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Effect of Ethyl Alcohol upon Splanchnic Hemodynamics. (27772)

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Various investigators have studied the effect of ethyl alcohol infusion upon hepatic circulation(1,2,3) with conflicting results. Some investigators have reported increases, others no change in hepatic blood flow. This study was undertaken to determine the effect of slow intravenous infusion of ethanol on estimated splanchnic blood flow and cardiac output in an attempt to define more clearly the parameters by which ethyl alcohol alters blood flow through the splanchnic vascular bed.

Methods. Adult mongrel dogs (15-20 kg) were anesthetized with sodium pentobarbital (30 mg/kg body wt). Under fluoroscopic guidance a catheter was placed in a hepatic vein. A second catheter was placed in the pulmonary artery to obtain mixed venous blood. A branch of the femoral artery was cannulated for recording of pressure and an infusion cannula was placed in the saphenous vein. Heparin was given to all animals (5 mg/kg body wt) during catheterization. Hepatic vein and femoral artery pressures were measured with Statham strain gauges, appropriate amplifying and recording equipment being used simultaneously and continuously throughout the experiment. Total oxygen consumption was determined from aliquots of expired air, collected by either a Tissot or Benedict-Roth spirometer. Respiratory gas samples were analyzed for O_2 and for CO_2 where possible by a Beckman oxygen and a Liston-Becker carbon dioxide analyzer. All blood samples were analyzed for oxygen and carbon dioxide content by a modification of the Van Slyke and Neill method(4). Hematocrit values were obtained by the Wintrobe tube technic. Hemoglobins were determined by the cyanemethemoglobin method.

Hepatic blood flow was measured by means of the bromsulphalein method(5). At 10-minute intervals 3 sets of samples were drawn for bromsulphalein (BSP) analyses and determinations of control splanchnic blood flow. Following the control period a total of 500 mg of 95% alcohol/kg body weight diluted with BSP was infused over a 60-minute period. During infusion samples were drawn at 15-minute intervals for BSP and alcohol analyses.

Alcohol concentrations were determined by a modification of the method of Westerfeld *et al.*(6) and Fleming and Stotz(7) on samples obtained from the femoral artery and hepatic vein.

The amount of alcohol metabolized per minute by the liver was calculated by the formula: (Art. alcohol-Hep. vein alcohol conc.) $\times$ EHBF (ml/min). Cardiac output was calculated by the direct Fick principle.

Splanchnic vascular and total peripheral re-

sistances were calculated by the relationships:

$$\frac{\text{Mean arterial pressure (mm Hg)} - \text{Mean hepatic pressure (mm Hg)}}{\text{EHBF (ml/min)}}$$

$$\frac{\text{Mean arterial pressure (mm Hg)}}{\text{Cardiac output (cc/sec)}}$$

The data were analyzed on an unpaired basis. A statistically significant difference was accepted at the 5% level.

Results. Upon completion of the 60-minute infusion of alcohol (500 mg/kg) arterial blood concentration was 84.6 mg %. The increase in alcohol concentration of arterial blood followed a linear relationship, $y = 1.08\times + 28.06$ (Fig. 1). Concurrent with increasing concentration of arterial alcohol there was a decreasing extraction of alcohol and BSP by the liver. Approximately 74% of the total amount of alcohol administered was metabolized.

Following infusion the arterial alcohol concentration decreased linearly, $y = -0.44\times + 53.25$ (Fig. 2), and an inverse correlation was observed between amount of alcohol extracted by the liver and concentration in the arterial blood.

The splanchnic blood flow did not change significantly during or following alcohol infusion (Table I). Extraction of BSP was decreased significantly for one hour after infusion.

There was little or no change in hepatic or systemic blood pressure during infusion of alcohol. However, after infusion the systemic pressure decreased significantly from control values. Hepatic pressures remained unchanged during the post-infusion period. No difference was noted in heart rate until after 60 minutes of alcohol infusion. The cardiac output did not change appreciably although it tended to decrease during the experiment.

Throughout infusion, CO_2 production exhibited a significant elevation, with subsequent increase in minute volume during the post-infusion period (Table I). The blood CO_2 content measured in arterial (47.2 vol % ± 1.3 vol %) and hepatic (49.8 vol % ± 1.1 vol %) blood samples, showed a significant decrease from the control during (39.2 ± 1.6 vol %) (44.2 ± 1.6 vol %) and after (37.5 ± 1.6 vol %) (41.3 ± 1.2 vol %), alcohol infusion. Arterial and venous blood oxygen remained relatively constant, as did total O_2 consumption throughout the study.

Discussion. Hepatic blood flow decreased slightly with gradual elevation of blood ethyl alcohol concentration to 84.6 mg %. Smythe *et al.*(1) reported that following 25 mg of alcohol by gavage, no change in hepatic blood flow occurred in anesthetized dogs, although Mendeloff(3) observed that in humans hepatic blood flow increased 45% over the control level with arterial concentrations of 10-65 mg % following a 50-80-minute infusion of a 5% alcohol solution. Mendeloff(3) varied the rate and total time of infusion. These

TABLE I. Summary of Data for Hepatic and Metabolic Functions Before, During, and Following Ethyl Alcohol Infusion.

	Control			During infusion 45 min			Post-infusion 20 min			
	N	Mean	S.E.	N	Mean	S.E.	N	Mean	S.E.	
Hepatic blood flow, ml/min	10	702.0	56.8	10	614.0	48.2	9	643.0	75.7	
% extraction of BSP	10	39.6	2.7	10	32.8	2.9	9	25.6	3.2	*
Splanchnic O_2 consumption, ml/min	10	38.0	6.8	10	45.6	6.4	9	47.1	6.0	
Heart rate/min	12	155.0	9.5	11	181.0	10.3	10	181.0	7.2	*
Mean hep. vein press., mm Hg	10	4.4	1.0	9	4.1	.8	9	3.5	.8	
Cardiac output, l/min	12	2.52	.39	11	2.03	.32	10	1.63	.28	
Mean arterial press., mm Hg	12	131.0	8.0	11	119.0	8.0	10	99.0	10.9	*
Vent. vol, l/min	10	3.84	.52	8	5.72	.85	8	6.83	.85	*
Total O_2 consumed, ml/min (STP)	12	86.0	13.2	11	91.0	31.5	10	86.0	12.0	
Total CO_2 produced, ml/min	9	72.0	5.6	8	89.0	4.7*	8	89.0	5.0	*
Heat production,† cal/M^2/hr	9	28.1	1.8	8	32.1	1.4*	8	30.4	2.7	

N = No. of animals. S.E. = Stand. error of mean.

* Unpaired—5% significance level. † Calculated only when R.Q. was available.

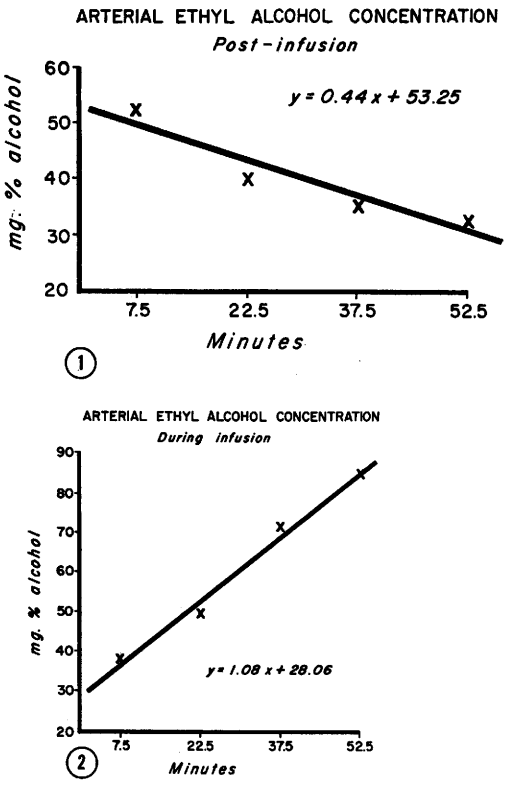

FIG. 1 and 2

variations may be responsible for the divergence in results. The rate and total time of infusion were maintained constant in the present study, which resulted in a similar progressive increase in blood alcohol concentration (Fig. 1, 2) in all animals.

The lowered hepatic blood flow was probably not due to decreased cardiac output, since the hepatic vascular resistance was significantly decreased. The fraction of the cardiac output going to the liver actually increased during infusion to 30.2% from a control of 27.9% and to a post-infusion value of 39.5%. Thus, some vasodilation within the splanchnic vascular bed must have taken place.

The ability of the liver to remove BSP was reported to be impaired in dogs(1) and in humans(3,8). In the present study the extraction of BSP decreased, particularly during the post-infusion period (Table I). This may have resulted from a direct depression of liver cells, or from an accumulation of metabolic products within the cells.

The increase in respiratory quotient was anticipated with the metabolism of alcohol. The ventilatory volume was raised in response to the greatly elevated levels of blood CO_2 during and after infusion. Total body heat production increased significantly during the infusion of alcohol, but dropped during the post-infusion period. This phenomenon was possibly related to the predominance of alcohol metabolism by the liver, since the fraction of O_2 consumed by the liver increased in both periods. The greatest amount of alcohol metabolism is known to take place within the liver(8). However, Larsen(8) has shown that a small and constant amount of ethyl alcohol also is metabolized extra-hepatically even over a large range of blood concentrations.

An inverse relationship existed between the alcohol metabolism and the arterial alcohol concentration. This is the converse of what has been found by Larsen(8) in human subjects. Possibly man has a larger capacity for metabolism of alcohol than the dog. Since extraction of BSP and metabolism of alcohol are both decreased, a depression of liver cells is suggested.

Summary. Hepatic blood flow was measured in adult mongrel dogs by the bromsulphalein method before, during and following constant infusion of 500 mg/kg ethyl alcohol. The blood alcohol concentration increased linearly to a maximum of 84.6 mg % and decreased linearly during the post-infusion period. An insignificant decrease in alcohol metabolism was observed with elevated blood ethanol levels. Extraction of BSP was decreased by alcohol administration. The respiratory quotient increased in response to elevated carbon dioxide production. Total body heat production increased during the infusion period. Ethyl alcohol did not alter hepatic blood flow significantly, but metabolic studies indicated hepatic oxidative depression.

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Differences Between the Normal Serum Protein Patterns of American Indian, Negro and Caucasian Subjects. (27773)

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Several investigators using salt fractionation or electrophoretic methods have reported on the differences observed between the normal serum protein fractions of Negroes as compared to Caucasians(1,2,3,4,5). They found that the albumin fraction was lower and the gamma globulin fraction higher in Negro subjects as compared to Caucasian subjects. The purpose of the present investigation was to compare the normal serum protein patterns of American Indian subjects with those of Negro and Caucasian subjects.

Materials and methods. The Indian subjects were high school students from 3 Indian Agency Schools located in Oklahoma and all were full-blooded Indians. The majority was Navajo, but other tribes were also represented. They live at the schools during the school term and return to their homes for the summer. Most of them reside in New Mexico and Arizona. The Negro subjects consisted of food handlers, students, and laboratory technicians, residing in Oklahoma City. The Caucasian subjects were recruits for the National Guard and reside in Oklahoma City. The subjects of all three groups were young males who appeared to be in good health.

Blood was collected by venipuncture from 45 subjects of each racial group (total 135 subjects). The serum was separated from the clotted blood and stored in the deep freeze at −20°C until used. Paper electrophoresis was carried out on the Spinco model RB apparatus following the procedure outlined in the Spinco Instruction Manual(6). Serum samples (0.006 ml) were placed on Schleicher and Schuell 2043-A mgl. paper strips which had been saturated with 0.075 ionic strength veronal buffer (pH 8.6). A current of 2.5 milliamps per cell was applied for 18 hours. The strips were stained with 0.1% bromphenol blue and scanned in a Spinco Analytrol B. The serum protein fractions are expressed as mean percentages. The data were subjected to an analysis of covariance using the method of Snedecor(7) to test for the effect of age. Duncan's(8) multiple range test was used to test for significant differences between the groups.

Results. The serum protein fractions, as determined by paper electrophoresis, are presented in Table I. There was no significant difference ($p>0.1$) between Indian and Negro groups in relation to mean percentages of serum albumin, beta globulin and gamma globulin fractions; however, these fractions were significantly different (albumin, higher; beta globulin and gamma globulin, lower) in the Caucasian group. The percentages of alpha 1 and alpha 2 globulins were similar ($p>0.1$) in the Negro and Caucasian groups, but significantly different in the Indian group. The percentage of alpha 1 fraction was higher and the alpha 2 fraction lower in the Indian group as compared to the Negro and Caucasian groups. The only significant difference between the serum protein patterns of the

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