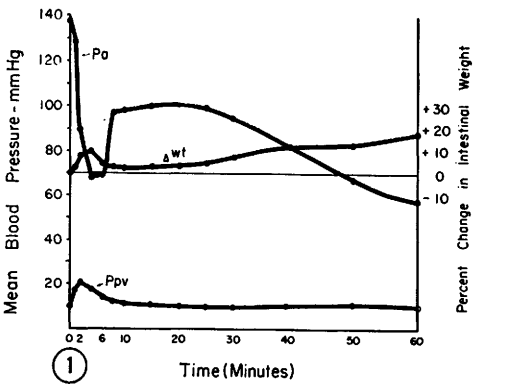

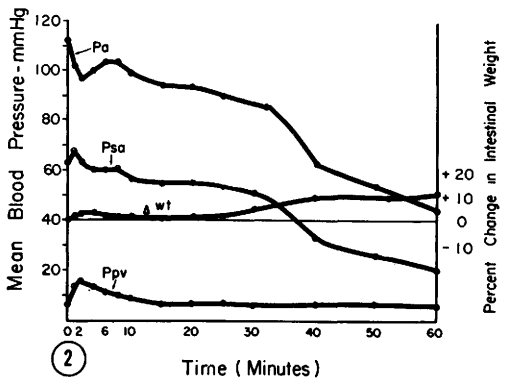

FIG. 1. Percentage changes in intestinal wt ($\triangle$wt) and absolute pressure changes in superior mesenteric artery (P_a) and portal vein (P_{pv}) in mature dogs at various times after administration of *E. coli* endotoxin. Avg data from 5 dogs.

FIG. 2. Percentage changes in intestinal wt ($\triangle$wt) and absolute pressure changes in superior mesenteric artery (P_a), mesenteric small artery (P_{sa}), and portal vein (P_{pv}) in immature dogs at various times after administration of *E. coli* endotoxin. Avg data from 6 dogs.

young dogs had their deciduous teeth. Older dogs had permanent teeth. The animals were fasted for 18-24 hours and anesthetized by intravenous injection of sodium pentobarbital. Blood pressures in the superior mesenteric artery (P_a) and portal vein (P_{pv}) were measured with P23AA Statham strain gauges by cannulating a branch of these vessels. Pressures were recorded with a meaning circuit on a Sanborn Recorder. In addition, the technic of Haddy and others(8) for determining pressures in small vessels was employed to measure pressures in mesenteric small arteries (P_{sa}) of the young dogs. The method used to estimate *in vivo* changes in weight of a loop of intestine has been described by Stish *et al.* (9). The absolute weight of the loop studied was determined at autopsy.

In both experimental groups, blood pressures and changes in weight of the intestinal loop were determined at various intervals (1, 2, 4, 6, 8, 10, 15, 20, 25, 30, 40, 50, and 60 minutes) following intravenous administration of 1 mg/kg of Difco (batch 0127:BB) *E. coli* endotoxin *via* the external jugular vein.

Results. Blood pressures and percentage changes in weight of an intestinal loop at the various intervals of time are presented in Fig. 1 (adult) and 2 (young). The maximum change in weight during the portal hypertensive phase occurred on the average at 4 minutes in both groups. However, the change is much greater in mature dogs (9.9%) than in young animals (2.9%). The difference between the two mean values was significant as determined by the *t*-test (p-value = 0.002). At 60 minutes, arterial pressures in both groups reached shock levels. Intestinal weight increased an average of 17.8% in adults and 11.1% in young dogs. These values were not significantly different (p-value $>$ 0.05).

The integrated time mean of the percentage change in intestinal weight, the integrated time mean of the change in portal pressure and their ratio for each dog for the first 10 minutes following endotoxin injection are presented in Table Ia (adult) and Ib (young). The average of the integrated time mean for the change in intestinal weight during part or all of the portal hypertensive period was greater in the adult dogs (p-value = 0.014). The integrated time mean elevation in portal pressure was not significantly different between the 2 groups. The ratio of these 2 variables was significantly greater in the adult dogs (p-value = 0.036).

Discussion. The earlier, and significantly greater, increase in intestinal weight in the adult group indicates that the initial vascular responses to endotoxin in the 2 groups may be different. Whether age was the only difference between the 2 groups is a question that cannot be answered unequivocally because all of the dogs were mongrels and were studied shortly after purchase. However there is no known difference in prior history of the 2 groups of animals, and the great likelihood is

TABLE I.

(a) Adult				(b) Young			
Exp.	A	B	A/B	Exp.	A	B	A/B
1	1.3	2.7	.48	1	1.6	6.7	.24
2	7.0	3.4	2.06	2	1.2	3.3	.36
3	6.7	9.7	.69	3	2.9	8.0	.36
4	5.2	8.2	.64	4	3.0	4.8	.63
5	5.4	3.8	1.42	5	.7	4.7	.15
				6	2.4	5.3	.45
Mean ± S.E.	5.1 ± 1.0	5.6 ± 1.5	1.06 ±.30		2.0 ±.4	5.5 ±.7	.37 ±.07

A = Integrated time mean of percentage change in intestinal weight for first 10 min. following endotoxin.

B = Integrated time mean of change in portal venous pressure in mm Hg for same period.

that factors related to age are responsible for the differences seen.

In 5 of the 6 young dogs the pressure in the mesenteric small artery (P_{sa}) was elevated at the end of the first minute. In the remaining case, P_{sa} did not change. In 2 other young dogs in which changes in intestinal weight were not recorded, this pressure (P_{sa}) was also elevated. Thus, 7 out of 8 young dogs showed an increase in P_{sa} at the end of the first minute following endotoxin, whereas in another study(10) on adult dogs P_{sa} decreased in 11 out of 13 cases.

Pressure in the mesenteric small arteries increased following the mechanical elevation of the portal venous pressure(10). Johnson and Selkurt(11) and Meyer(10) noted an increase in intestinal vascular resistance following mechanical increase in the venous pressure. Thus, the administration of endotoxin in young dogs may increase vascular resistance which prevents the initial arterial hypotension. The average change in intestinal weight in young dogs during the first 10 minutes following endotoxin is not significantly different than the average change previously observed in adult dogs(3) or young dogs (unpublished observations) during a 10-minute period of mechanical increase of the venous pressure. However, the average rise in intestinal weight in the adult is significantly different from that observed following mechanical elevation of the portal pressure(3).

In young dogs, increased arteriolar resistance may explain the decreased amount of intestinal pooling or loss of fluids immediately following endotoxin injection. In adult dogs, the increased weight is associated with increased loss of albumin to the intestinal tissue as observed by Aust and others(12) and has been attributed to a decrease in the segmental resistance between the intestinal small artery and venule and a substantial rise in the resistance in the intestinal small vein segments (13).

Histamine, or a histamine-like substance, has been implicated as one of the chemical mediators of endotoxin shock in adult dogs (2, 14). Feldberg(15) has indicated that the histamine content of certain tissues may increase with age in some species; however dogs were not investigated. Young dogs, possibly with a low histamine level in the intestinal tissues, may tend, after endotoxin administration, to respond for a short period like animals in which the venous pressure is mechanically elevated.

Summary. In dogs, susceptibility of the intestine to pooling of blood and tissue fluid during the portal hypertensive phase of endotoxin shock is diminished in younger animals. Pressure changes in large and small vessels of the mesentery and changes in intestinal weight per increment in portal pressure of young dogs given endotoxin were similar to the changes previously observed during mechanical elevation of the portal pressure suggesting analogous mechanisms are involved. Thus, during the early period, lesser effects of endotoxin (1 mg/kg) upon the amount of pooling in intestines of immature dogs may be due to an increase in arteriolar resistance, in contrast to the circumstances in older animals in which a decline in arteriolar resistance appears to occur after endotoxin administration.

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Effects of Added Casein on Goitrogenic Action of Different Dietary Levels of Soybeans.* (27535)

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In at least 14 papers, from 1933 onward, it has been reported that diets containing soybeans (*Glycine max*) or soybean products cause enlargement of the thyroid gland in the rat, chick, guinea pig, rabbit or human. Greer (1,2) has reviewed many of these findings, and has suggested that soybean diets may be goitrogenic simply because they have a low iodine content. Some of the soybean diets reported as goitrogenic contained only a small proportion of beans. Hence in these studies it seems possible that the goitrogenic effect of the beans was not manifested, with the result that the thyroid enlargement seen could have been due solely to iodine deficiency. To shed light on these questions, one of the experiments in the present study was designed to measure and compare the goitrogenic effects of low and high dietary levels of soybeans.

An observation on which there has been unanimity is that heating of soybeans reduces or obliterates their goitrogenic property(3). Moreover, the best studied of the known toxic factors of the soybean, the trypsin inhibitor, is similarly reported to be heat labile(4). This similarity raises a question as to whether the two effects might have the same basis, and has suggested the remaining experiments reported here. These experiments were designed to determine whether protein supplementation of raw soybeans, as is known to reduce or eliminate the growth-retarding effect of the soybean trypsin inhibitor(4), has an effect on the goitrogenic property of soybeans.

Materials and methods. The soybeans used were obtained from an oil processing plant (courtesy of Dr. H. W. Howard, The Borden Co.). The beans, of a small, yellow, black hilum variety, were ground in the laboratory, with care to avoid frictional heating. Soybean meal made from the same lot of beans was also obtained. This meal is the residue from fat extraction of soybeans, after which the meal is "toasted" and ground.

The diets designated 35 and 35CAS (Table I) contained 35% by weight of raw soybeans; those designated 60 and 60CAS contained 60% of raw soybeans. To equate the fat and

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