emulsified, dried and tested for radioactivity content with a Geiger Tube Detector. (2) Results showed only a narrow range of radioactivity for each organ specimen calculated as a product of the average blood radioactivity in the same group of mice (amputated at the same time). (3) The calculated and tabulated data show that a significant proportion of $CrP^{32}O_4$ was translocated into the liver from the tail; for Y^{90} the initial storage in the tail was very high, but some translocation occurred, presumably by excretion. (4) The pattern of Y^{90} and $CrP^{32}O_4$ distribution in the body after injection into the tail was comparable to delayed results of intravenous injection; this resemblance was interpreted by high vascularization of the tail. (5) It was concluded that the method of serial tail amputation may be useful for outlining the dynamics of isotopes spread in bodies of experimental animals.

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Effects of Ethyl Alcohol on Cardiac Output and Its Distribution in the Rat.* (24122)

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Ethyl alcohol is generally considered to increase peripheral blood flow. Particular interest has been directed to its possible effects as a coronary and cerebral vasodilator. The present studies were designed to determine whether alcohol influences the cardiac output and its distribution in the albino rat.

Methods employed in determination of cardiac output and regional uptake of indicators have been described(1,2). The conditions in which the fractional distribution of an indicator and the fractional distribution of the cardiac output correspond with each other have also been indicated(1,2). The cardiac output and the uptake fraction of all organs other than the brain were measured with Rb^{86}. Iodoantipyrine (I^{131}) was used in the brain studies. Female rats of Sprague-Dawley strain were used unless otherwise noted. Animals weighed 200-250 g after an 18 hour fast during which they were allowed free access to water. Each animal received 5 ml 20% alcohol by intraperitoneal injection. This amount was sufficient to produce light anesthesia. Five to 10 minutes after administration of the alcohol, either $Rb^{86}Cl$ or iodoantipyrine (I^{131}) was given in 0.4 ml by injection into an exposed femoral vein. Determination of cardiac output was made with Rb^{86} in animals in which the carotid artery had been catheterized with a short length of polyethylene tubing. Blood samples were collected at 0.67 second intervals, using a sample collector described elsewhere(3), and the arterial concentration curve of indicator constructed. Cardiac output was calculated as described(1). Other animals were employed for determination of Rb^{86} or iodoantipyrine (I^{131}) uptake by the organs at 15 or 30 seconds after administration. At these times, all organs other than brain have the same extraction ratio for Rb^{86} as the whole body; the fraction of Rb^{86} appearing in an organ, therefore, describes the fraction of cardiac output which perfuses it. Cerebral blood flow, which cannot be meas-

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TABLE I. Effect of Alcohol on Fractional Distribution of Iodoantipyrine (Brain) and Rb^{86} (Other Organs) at 15-30 Sec. after Injection in Rats.

	Pentobarbital			Alcohol		
	# rats	Avg	S.D.	# rats	Avg	S.D.
Heart	8	2.9	.5	20	3.8	.7 *
Lungs	12	3.7	.7	20	3.9	.9 *
Kidneys	8	18.7	5.5	20	12.7	3.0 *
Liver	12	7.6	1.0	16	7.4	1.6
Gut	12	19.3	4.3	16	17.4	3.6
Skin	12	6.4	.9	16	5.7	1.1
Spleen	12	1.3	.5	20	.7	.3
Brain†	14	.40	.10	16	.76	.17*

* Significant at 1% confidence level.
† Values converted to ml/g/min.

ured with Rb^{86}, was determined with iodoantipyrine (I^{131}) for which the brain and whole body have the same extraction ratio during the first 30 seconds after injection. Control animals were anesthetized with sodium pentobarbital 40 mg/kg unless otherwise noted.

Results. Cardiac output in alcohol treated rat. The average cardiac output in 5 rats receiving alcohol was 217 ml/kg/min (range: 180-243). The value did not differ appreciably from that found in 40 control animals of 200-210 g (225 ml/kg/min).

Rb^{86} uptake by organs of alcohol treated rats. The results in 32 alcohol treated rats are presented in Table I. Three organs, other than brain, show significant differences from values in normal controls. The coronary uptake fraction rose from 2.9 $\pm$ 0.5 (S.D.) in normals to 3.8 $\pm$ 0.7 in alcohol treated animals. Splenic uptake fell from 1.3 $\pm$ .5% to .7 $\pm$ .3 (S.D.) % of the injected dose in alcohol treated animals. The renal fraction fell after alcohol treatment. In normal animals the renal fraction was 18.7 $\pm$ 5.5 (S.D.) %; after alcohol, the value was 12.7 $\pm$ 3.0% of the injected dose.

Cerebral blood flow in alcohol treated rats and mice. Alcohol elevated calculated cerebral blood flow from 0.40 $\pm$ .10 ml/g/min to 0.76 $\pm$ .17 ml/g/min in rats. Flow values were calculated by multiplying body weight in kg by the average cardiac output/kg in each animal; this value was multiplied by fractional uptake of label by the brain in each animal and divided by brain weight in grams. Control values are based on rats anesthetized with sodium pentobarbital. Since the effect observed might have been due to a diminution from the normal, due to pentobarbital anesthesia rather than an increase from the normal due to alcohol, an attempt was made to administer the label by tail vein in unanesthetized animals. Because of the difficulty of making a successful venipuncture in the unanesthetized rat, a comparison of untreated, pentobarbitalized, and alcohol treated Albino Swiss mice was made. Anesthesia was induced with 1 mg of pentobarbital sodium given intraperitoneally or with 1 ml of 20% alcohol by the same route. Unanesthetized animals were loosely restrained in a 20 mm glass tube. Indicator injections of 0.2 ml were made into a tail vein. The animals were killed 10-15 seconds after injection of indicator.

The fractional uptake of iodoantipyrine by the brain in 4 conscious mice averaged 2.8% of the injected dose (range 2.1-3.6%). Three animals anesthetized with pentobarbital showed a cerebral uptake of label averaging 1.9% of injected dose (range 1.8-2.1%). Three animals which received alcohol had an average cerebral uptake of indicator of 4.2% of the injected dose (range 3.5-4.6%).

Discussion. The present experiments show that ethyl alcohol in the doses used is without effect on the cardiac output of the rat. Uptake of Rb^{86} by the heart is increased; renal and splenic uptake of this isotope is reduced. Alcohol increases cerebral uptake of iodoantipyrine. Since, in the experimental circumstances used, organ uptake parallels flow distribution, these findings suggest that alcohol increases blood flow to heart and brain while reducing blood flow to kidneys and spleen.

Increased coronary flow is in accord with clinical observation(4) that ethyl alcohol may alleviate anginal pain. Increase in coronary circulation has been more directly demonstrated after either intravenous or intracoronary injection of alcohol in the dog(5).

The reduction in the fractional uptake of Rb^{86} by the kidney was large. The failure of Smythe *et al.*(6) to detect renal blood flow changes in the dog may have been due to a species difference or to administration of pen-

tobarbital before the alcohol. The effect of alcohol on renal plasma flow in the absence of pentobarbital does not appear to have been investigated by bladder clearance methods.

The failure of alcohol to influence splanchnic uptake of Rb^{86} is in accordance with previous findings that alcohol does not influence splanchnic blood flow in the dog(6). The reported increases in splanchnic blood flow in man(7) may have been due to a species difference or to use of smaller doses in human subjects. The present studies show that in the rat distribution of splanchnic blood flow between hepatic artery and portal inflow other than the spleen is not altered by alcohol. The apparent effect of alcohol on the spleen may have resulted from alterations in the spleen due to pentobarbital(8) rather than from a true reduction in splenic blood flow due to alcohol.

The failure of alcohol to affect uptake of Rb^{86} by the skin appears at first to be inconsistent with the observations of increased skin blood flow by Abramson *et al.*(9) in man after alcohol. It should, however, be noted that these authors found that though the blood flow to the hand was increased by alcohol, the blood flow to arm and leg was unaffected, suggesting that the vasodilatation produced by alcohol may be restricted to a small portion of the skin.

The most striking changes produced by ethyl alcohol are on cerebral uptake of iodoantipyrine. Increased cerebral blood flow has been reported in stuporous subjects with blood alcohol levels of 320 mg %(10). Actual intake of alcohol by the subjects was unknown; neither was their nutritional status ascertained; smaller doses of alcohol given by vein in more normal subjects appear to be without effect on cerebral blood flow(10,11). From findings in the unanesthetized mice, it appears that alcohol increases cerebral blood flow above the normal value; although the value with pentobarbital is lower than that in the conscious mouse, the difference may be attributable to a response of the conscious animal to the procedure of handling, restraint, and injection rather than to any specific effect of the pentobarbital. In either case, alcohol increases cerebral flow fraction well above the conscious level or that observed in pentobarbital anesthesia.

Summary and conclusions. (1) Ethyl alcohol does not influence cardiac output of the rat in doses of 5 ml of 20% by volume solution in 200-250 g rats. (2) Blood flow values to the major organs calculated from the fractional uptake of Rb^{86} or iodoantipyrine (I^{131}) show the following: cutaneous blood flow (considering the skin as a whole) hepatic arterial inflow, portal flow other than splenic, and bronchial blood flow are unaffected by alcohol; coronary blood flow is increased 31%; renal blood flow is reduced 32%; cerebral blood flow is 90% greater in the alcohol treated than in the pentobarbitalized animal.

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