Changes in pulmonary hemodynamics and lung function associated with an acute intravenous dose of ethanol

by

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LIST OF ABBREVIATIONS

a	arterial
a-c/u	alpha-chloralose and urethane
bar	barometric
BE	base excess
BEC	blood ethanol concentration
C	concentration
C_L	lung compliance
cm	centimeter
COLD	chronic obstructive lung disease
DAP	diastolic arterial pressure
dL	deciliter
e	mixed expired
es	esophageal
et	end tidal
ECG	electrocardiogram
ECO_2	expired carbon dioxide
F	airflow
F_e	concentration of nitrogen in collected expired air
F_i	concentration of nitrogen in inspired oxygen
F_o	concentration of oxygen in alveoli at the end of the washout
F_a	concentration of nitrogen in the alveoli at the onset of the washout
f	respiratory frequency
FiO_2	fraction of inspired oxygen

FRC	functional residual capacity
HCO_3^-	bicarbonate
Hg	mercury
Hgb	hemoglobin concentration
HR	heart rate
i	ideal
Kg	kilogram
L	liter
mg	milligram
min	minute
mm	millimeter
P	pressure
PIF	peak inspiratory air flow
PCO_2	partial pressure of carbon dioxide
PO_2	partial pressure of oxygen
$\dot{Q}$	cardiac output
$\dot{Q}s/\dot{Q}t$	physiological shunt
R	airway resistance
RQ	respiratory exchange ratio
Sat	hemoglobin percent saturation
$\dot{V}_A$	alveolar minute ventilation
$\dot{V}A/\dot{Q}$	ventilation-perfusion ratio
V_{ads}	apparatus dead space, (approximately 55 ml)
vap	water vapor
V_{ds}	physiological dead space

$\dot{V}CO_2$	carbon dioxide production
$\dot{V}O_2$	oxygen consumption
V_T	tidal volume
V_W	washout volume

INTRODUCTION

Ethanol is the most popular mood-altering drug in the world and has probably been used by mankind since before recorded history. This project was designed to investigate the possibility of a detrimental effect of an acute, low dose of ethanol on pulmonary function. There has been extensive research on the detrimental effects of ethanol on several systems, organs, and tissues. Yet, there has been relatively little investigation of the possible toxic effects of alcohol consumption on the pulmonary system.

Only recently has evidence been reported that would indicate the possibility of a direct toxic effect of alcohol on the lung itself. There is ample evidence to indicate that the effects of alcohol on other systems may indirectly affect the pulmonary system. An excellent review of these possibilities has been provided by Heineman (1977).

Several authors have reported findings that indicate chronic alcohol consumption may lead to a higher incidence of symptoms resembling those seen in Chronic Obstructive Lung Disease (COLD) (Banner, 1973, Emergil et al., 1974, Saric et al., 1976, Emergil and Sobol, 1977). Others have shown that acute exposure to ethanol can cause changes in ventilatory regulation, and some lung volumes (Sahn et al., 1975, Johnstone and Rier, 1973). Whether the possible changes

caused by repeated acute exposure to ethanol could cause permanent damage to the lung is unknown.

This project was designed to determine if changes in lung function and pulmonary hemodynamics occur with blood ethanol concentrations (BEC) less than 100 mg/dL. This blood level was chosen as being a typical consequence of many social drinking situations.

LITERATURE REVIEW

Most of the interest in the toxic effects of alcohol consumption has been directed toward the pathologic changes in various tissues and organs and the concurrent derangements of their function. Research has primarily concerned itself with the toxic effects of alcohol on the structure and function of the heart, liver, brain, gastrointestinal system, and skeletal muscle. Relatively little attention has been directed toward the pulmonary system. This review will be limited to literature concerning the influence of alcohol on the function of the pulmonary system.

Population Studies

Several population studies have shown that there is reason to suspect a link between the consumption of alcohol and the incidence of specific pulmonary disease patterns. Banner (1973) studied the pulmonary function of thirty patients admitted to an alcoholic detoxification center. He found consistent derangements in lung volumes, airflows and diffusion capacities. The changes were judged greater than could be accounted for by the effects of only smoking. The observed changes were reminiscent of a mild obstructive pattern. Emergil et al. (1974) conducted a similar study and his findings largely confirmed those of Banner (1973). Again, there was a high incidence of abnormal airflow patterns,

reduced lung volumes, and a very consistent reduction in diffusion capacity. These changes were shown to be greater than could be attributed to only cigarette smoking. Saric et al. (1976) conducted a large population study using factory workers. His findings correlated alcohol consumption with the incidence of a Chronic Nonspecific Lung Disease pattern. They also attempted to account for the effects of both age and smoking habits. A subsequent study by Emergil et al. (1974) of former alcoholics, members of Alcoholics Anonymous, showed that the obstructive lung (pulmonary) characteristic pattern observed in the alcoholic tended to persist with abstinence. However, the consistent decrease in the diffusion capacity seen in the alcoholics was not found in the former alcoholics. Cohen et al. (1980) measured the pulmonary function of 2,539 subjects in a longitudinal study concerning the effects of alcohol consumption on the incidence of airway obstruction. They found that the initial significant correlations between alcohol consumption and the reduction of the timed forced expired volume (FEV_1) to forced vital capacity (FVC) ratio disappeared when the averages were corrected for other contributing factors. These factors included age, sex, race, socioeconomic status, cigarette smoking, ABO blood type, Rh blood type, ability to taste Phenylthiocarbamide and familial component (whether subjects were relatives

of patients with pulmonary disease). They concluded that any effect that alcohol consumption has on the development of pulmonary disease is probably due to an indirect influence and not a cause-effect type of relationship. They stated:

> Although we cannot rule out a role for alcohol in the development of pulmonary disease, its impact, if any, is probably the result of interaction with other intrinsic or extrinsic factors associated with alcoholism, if not deriving primarily from those other factors.

These conclusions are supported by the findings of Sarkar and Gupta (1980). Their study used ten chronic alcoholics who were nonsmokers and had no history of respiratory disease. They found that all of the parameters of pulmonary function measured were within normal limits. They concluded that alcoholism had little direct influence on respiratory function and that the changes which were observed were probably due to changes in liver function.

Alcohol and the Control of Respiration

There has been a long-standing controversy concerning the effects of alcohol on respiration. Mackenzie and Hill (1910) reported that men given a half ounce dose of alcohol could increase their breath holding time by one-third. Higgins (1917) duplicated their experiment as part of his study and confirmed their results. He attributed the

apparent depression of respiratory drive to ". . . the decreased appreciation of muscular fatigue by the brain." He also reported that alcohol had an inconsistent effect on respiration. The same dosage given to different subjects would sometimes stimulate and sometimes depress their respiration. Hitchcock (1941) reported that alcohol had a slight stimulatory effect on respiration but that the effect was so slight as to be ". . . of little practical importance." He further stated that the effects of alcohol on respiration were ". . . chiefly of academic interest."

Loomis (1952) found that moderate blood ethanol concentrations, less than 287 mg/dL, had little effect on the respiration of dogs, while nearly lethal concentrations produced a definite depression of respiration. Klingman and Haag (1958) found that most dogs receiving lethal oral doses of alcohol died of respiratory failure, though approximately thirty-five percent died of cardiac failure. However, dogs given their lethal dosage intravenously always died of respiratory failure.

Johnstone and Witt (1972) observed that patients admitted for treatment of severe alcohol intoxication showed no reduction of minute ventilation. Sahn et al. (1975) showed that moderate doses of alcohol produced no alveolar hypoventilation in patients with Chronic Obstructive Lung Disease (COLD).

Several authors have demonstrated alterations in the control of breathing with acute exposure and as a consequence of long exposure to alcohol. Changes in both the response to low oxygen (hypoxic ventilatory drive) and high carbon dioxide (hypercapnic ventilatory drive) have been observed with moderate doses of alcohol. Higgins (1917) found that alcohol tended to cause a reduction in the alveolar carbon dioxide tensions in humans. He interpreted this as the result of an increased sensitivity of the respiratory center to carbon dioxide. Loomis (1952) found that dogs showed a decreased response to hypoxia, but the responses were not measured at blood levels below 287 mg/dL.

Rosenstein et al. (1968) found that ethanol injected into the cerebrospinal fluid of cats caused a reduced response to hypercapnia. The effects were demonstrated even when the preparations were decerebrated and vagotomized. They concluded that this indicated a central effect rather than an alteration of the peripheral chemoreceptors.

Johnstone and Rier (1973) found a similarly depressed respiratory response to hypercapnia in humans given alcohol intravenously. The depression was increased in a dose dependent manner. It is of interest that they found that the largest response was observed after the blood levels had already peaked. They attributed this delay to the early stimulatory effects of intoxication.

Sahn et al. (1975) investigated the changes in both hypoxic and hypercapnic ventilatory drives in humans given an oral dose of alcohol. Unlike Johnstone and Rier (1973), they maintained isocapnic conditions during the hypoxia and found there was still ". . . a moderate blunting of the hypoxic ventilatory drive in all eight subjects." The responses to hypoxia tended to return toward normal even while the blood alcohol levels were relatively high. They speculated that the ventilatory control mechanisms might develop an acute tolerance to the "true drug" effect of ethanol. Their study of the hypercapnic ventilatory drive showed that there was a significant depression which did not occur until seventy minutes after ingestion of a moderate alcohol dose while blood ethanol concentrations peaked at twenty minutes. In a later study, Sahn et al. (1979), showed that patients who already had chronic alveolar hypercapnia, those suffering from COLD, showed no tendency toward alveolar hypoventilation after moderate doses of alcohol.

Pulmonary Function

Several authors have reported alterations in pulmonary function as a result of both chronic and acute exposure to alcohol dosages. These alterations include changes in diffusion capacity, changes in several lung volumes, changes in

specific air flows, and changes in the hemodynamic responses to hypoxia.

Higgins (1917) found an increase in alveolar PCO_2 after an alcohol dose. He postulated that the increase might be due to a bronchoconstrictor effect of alcohol. Subsequent measurement of the physiological dead space (V_{ds}) showed that this was not the case since there was never a decrease in V_{ds} as would be seen with bronchoconstriction, and there was occasionally an increase in V_{ds}, indicating a bronchodilatation. Measurement of total lung ventilation ($\dot{V}_E$) showed a slight decrease associated with alcohol dosage. He attributed the decrease in ventilation to a decrease in CO_2 production ($\dot{V}CO_2$). Hitchcock (1941) chose to express ventilation as the ventilatory equivalent, the volume of air breathed per 100 ml of oxygen absorbed. He considered this value superior to $\dot{V}_E$ since it took into account the changes in oxygen consumption. Using this value, he found that there was a stimulatory effect soon after ingestion of alcohol that gave way to a depressant effect within one hour. Although not directly stated as such, his data supports the earlier findings concerning increases in V_{ds}.

Johnstone and Rier (1973) showed that there may be some changes in lung volumes associated with an acute dose of alcohol. They gave three intravenous doses, 0.35, 0.70, and 1.05 ml/Kg over a one hour period to human subjects. These

doses resulted in average blood ethanol concentrations of 40, 99, and 121 mg/dL. They found that vital capacity (VC) was reduced in a dose dependent manner. They also measured V_{ds} and found that there was a corresponding trend toward an increase in V_{ds} with increased blood levels of alcohol, but this trend never became significant.

Other Factors Involved with Ethanol Responses

A complete spirometric analysis of pulmonary function was carried out by Banner (1973) on chronic alcoholics. Since almost all alcoholics also smoke cigarettes, he applied a correction factor to adjust for the changes associated with cigarette smoking. He found that the subjects showed no significant differences in total lung capacity (TLC), vital capacity (VC), or residual volume (RV) from the normal population range. However, there was a slight impairment of airflows and a significant decrease in FEV_1. The ratio of FEV_1/FVC trended towards a decrease, but the changes were not statistically significant. Measurements of lung compliance and resistance to airflow showed inconsistent responses. The most consistent derangement found that correlated with alcohol consumption was a decrease in the diffusion capacity of the lungs, measured by single breath diffusion of carbon monoxide (SBDCO). Banner postulated that the pulmonary mechanics indicated an alveolo-

capillary block, rather than a decrease in the area available for diffusion or a decrease in capillary blood flow.

Emergil et al. (1974) conducted a very similar study of chronic alcoholics and found that all of the subjects studied exhibited some form of respiratory disorder. They found that there were decreases in TLC, RV, VC, FEV_1, and SBDCO that progressively decreased as the history of alcohol consumption increased. He concluded that the consumption of alcohol lead to the production of the symptoms of COLD. He went on to say,

> . . . our data suggest that alcohol alters pulmonary function independent of the effects of cigarette smoking or previous pulmonary infection. Alcohol appears to produce a pulmonary disease which is basically obstructive in its characteristics. This obstructive disease is usually associated with impaired diffusion capacity and relatively low lung volumes . . . significant correlation between the alcohol consumption and lung volumes suggests that alcohol may have a direct effect on the lungs.

A later study by Emergil and Sobol (1977) on former alcoholics indicated that some of the changes associated with chronic alcohol consumption may reverse themselves with abstinence while others do not. They studied members of Alcoholics Anonymous and found that there was a high incidence of abnormal expiratory airflow rates and elevated RV/TLC ratios. They stated,

> . . . it can be seen . . . that the common functional abnormality of alcoholics (namely obstructive pulmonary disease) does not appear to be reversible with abstinence.

However, the almost universally consistent decreased diffusion capacity found in the alcoholics was shown to be apparently reversible with abstinence. The former alcoholics had significantly higher diffusion capacities than those found in the chronic alcoholics. These differences were not due to differences in hemoglobin concentration or smoking history.

Two studies of large populations not selected for either pulmonary disorders or alcoholism showed conflicting results. Saric et al. (1976) studied respiratory parameters in a large population of factory workers. They found that decreases in FVC were not associated with alcohol consumption but decreases in FEV_1 were significantly correlated with alcohol consumption. They attempted to correct for the effects of age and smoking habits and found that alcohol was still significantly associated with decreased FEV_1. They concluded that alcohol consumption was related to the occurrence and rate of Chronic Nonspecific Lung Disease.

On the other hand, Cohen et al. (1980), in a "longitudinal community dwelling study", found that although alcohol consumption could be correlated with decreased FEV_1/FVC ratios, this significant relationship disappeared when the results were corrected for other contributing factors, as mentioned previously.

Sarkar and Gupta (1980) tried to eliminate any influence

that smoking and previous respiratory infection might have on lung function in alcoholics by measuring the pulmonary function of ten nonsmoking alcoholics with no history of respiratory infection. They measured VC, RV, TLC, FEV_1, FEV_1/FVC, maximum mid-expiratory flow rate (MMFR), peak expiratory flow rate (PEFR), maximum ventilatory volume (MVV), and SBDCO. The mean values for all the tests were within normal limits, though RV, FEV_1, FEV_1/FVC, MMFR, MVV, and SBDCO were shown to be statistically larger than the normal mean predicted values.

Pulmonary Hemodynamics

Doekel et al. (1978) investigated the pulmonary hemodynamic responses to acute alcohol doses administered to dogs both orally and intravenously. They measured pulmonary arterial pressure (PAP), systemic arterial pressure (SAP), pulmonary arterial wedge pressure (PAWP), and cardiac output ($\dot{Q}$). They found that when blood ethanol concentrations rose above 100 mg/dL there was a significant increase in both PAP and pulmonary vascular resistance (PVR) which was calculated by the formula $(PAP-PAWP)/\dot{Q}$. The dogs were mechanically ventilated to maintain a constant blood pH. Neither melcofenamate, an inhibitor of vasoconstrictive prostaglandin synthesis or phenoxybenzamine, a blocker of alpha receptors inhibited the increases

in PAP and PVR caused by ethanol. However, the increase in PVR was abolished by exposure to hyperoxia and potentiated by exposure to hypoxia. The normal response to hypoxia is an increase in PVR as a result of reflex hypoxic vasoconstriction. There are only a few known compounds that potentiate this reflex.

Metabolic Rate

Only a few investigators have reported on possible changes in basal metabolism caused by treatment with alcohol. These changes could be seen by noting shifts in the $\dot{V}O_2$, $\dot{V}CO_2$, and respiratory exchange ratio ($RQ = \dot{V}CO_2/\dot{V}O_2$). Higgins (1917) measured the oxygen consumption in humans given a small dose of alcohol. He found that there were only small changes in $\dot{V}O_2$ associated with alcohol treatment. Based on the $\dot{V}O_2$ data, he concluded that there was no change in the basal metabolism of normal men given alcohol. He also noted a decrease in the $\dot{V}CO_2$ which would mean that RQ would have been stable or decreased during the alcohol treatment. Johnstone and Rier (1973) also measured the $\dot{V}O_2$, $\dot{V}CO_2$, and RQ in humans treated with intravenous doses of alcohol. They reported slight decreases in $\dot{V}CO_2$ and slight increases in $\dot{V}O_2$. Their measurements of the respiratory quotient showed a significant decrease after the inter-

mediate dosage of alcohol, but this effect was inconsistent since it was not repeated after the higher dosage.

Blood Gases

Many of the authors previously quoted also noted derangements in blood gas tensions, acid-base equilibrium and oxygen saturation of blood in their subjects exposed to alcohol. Klingman and Haag (1958) reported significant decreases in blood pH values in dogs given lethal doses of alcohol. They also noted significant increases in both hemoglobin and hematocrit levels. Johnstone and Witt (1972) reported a mild metabolic acidosis, increased $PaCO_2$, and normal PaO_2 in patients admitted for emergency treatment of severe alcohol intoxication. The study by Emergil et al. (1974) noted oxygen saturations at the lower limit of the normal range in chronic alcoholics. Smith et al. (1975), noted trends toward decreased blood pH and increased blood $PaCO_2$ in mice treated with alcohol. Doekel et al. (1978) reported values that indicate a trend toward decreased PaO_2 and increased $PaCO_2$ in dogs given a moderate dose of alcohol. Sahn et al. (1979) followed the whole blood $PaCO_2$, PaO_2, pH and serum bicarbonate in patients given a moderate oral dose of alcohol. They found significant decreases in both blood pH and serum bicarbonate associated with the treatment with no significant changes in $PaCO_2$ and PaO_2. None

of the observed changes exceeded the normal physiological limits, but they stated that the mild acidosis observed was of metabolic origin. Sarkar and Gupta (1980) measured the $PaCO_2$, PaO_2, and pH in eight of ten nonsmoking chronic alcoholics and stated that they were within normal limits both at rest and after exercise. They did find an abnormal response to breathing 100% oxygen for twenty minutes. They found no changes that could be directly attributed to alcoholism and stated,

> The true shunt noted in all subjects who underwent blood gas studies is probably related to liver disease.

MATERIALS AND METHODS

Experimental Design

Sixteen adult mongrel dogs (15.6-36.3 Kg) were used in this study. These dogs were obtained from Laboratory Animal Resources at Iowa State University. The animals were randomly divided into Group I that consisted of eight dogs infused with ethanol and Group II that were infused with normal saline.

The dogs were anesthetized initially with sodium thiopental (5.44 mg/Kg), and maintained with a solution of alpha-chloralose (38 mg/Kg) (a-c) and urethane (375 mg/Kg) (a-c/u). Depth of anesthesia was estimated by peripheral signs and continuous recordings of respiratory parameters. Additional doses of a-c/u were administered as needed to maintain the plane of anesthesia.

The experiment was designed to follow the changes in the various recorded and calculated parameters over a 200 minute period. Samples were taken initially at T0 and at subsequent 20 minute intervals until T10. The infusion commenced after the initial samples and recordings were collected and continued until the calculated volume (2 ml/Kg) of either saline or 50% ethanol had been administered. Measurements of Functional Residual Capacity (FRC) were taken at least 15 min before T0, immediately after completion of the infusion (T6 or T7), and again after the T10 samples. The infusion lasted

an average of 132 minutes for both experimental groups.

Experimental Techniques

Pulmonary dynamics and systemic hemodynamics

The dogs were strapped in dorsal recumbency on a thermal pad, intubated and cannulated. After all recording transducers were connected and the dog appeared to be physiologically stabilized, the first set of blood and air samples were collected. At the same time, a set of continuous recordings (0.5 mm/sec for 2 min, 25 mm/sec for 1 min) on a Beckman 611 recorder included: airflow (F) measured by a Fleish #0 pneumotach and Statham differential pressure transducer. Airflow (F) was electrically integrated to give tidal volume (V_T). Arterial blood pressure (AP), right ventricular blood pressure (RVP), esophageal pressure (P_{es}) were all recorded with Statham pressure transducers. ECG (lead II) and a continuous recording of expired percent carbon dioxide (ECO_2) from a Beckman LB-1 on-line CO_2 analyzer connected to an end tidal sampler completed the list of recorded paramenters.

Measurement of functional residual capacity

Functional Residual Capacity (FRC) was measured in 4 dogs from Group I and 5 dogs from Group II. FRC was measured using the technique of multiple breath nitrogen

washouts.

The dogs were attached to a combination pneumotach and nitrogen analyzer. Both instruments presented digital output and analog output. The pneumotach was used to measure expired tidal volume with the analog output going to channel 1 of a Brush recorder. The analog output from the nitrogen analyzer went to channel 2 of the same recorder. A valve on the inspiratory port allowed the dogs to breath either room air or 100% oxygen.

After the respiratory pattern of the dogs had stabilized, the animal was switched from breathing room air to pure oxygen during an expiration. Simultaneously, an evacuated meteorological balloon was attached to the expiratory port of the pneumotach for collection of the expired washout air. The nitrogen content of each expired breath and the volume of each breath were monitored on the two channels of the Brush recorder (see sample recording, Figure 1). When the concentration of nitrogen in the expired air fell below 10%, the dogs were removed from the pneumotach. The air collected during the washout was then forced through the nitrogen analyzer for measurement of the nitrogen concentration in the collected gas.

Figure 1. Recording used for calculation of functional residual capacity (FRC)

A. Percent nitrogen

F_a - concentration of nitrogen in the alveoli at the end of the washout

F_e - concentration of nitrogen in collected expired air

F_i - concentration of nitrogen in inspired oxygen

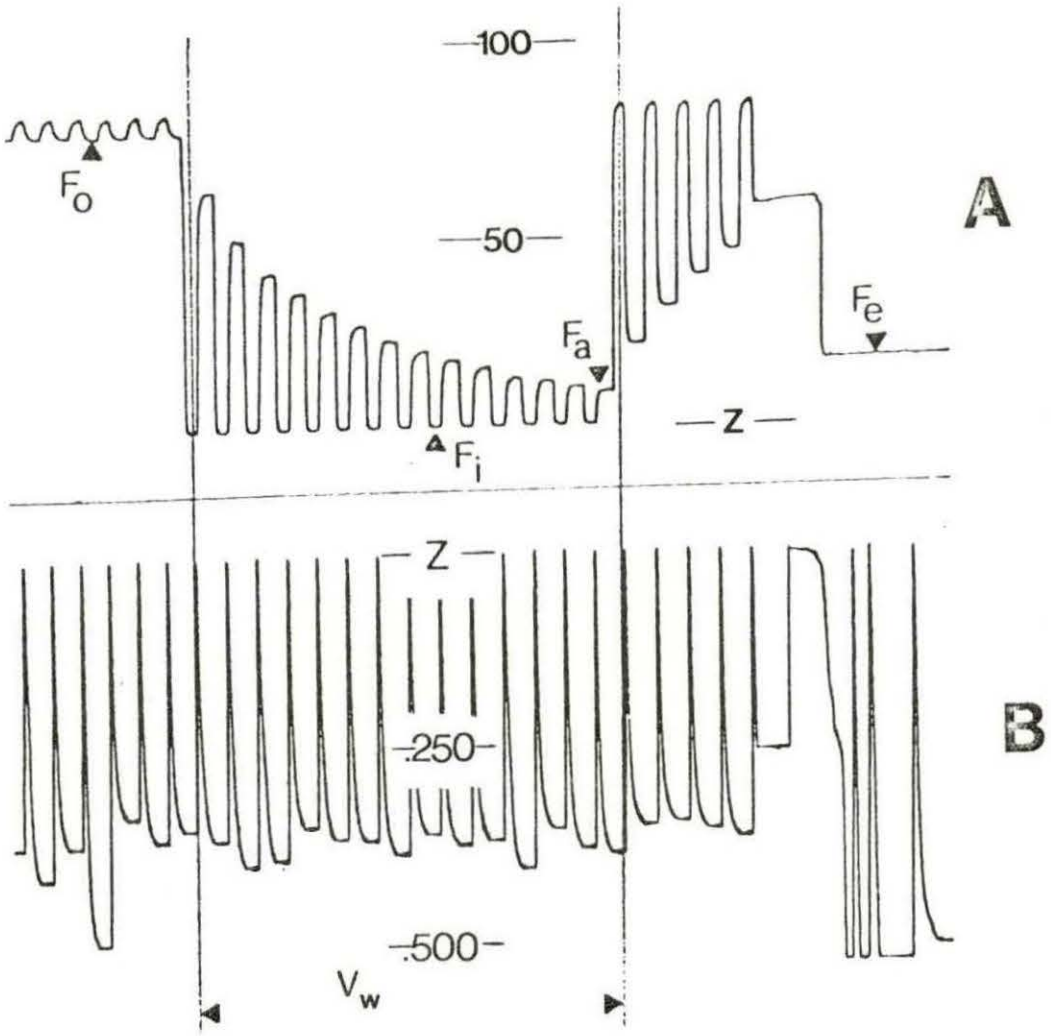
F_o - concentration of nitrogen in the alveoli at the onset of the washout

Z - zero line

B. Expired volume (L)

V_w - total volume of air expired during the washout

Z - zero line


100
50
F_o
F_a
F_e
F_i
Z
A
Z
250
500
V_w
B

Surgical techniques

A single incision on the neck was used to expose both the external jugular veins and the right common carotid arteries for cannulation. A Swan-Ganz catheter connected to a Statham pressure transducer was introduced into the right external jugular vein and the tip positioned in the right ventricle. The catheter positioning was verified by the characteristic right ventircular pressure wave form. This catheter was used for collection of the anaerobic mixed venous blood samples and recording of the right ventricular pressure (RVP). Systemic arterial pressure (SAP) and anaerobic arterial blood samples were collected from another cannula in the right common carotid artery connected to a Statham pressure transducer. This cannula was advanced approximately 10 cm towards the heart and tied in place. A third cannula was introduced into the left external jugular vein, advanced toward the heart approximately 8 cm and tied in place. This cannula was utilized for the infusions of either alcohol solution or saline. All blood vessels were ligated cranially to the cannulation site. All cannulas were maintained patent by periodically flushing with heparinized saline (10 USP units/ml).

Blood and gas sample analysis

The blood and gas samples consisted of duplicate anaerobic arterial and mixed venous blood samples collected in 3 ml plastic syringes wetted with heparin (1000 USP units/ml) and a sample of mixed expired air collected in modified meteorological balloons.

The blood samples were refrigerated at 4°C immediately after collection. Analysis of the mixed expired air samples were completed less than one hour after collection in order to minimize the changes due to diffusion. Both the blood samples and mixed expired air samples were analyzed on an Instrumentation Laboratories 513 Blood Gas Analyzer. Measured blood parameters included: pH, and partial pressures of carbon dioxide (PCO_2) and oxygen (PO_2). The values for base excess (BE), bicarbonate (HCO_3^-), and total carbon dioxide (tCO_2) were calculated by the blood gas analyzer. A separate blood sample was used for the measurement of hemoglobin in g/100 ml via the cyanomethemoglobin method. The arterial blood samples for each time period were pooled and used for the measurement of blood ethanol concentrations (BEC) by enzyme NDA-ADH assay (Sigma No. 331-UV).

Measured and Intermediate Calculated Parameters

A. The following values were used to calculate several parameters:

1)	partial pressure of mixed venous carbon dioxide		$P\bar{v}CO_2$	mmHg
2)	partial pressure of arterial carbon dioxide		$PaCO_2$	mmHg
3)	partial pressure of arterial oxygen		PaO_2	mmHg
4)	partial pressure of mixed expired carbon dioxide		$PeCO_2$	mmHg
5)	partial pressure of mixed expired oxygen		PeO_2	mmHg
6)	partial pressure of end tidal carbon dioxide		$PetCO_2$	mmHg
7)	barometric pressure		Pbar	mmHg
8)	concentration of hemoglobin	Hgb	g/100 ml	
9)	tidal volume		V_T	L
10)	respiratory rate	f	breaths/min	
11)	pH of both arterial and venous blood			

B. The following values were constant in all experiments:

1)	fraction of inspired oxygen	FiO_2	.2093
2)	saturated water vapor pressure	Pvap	47 mmHg

C. The following were intermediate calculations:

1) percent saturation of hemoglobin, calculated from a nomogram (Rossing and Cain, 1966) using pH and PO_2 and assuming a temperature of 37°C.

   a) arterial Hgb saturation — aSat ml/100 ml (%)

   b) venous Hgb saturation — vSat ml/100 ml (%)

2) arterial oxygen concentration — ml O_2/100 ml

   $CaO_2 = (1.34 \times Hgb) \times aSat$

3) mixed venous oxygen concentration — ml O_2/100 ml

   $C\bar{v}O_2 = (1.34 \times Hgb) \times vSat$

4) ideal oxygen concentration — ml O_2/100 ml

   $CiO_2 = (1.34 \times Hgb) \times 100\%$

D. The following values were calculated using the variables from A, B, and C using a WANG minicomputer:

1) ratio of physiological dead space to tidal volume

   $V_{ds}/V_T = (PaCO_2 - PeCO_2)/PaCO_2$

2) volume of physiological dead space

   $V_{ds}(L) = (V_{ds}/V_T) \times V_T$

3) alveolar minute ventilation

   $\dot{V}_A$ (L/min) $= (V_T - V_{ds}) \times f$

4) oxygen consumption

   $\dot{V}O_2$ (L/min) $= FiO_2 - (PeO_2/(Pbar-Pvap)) \times V_T \times f$

5) cardiac output

   $\dot{Q}$ (L/min) $= \dot{V}O_2/(CaO_2 - C\bar{v}O_2)$

6) carbon dioxide production

$\dot{V}CO_2$ (L/min) = ($PetCO_2$/Pbar - Pvap) x $\dot{V}_A$

7) respiratory exchange ratio

$RQ = \dot{V}CO_2/\dot{V}O_2$

8) ventilation to perfusion ratio

$\dot{V}A/\dot{Q} = \dot{V}_A/\dot{Q}$

9) percent physiological shunt

$\dot{Q}s/\dot{Q}t = 100 \times (CiO_2-CaO_2)/(CiO_2-C\bar{v}O_2)$

E. Calculation of lung compliance and resistance:

1) Lung compliance and resistance were calculated using the simultaneous recordings of airflow, tidal volume, and esophageal pressure (see sample recording, Figure 2). A line drawn perpendicularly through the three traces at the end of inspiration or at the time of zero airflow determines a tidal volume and a measurement of esophageal pressure that is due only to the elastic resistance of the lung. Since there is no airflow at that moment, no effort is required to overcome airway resistance to airflow. Lung compliance is calculated using the tidal volume (V_T) and esophageal pressure at zero airflow (P_{esT}) with this equation:

C_L (L/cm H_2O) = V_T/P_{esT}

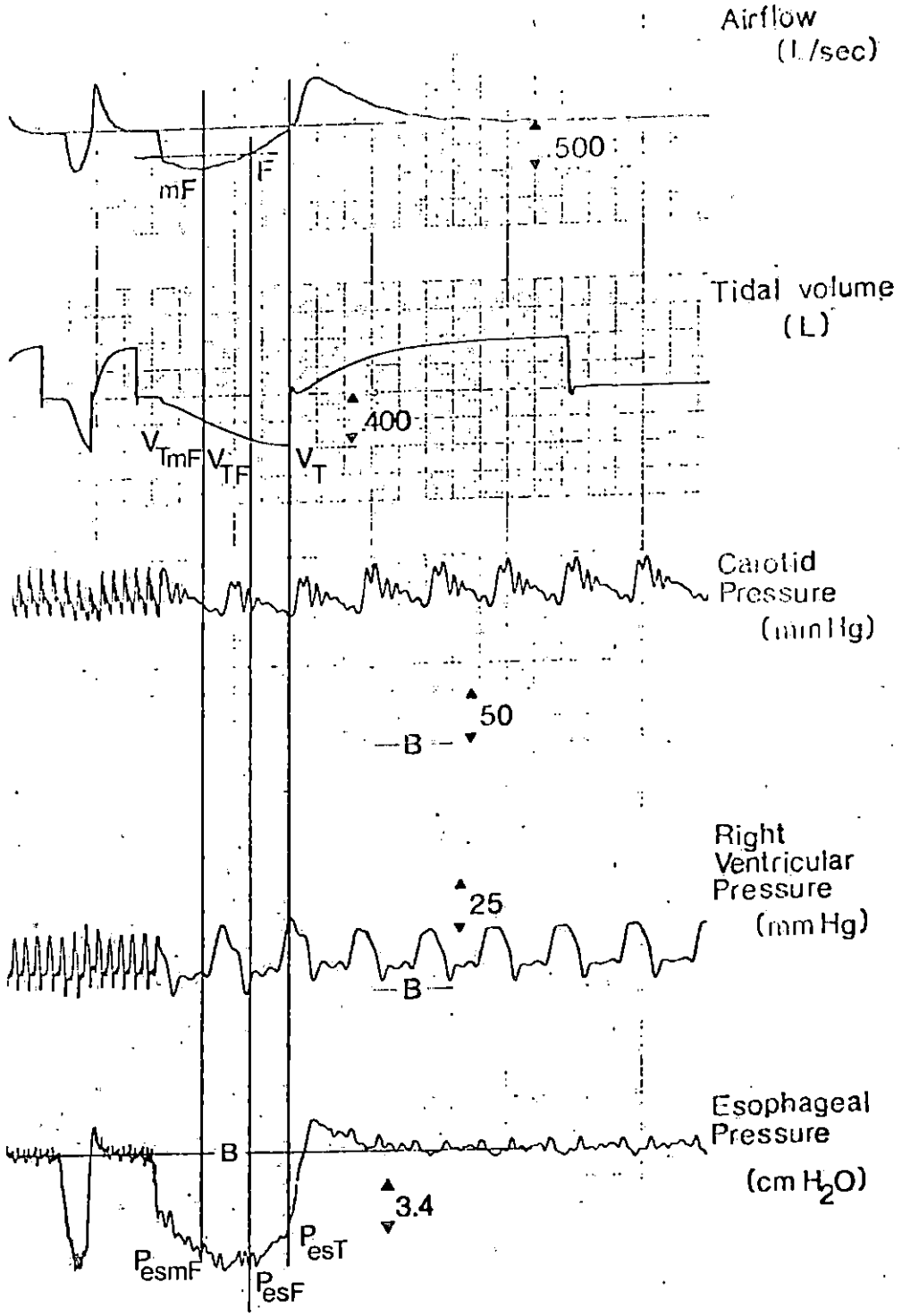
Since lung compliance is constant throughout the tidal volume, it can be used to calculate the esophageal pressure needed to overcome elastic resistance at a lung volume. A

Figure 2. Recording used to calculate lung compliance (C_L) and airway resistance (R)

F = standard airflow
mF = peak inspiratory airflow (PIF)

V_T = maximum tidal volume
V_{TF} = tidal volume at standard airflow
V_{TmF} = tidal volume at PIF

P_{esT} = esophageal pressure at maximum tidal volume
P_{esF} = esophageal pressure at standard airflow
P_{esmF} = exophageal pressure at PIF


Airflow
(L/sec)
500
mF
F
Tidal volume
(L)
400
V_{TmF}
V_{TF}
V_T
Carotid
Pressure
(mm Hg)
50
B
Right
Ventricular
Pressure
(mm Hg)
25
B
Esophageal
Pressure
($cm H_2O$)
B
3.4
P_{esmF}
P_{esF}
P_{esT}

line drawn perpendicularly at a desired airflow determines a value for tidal volume at a flow (V_{TF}), an esophageal pressure at a flow (P_{esF}) and a value for airflow (F) (see sample recording, Figure 2). The esophageal pressure due to elastic resistance, or compliance pressure is calculated using this equation:

$$P_{esC_L} (cm\ H_2O) = V_{TF}/C_L$$

This pressure is subtracted from the total esophageal pressure measured at an air flow to give the pressure generated to overcome airway resistance to airflow:

$$P_{esR} (cm\ H_2O) = P_{esF} - P_{esC_L}$$

2) The resistance of the airways to airflow is then calculated with the equation:

$$R\ (cm\ H_2O/L/sec) = P_{esR}/F$$

This value was calculated both at the moment of maximum inspiratory airflow and at a predetermined airflow when tracings were suitable. At least two, and when possible, three breaths were measured and the results averaged to give values for lung compliance and airway resistance to airflow at a predetermined flow and at the point of maximum airflow at each sample period.

F. Calculation of FRC:

$$FRC\ (L) = \frac{(V_w + V_{ads}) \times (F_e - F_i)}{(F_o - F_a)}$$

The recordings yield the following values: (see sample recordings, Figure 1)

V_w(L) = volume of air expired during the washout

F_e = concentration of nitrogen in the collected expired air

F_i = concentration of nitrogen in the inspired oxygen

F_o = concentration of nitrogen in the alveoli at the onset

F_a = concentration of nitrogen in the alveoli at the end of the washout

V_{ads} = dead space volume of the apparatus (approx. 55 ml)

Data Analysis

In order to correct for some of the inherent variability between animals, the data was normalized by determining the deviation of each parameter from the control, T0, values. The majority of parameters are presented as percent change from control. The values for hemoglobin saturation, blood pH, P_{CO_2}, and P_{O_2} are presented as absolute changes. This is because small changes in these parameters, which may not be large percentages of control values, may be physiologically very important. All figures presented were plotted

by the SAS computer system. All data presented in figure form is also presented in tables in the Appendix.

An analysis of variance was run on the values at each sample period to test for a treatment difference. A p-value of less than 0.05 was taken to indicate a statistically significant difference between the experimental groups. A p-value greater than 0.05 but less than 0.10 was taken to indicate a significant trend for a difference between the groups.

RESULTS AND DISCUSSION

Infusion Parameters

Infusion time

Each animal received an infusion volume based on body weight. Table 1 represents the average weights and infusion times of the dogs in group I, group II and both groups together. The infusion rate was constant at 0.388 ml/min, therefore the infusion times varied with body weight.

Table 1. Mean body weights and infusion times for each experimental group and for the combined groups

Group	n	Body weight	Infusion time
I	8	24.4 ± 1.9 Kg[a]	126 min
II	8	26.8 ± 2.7 Kg	138 min
I+II	16	25.6 ± 1.6 Kg	132 min

[a]Mean ± S.E.M.

For the sake of simplicity, the data presented here will use the mean infusion time for both groups together. Thus, the infusion time is considered to start from T0 to midway between T6 and T7.

Blood ethanol concentration (BEC)

Figure 3 is a plot of BEC versus sample period. The peak BEC was measured at T6 and did not exceed 50 mg/dL. These moderate BEC levels have seldom been used in the literature. Most researchers use levels far above 100 mg/dL (Loomis, 1952, Klingman and Haag, 1958, Doekel et al., 1978, Nakano and Kessinger, 1972). The possible effects of an acute low dose of alcohol and low BEC have largely been ignored in the literature.

Respiratory Parameters

Changes in respiratory parameters would include changes in ventilation, lung volumes, and pulmonary mechanics. This project assessed changes in ventilation by measuring alveolar minute ventilation ($\dot{V}_A$). This is influenced by changes in tidal volume (V_T) and respiratory frequency (f). Other lung volumes measured include the physiological dead space (V_{ds}) and Functional Residual Capacity (FRC). Changes in pulmonary mechanics were quantified by measuring lung compliance (C_L), airway resistance (R), and the peak inspiratory (PIF) and expiratory (PEF) airflows.

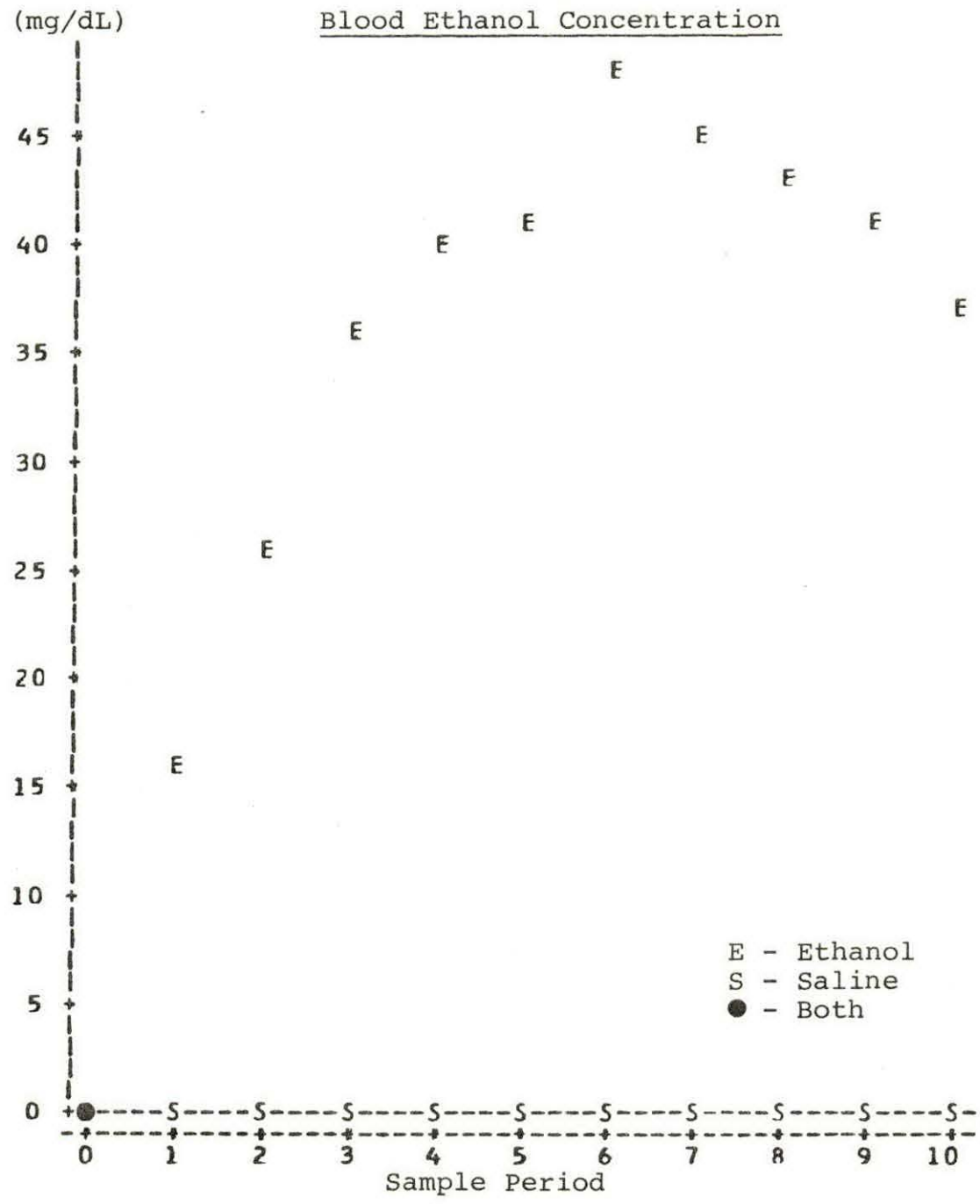


Figure 3. Mean blood ethanol concentration (BEC)

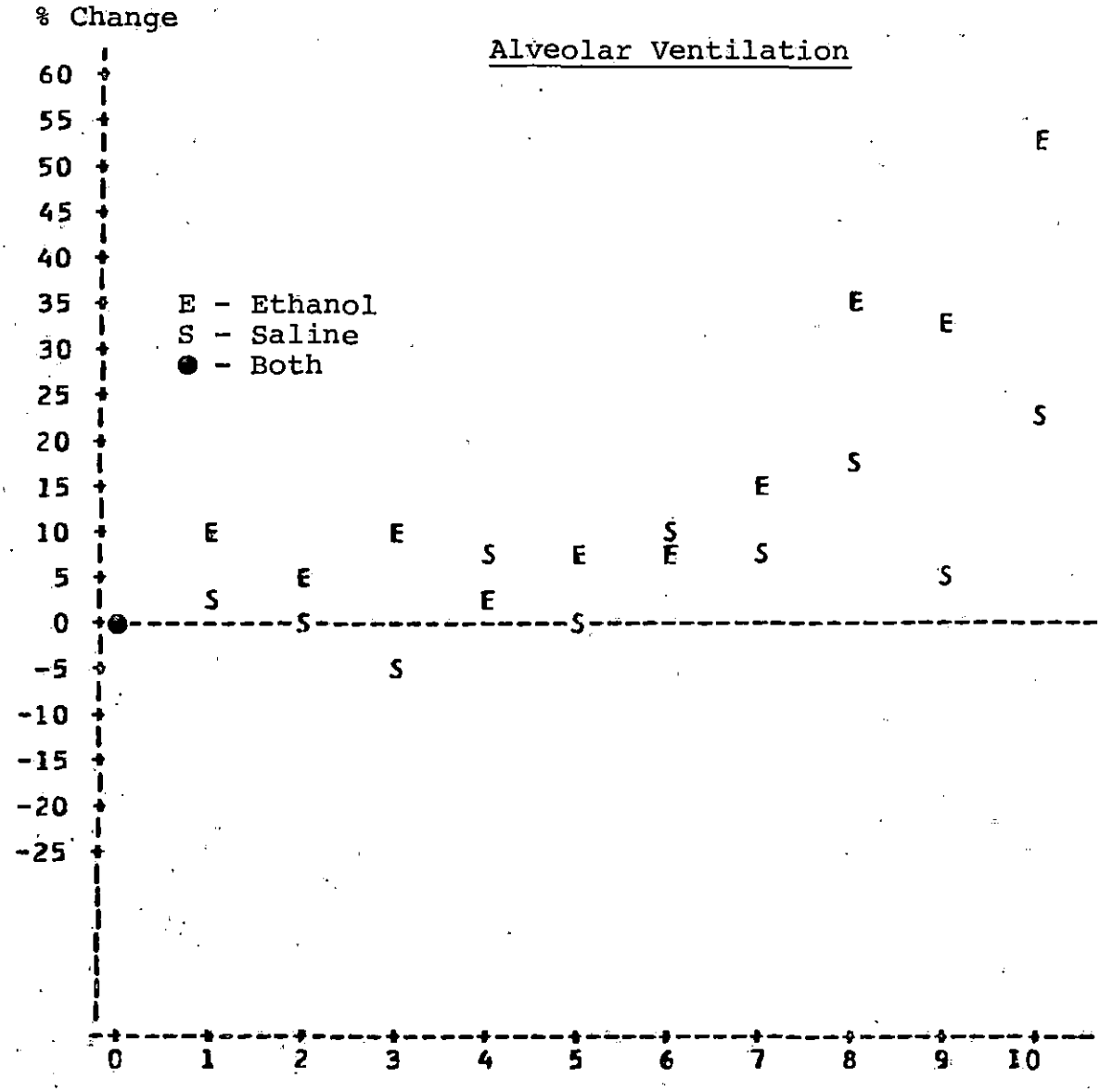
Ventilation

As can be seen in Figure 4, $\dot{V}_A$ shows a tendency to increase in both Group I and Group II over the experimental period. Both groups are nearly identical until T8. At this time, the ethanol treated group begins to show a trend toward an increase in $\dot{V}_A$ over that shown by the saline treated group (largest percent change at T10: E = 53.1 ± 6.3[1], S = 22.8 ± 16.8).

Changes in $\dot{V}_A$ must be associated by either a change in V_T or f or both. Figure 5 shows that part of the increase seen in both groups is due to a moderate increase in V_T. Group I shows the largest increase at T6 (13.6 ± 11.3 percent) while the Group II animals show their largest change at T9 (12.8 ± 5.0 percent). However, the trend is consistent and there is no evidence of a statistical difference between the two groups.

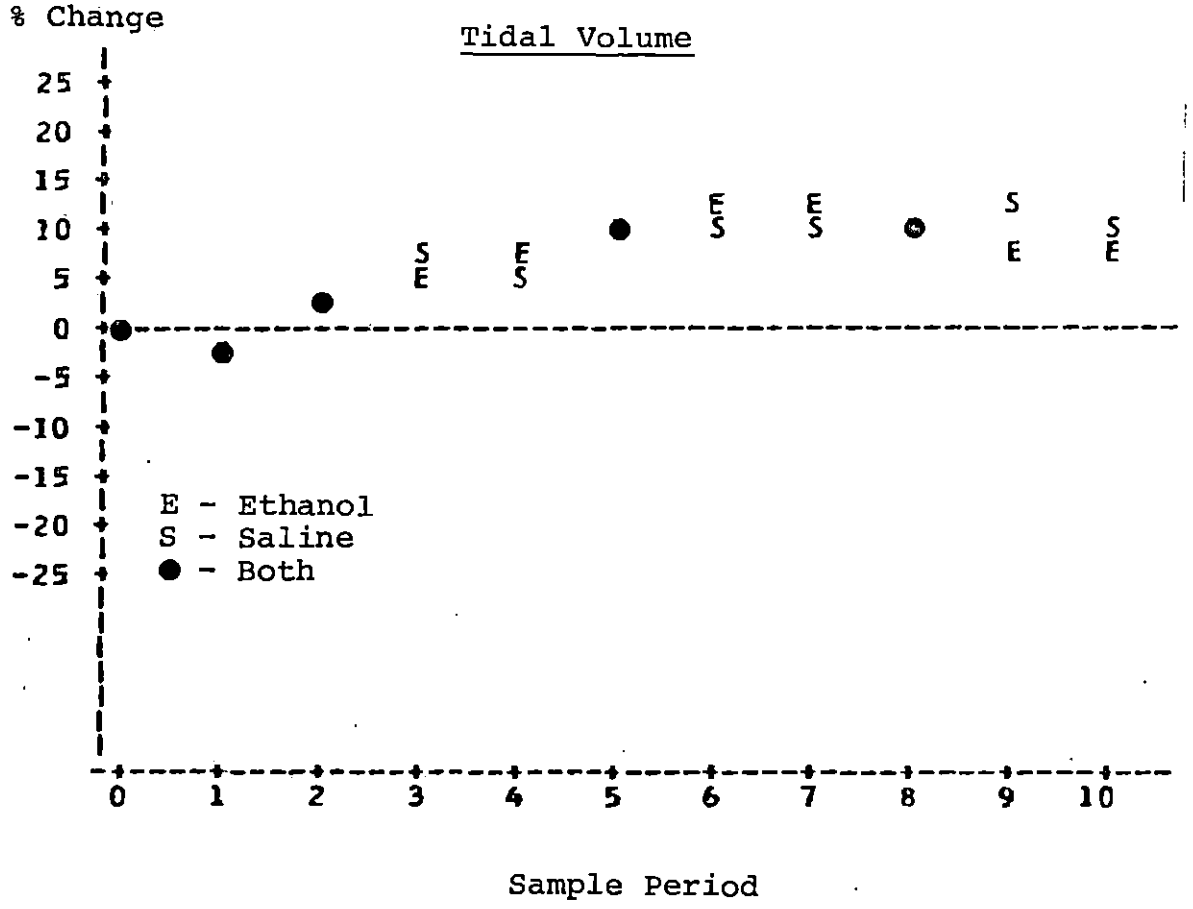
The difference in $\dot{V}_A$ is largely due to differences in f. Figure 6 shows the changes in f and it is apparent that there is no difference between the two groups until after T7. This increase in f occurs after BEC has peaked and is actually decreasing, so it is difficult to attribute this response to the ethanol treatment. The possibility of a delayed response does exist. Klingman and Haag (1958)

[1]Mean ± S.E.M.



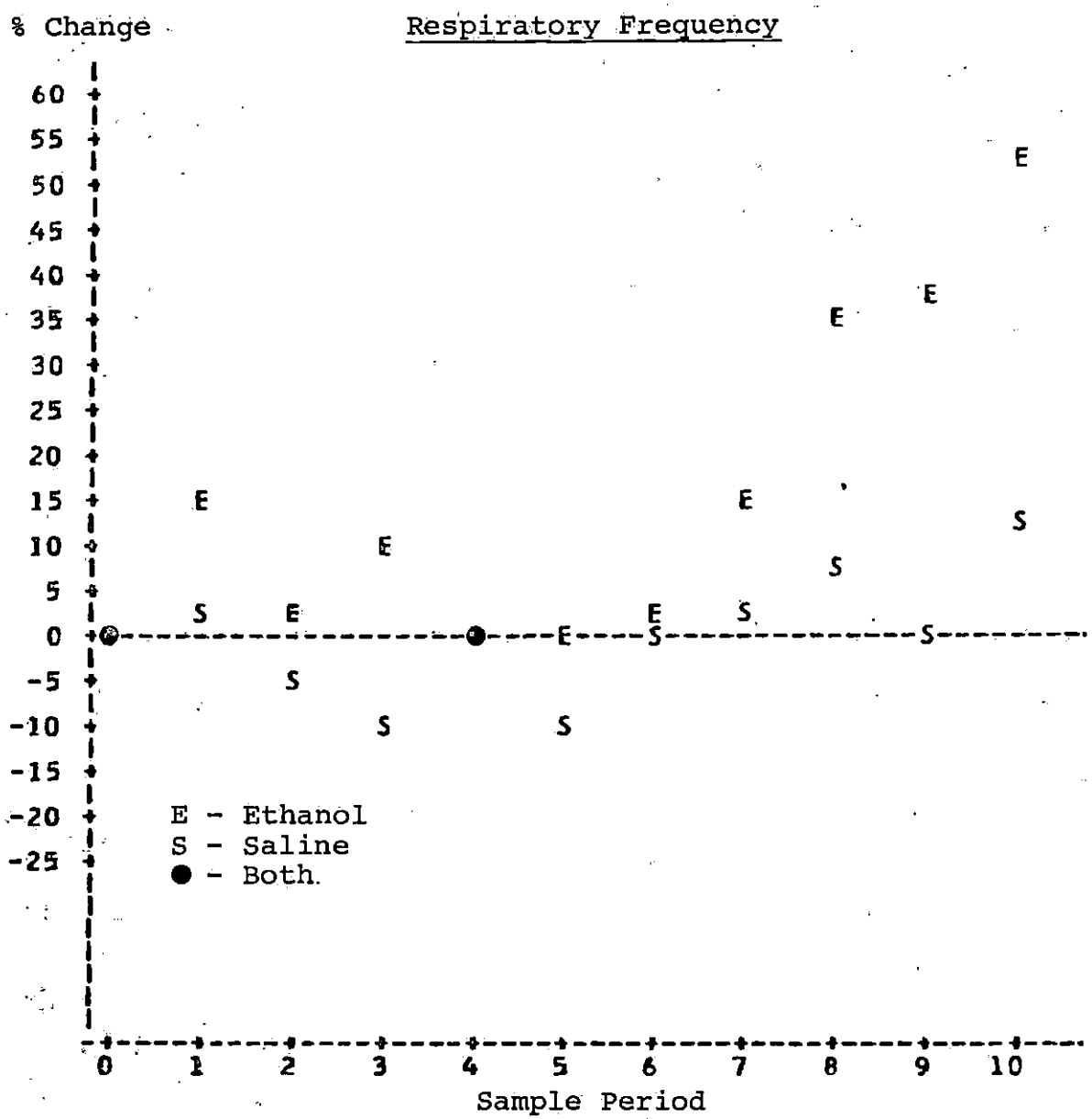
T0 values:
E 1.658 ± 0.224 L/min
S 2.215 ± 0.268 L/min

Figure 4. Percent change in alveolar ventilation ($\dot{V}_A$)



T0 values:
E 0.366 ± 0.040 L
S 0.348 ± 0.021 L

Figure 5. Percent change in tidal volume (V_T)



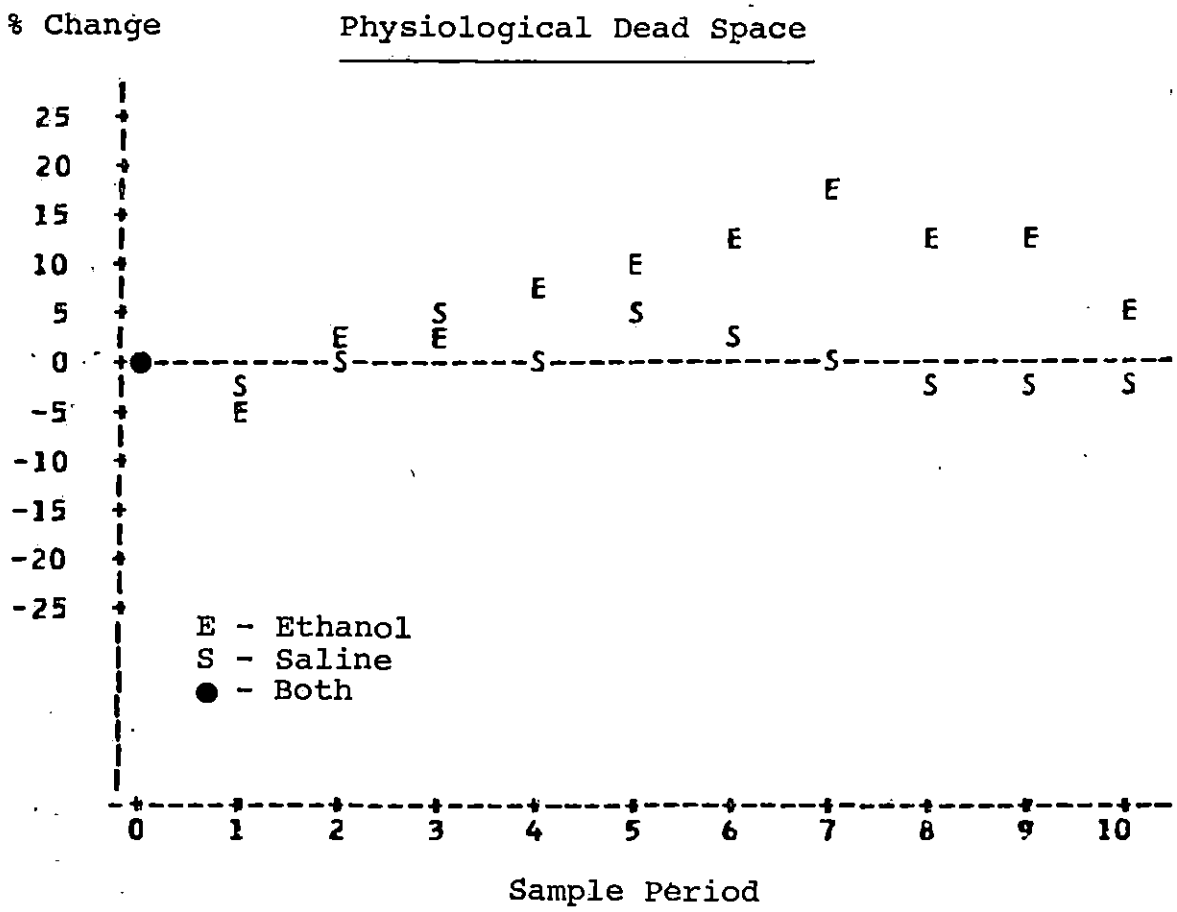
T0 values:
E 9.3 ± 0.7 breaths/min
S 11.7 ± 1.3 breaths/min

Figure 6. Percent change in respiratory frequency (f)

noted that dogs treated with lethal doses of ethanol, either orally or intravenously, always died after the BEC had peaked and was decreasing. However, they were dealing with a mean peak BEC of greater than 600 mg/dL. It is perhaps just as important to note that there is no indication of respiratory depression at these low BECs. This is in agreement with both Loomis (1952) and Klingman and Haag (1958), who reported no tendency for respiratory depression at low BECs in dogs. This conclusion is also in agreement with the findings of Johnstone and Witt (1972), Johnstone and Rier (1973) and Sahn et al. (1979) in human subjects.

Lung volumes

As previously mentioned, V_T shows a progressive increase in both groups. The basis for this increase remains unclear. Figure 7 illustrates the changes in V_{ds}, the volume of inhaled air that does not participate in gas exchange. It is evident that there is little deviation from the control values in the Group II animals with the largest increases occurring at T3 and T5 (3.8 $\pm$ 2.8 percent and 3.8 $\pm$ 4.6 percent, respectively). The Group I dogs show a consistent trend toward a moderate increase in V_{ds}. This curve is very similar to the one for BEC, strongly indicating the possibility of a relationship, though a statistically significant difference between the treatment groups is never established.



T0 values:
E = 0.181 ± 0.017 L
S = 0.169 ± 0.013 L

Figure 7. Percent change in physiological dead space (V_{ds})

Figure 8 shows the percent change in FRC volume left in the lung after expiration. FRC is measured after the end of the infusion and again after the last sample period. The ethanol treated group showed an increase in FRC at the end of the infusion, which subsequently decreased when measured after T10. The progressive decrease in FRC seen in the Group II animals may be due to the progressive edema associated with prolonged dorsal recumbency. The increase in FRC in the Group I dogs is all the more impressive in light of this trend. An analysis of variance between the treatment groups reveals no significant differences, although the values are approaching significance at peak BEC ($p = 0.084$). Any analysis utilizing a low number of subjects will have difficulty showing statistically significant differences between the groups, even though the differences may be physiologically significant. To find values even approaching significance is impressive under these circumstances.

The changes in FRC and V_{ds} are consistent with one another. One possible mechanism for an increase in V_{ds} would be a bronchodilation. This would increase the volume of the terminal bronchioles without increasing the area available for gas exchange. This would also cause an increase in volume for FRC since there would be a larger volume left in the lung after a normal expiration. Higgins (1917) suspected that alcohol would cause a

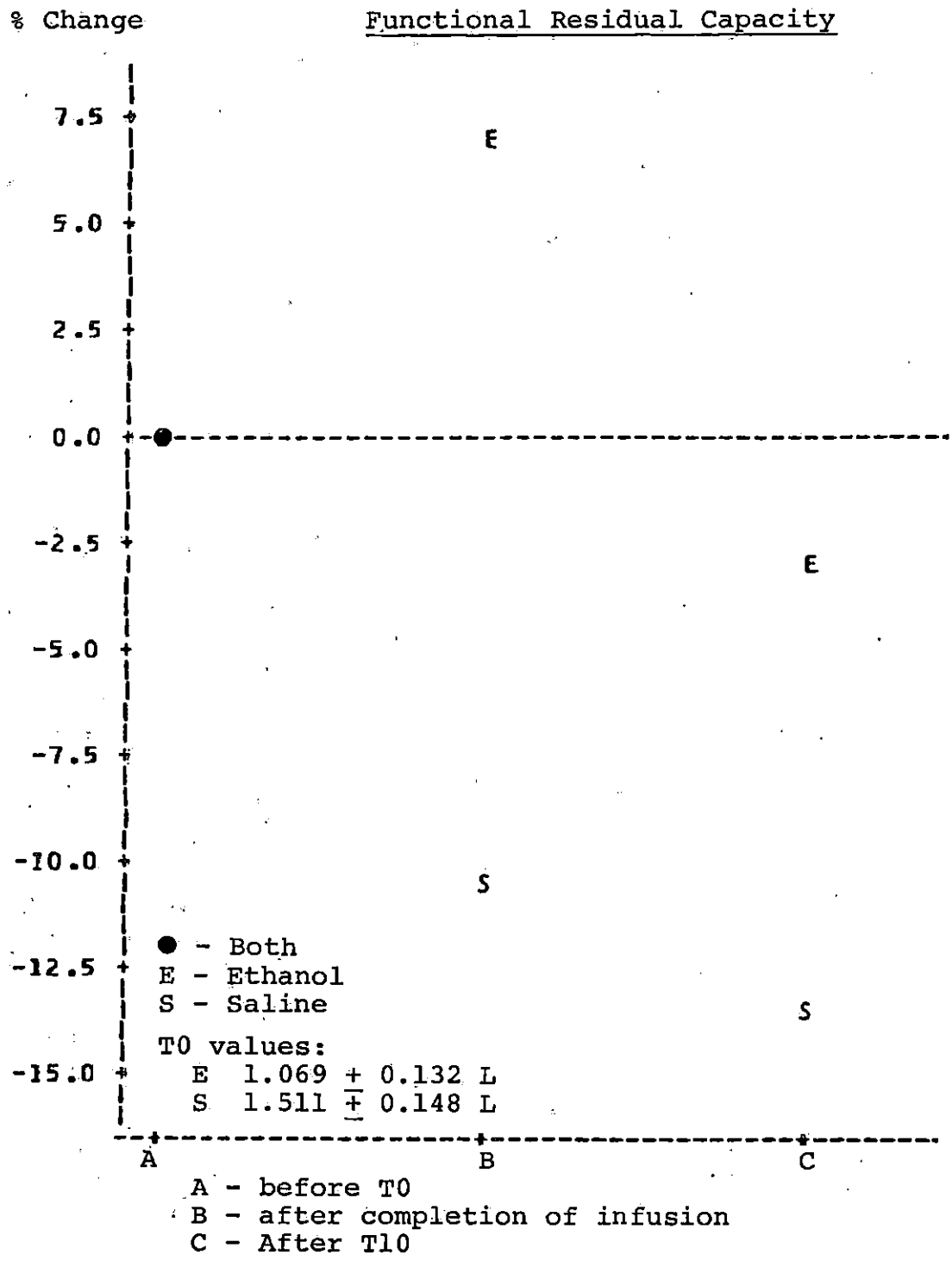


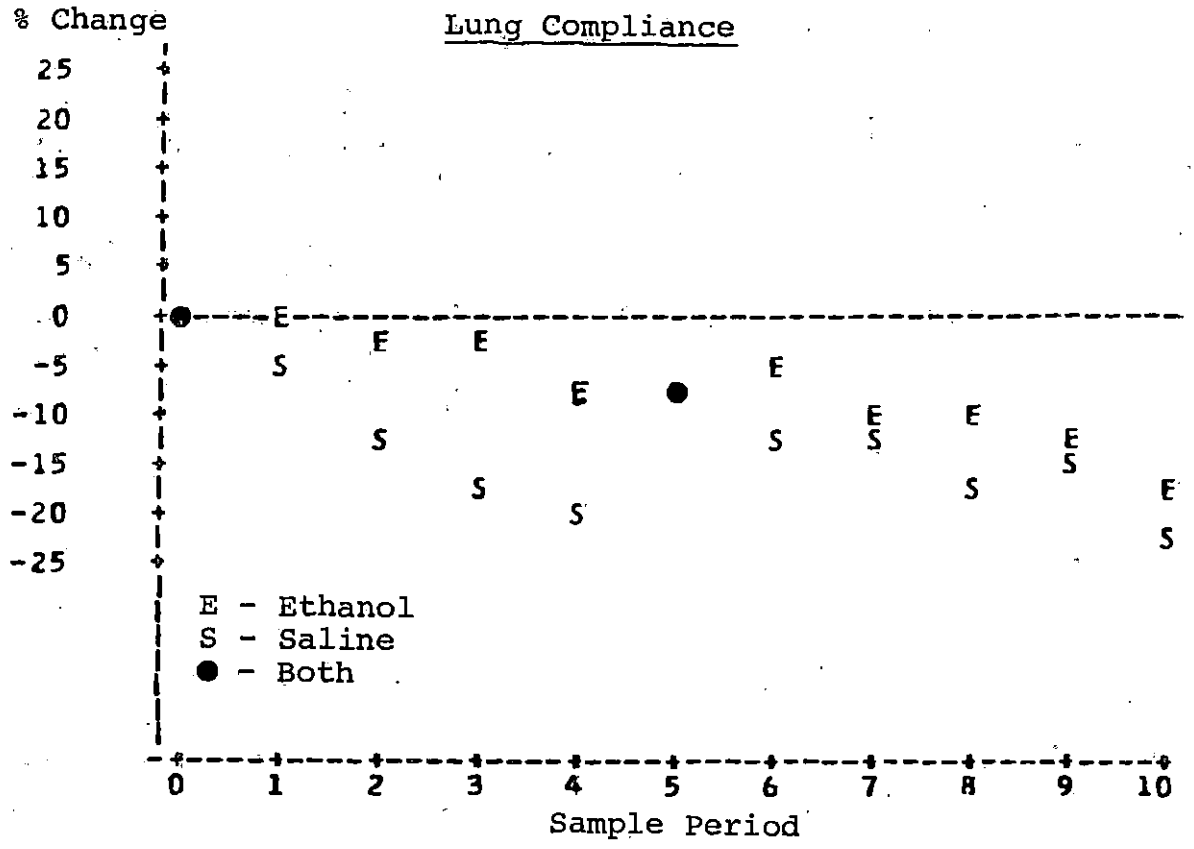
Figure 8. Percent change in functional residual capacity (FRC)

bronchoconstriction, and a consequent decrease in V_{ds}. His experiments revealed no tendency for a decrease in V_{ds}, but he observed an occasional increase in V_{ds} in response to an oral dose of alcohol in humans, indicating a bronchodilitation. Johnstone and Rier (1973) also reported values that indicated increases in V_{ds} could be linked with BEC, though the changes were not statistically significant. These findings support their reports.

Pulmonary mechanics

Measurement of C_L gives an indication of the changes in lung tissue elasticity. The calculated value for C_L depends on V_T and the esophageal pressure at that volume (P_{esT}). Figure 7 shows that C_L tends to decrease in both groups over the course of the experiment. For this to occur, either a larger subatmospheric pressure is required to inspire the same volume of air or a smaller volume requires the same pressure. In any case, a decrease in C_L indicates an increase in elastic resistance which could be due to a possible interstitial edema or decrease in the surface active material present in the alveoli. Changes in C_L reflect physiological changes at the alveolar level. As seen in Figure 9, there is little indication of any differences in response that can be attributed to the ethanol treatment.

Resistance (R) is a measurement of how much effort is



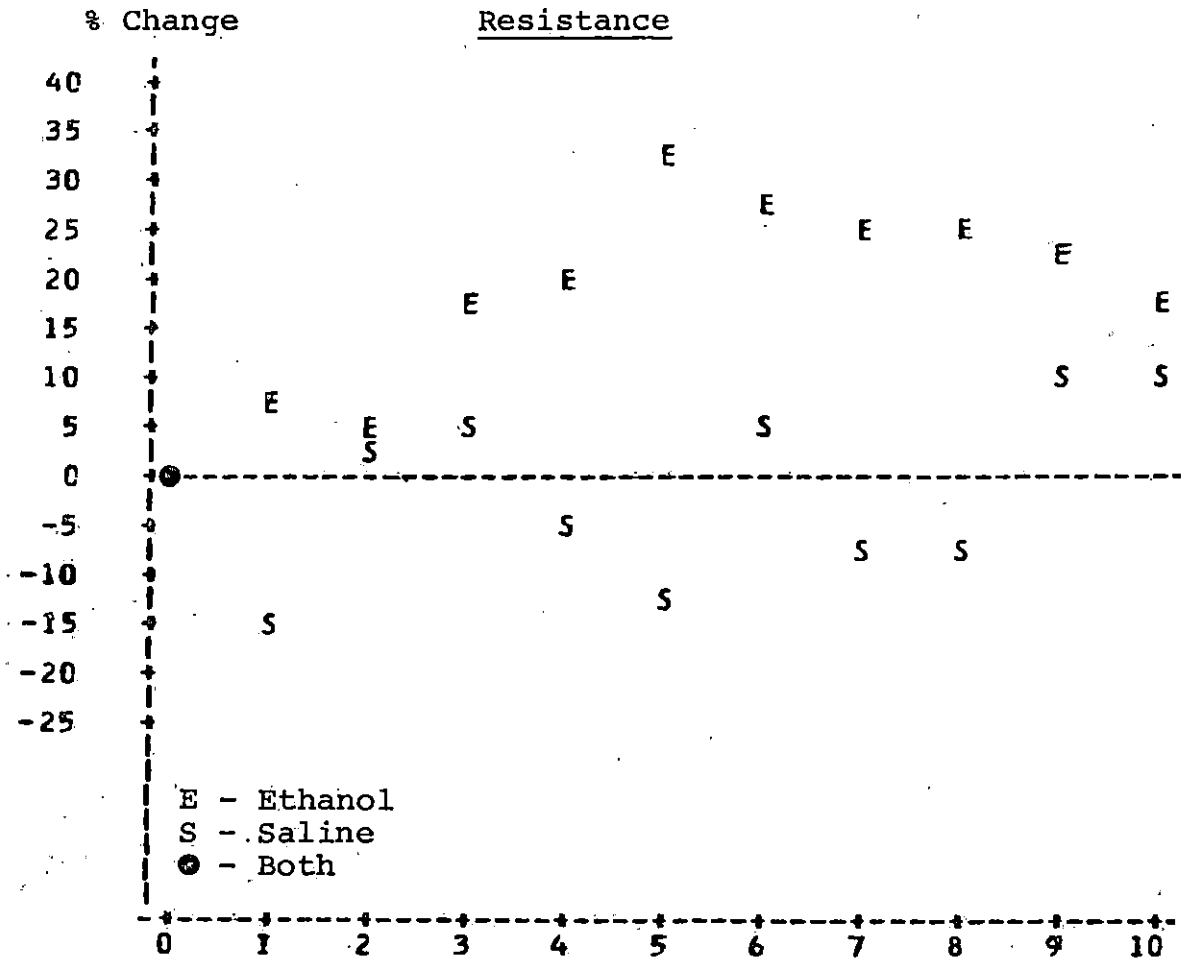
T0 values:
E 0.062 ± 0.012 L/cm H_2O
S 0.001 ± 0.012 L/cm H_2O

Figure 9. Percent change in lung compliance (C_L)

required to move air through the airways. Its calculation depends on airflow (F) and the esophageal pressure due to resistance (P_{esR}). An increase in R, with C_L remaining constant, is due to either a reduction of F, with P_{esR} remaining constant or a larger P_{esR} required to induce the same F.

As can be seen from Figure 10, there is a great deal of variability in the measurement for R. This is due to a low number of subjects with recordings that could be used for calculation of R. There seems to be little tendency for the Group II animals to show a consistent deviation from the control values. The Group I dogs show a very consistent increasing trend to a peak at T5 (33.7 $\pm$ 9.5 percent) and thereafter declining. There is a significant trend for a difference between the two groups at T5. In addition, this increase in R seems to correlate with BEC. As can be seen from Figure 11, there is no evidence of a change in peak inspiratory flow (PIF) that could account for the change in R. Both groups show a progressive increase in PIF that peaks at T10. There is no indication of any difference between the two groups. Though not presented here, peak expiratory flows (PEF) mimicked PIF.

A possible explanation for an increase in R would be a constriction of the upper airways. A very small decrease in airway diameter can cause large increases in R.

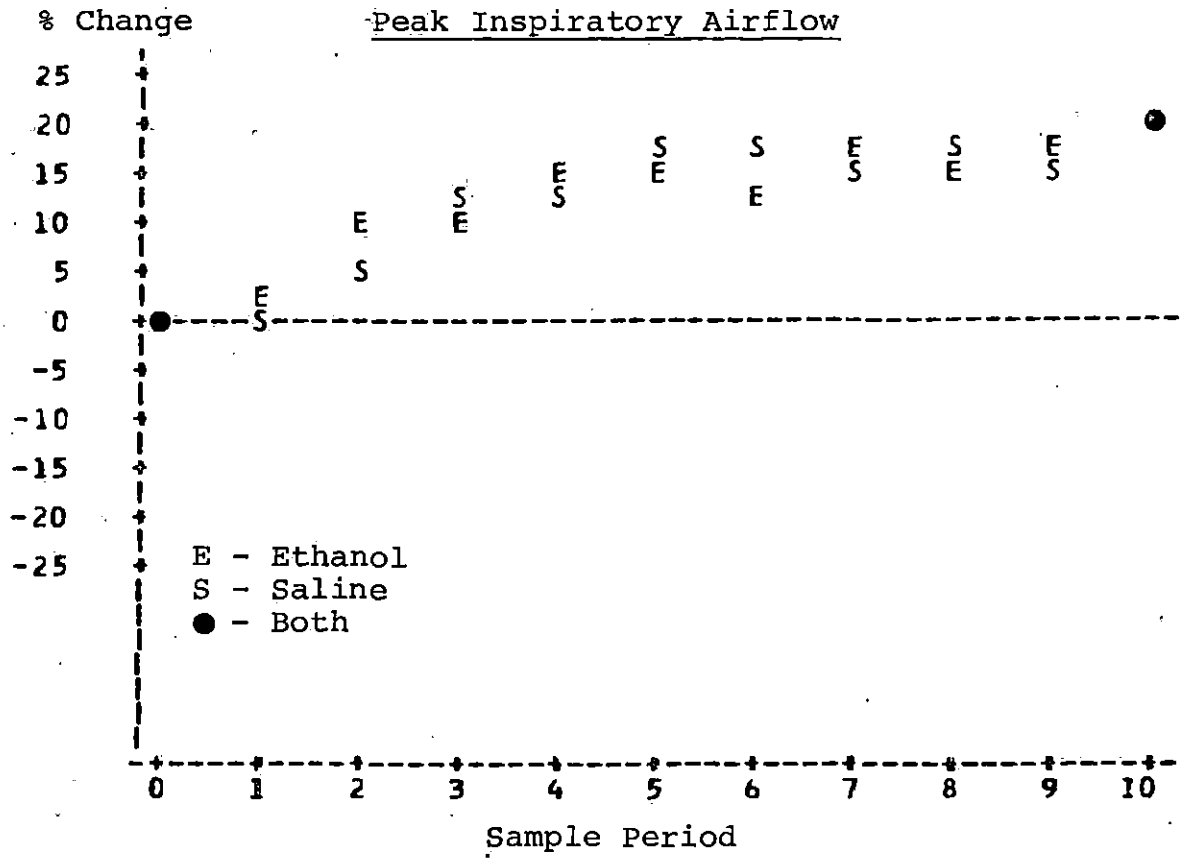


T0 values:

E 7.058 ± 0.880 cm H_2O/L/sec

S 7.584 ± 2.276 cm H_2O/L/sec

Figure 10. Percent change in resistance (R) measured at peak inspiratory airflow



T0 values:

E 0.368 ± 0.022 L/sec

S 0.429 ± 0.014 L/sec

Figure 11. Percent change in peak inspiratory airflow (PIF)

Most of the measurements of pulmonary mechanics in the literature require voluntary cooperation by the subject. Thus, it is difficult to compare these values taken during passive breathing. However, it is pertinent to note that Emergil et al. (1974) reported a reduction of Maximal Mid-Expiratory Flow (MMF) in chronic alcoholics.

Respiratory parameter interaction

None of the systems discussed, i.e., ventilation, lung volumes, or lung mechanics operate independently. Changes in one set of parameters will affect all the other parameters. Some of this interaction is illustrated in the following figures.

Figure 12 is a composite of the Group I changes in f, R, V_T, and C_L. The same parameters for Group II are presented in Figure 13. The most obvious differences between the two groups are in the plots for f and R. These changes reflect changes in V_T and C_L.

The normal response to an increased R is a reduced f and increased V_T. The normal response to a decrease in C_L is an increase in f with a reduction in V_T. These changes minimize the work needed to maintain a normal ventilation; either slower, deeper breaths or faster, more shallow breaths, depending on which will minimize the work of breathing.

In the Group I dogs, there is a moderate decrease in C_L.

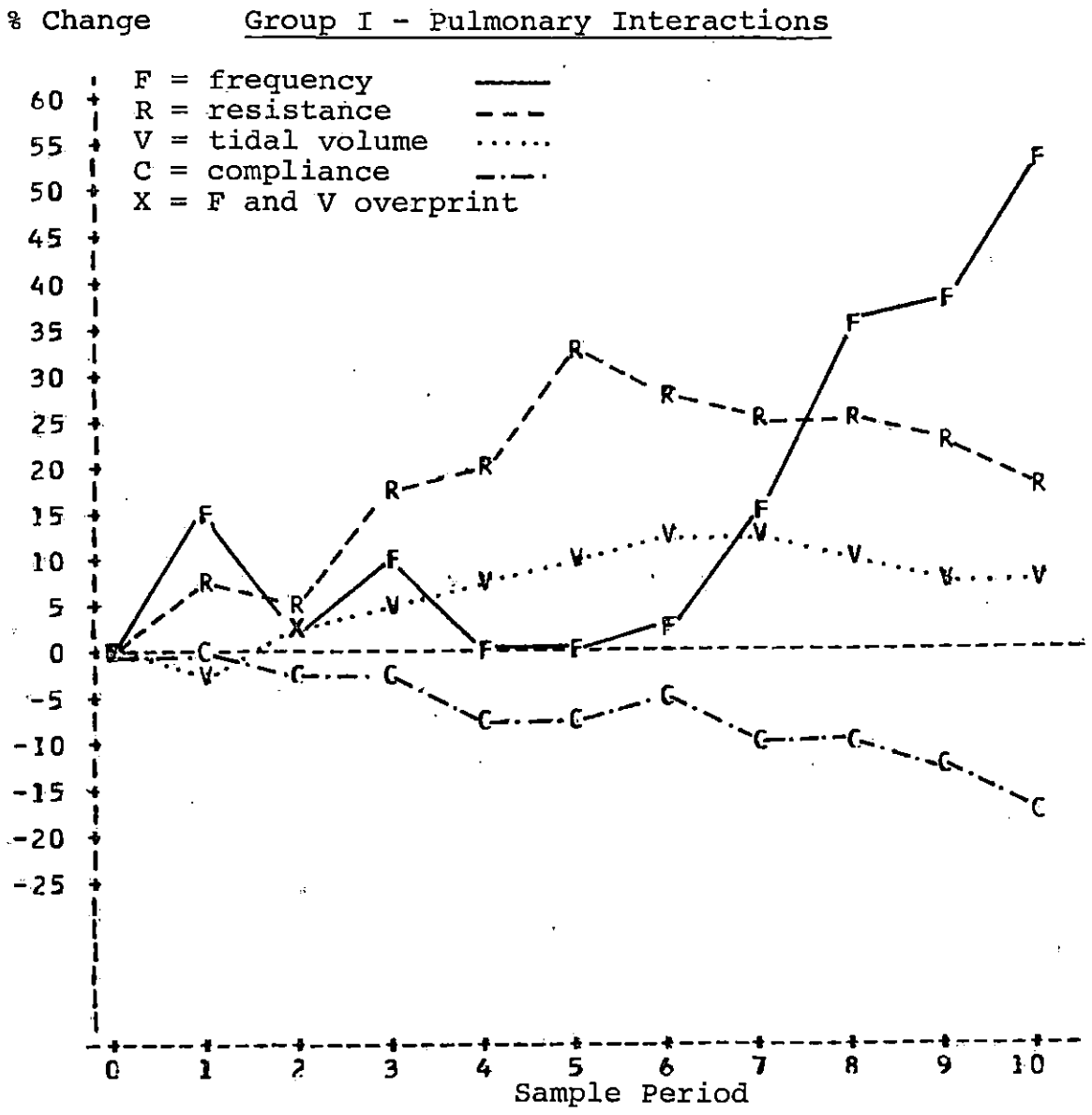


Figure 12. Composite of the percent change in respiratory frequency, airway resistance, tidal volume and lung compliance for the ethanol infused treatment group

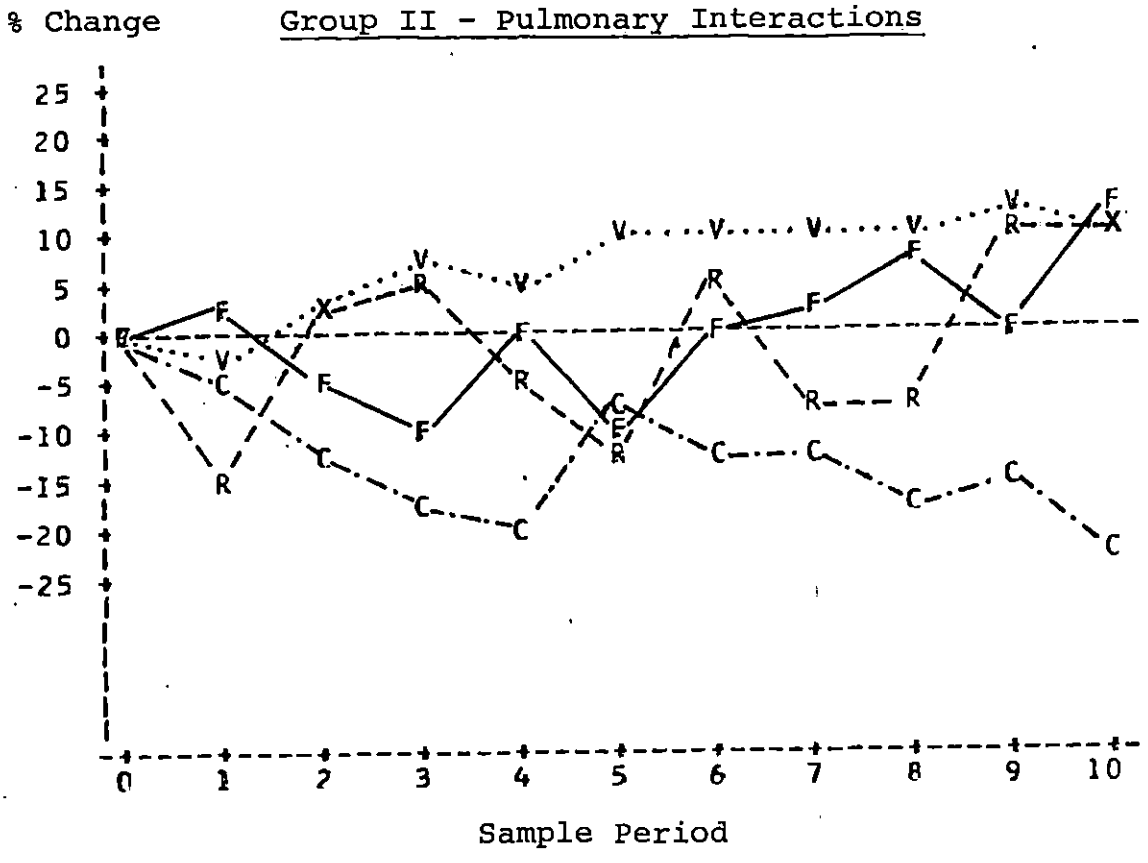


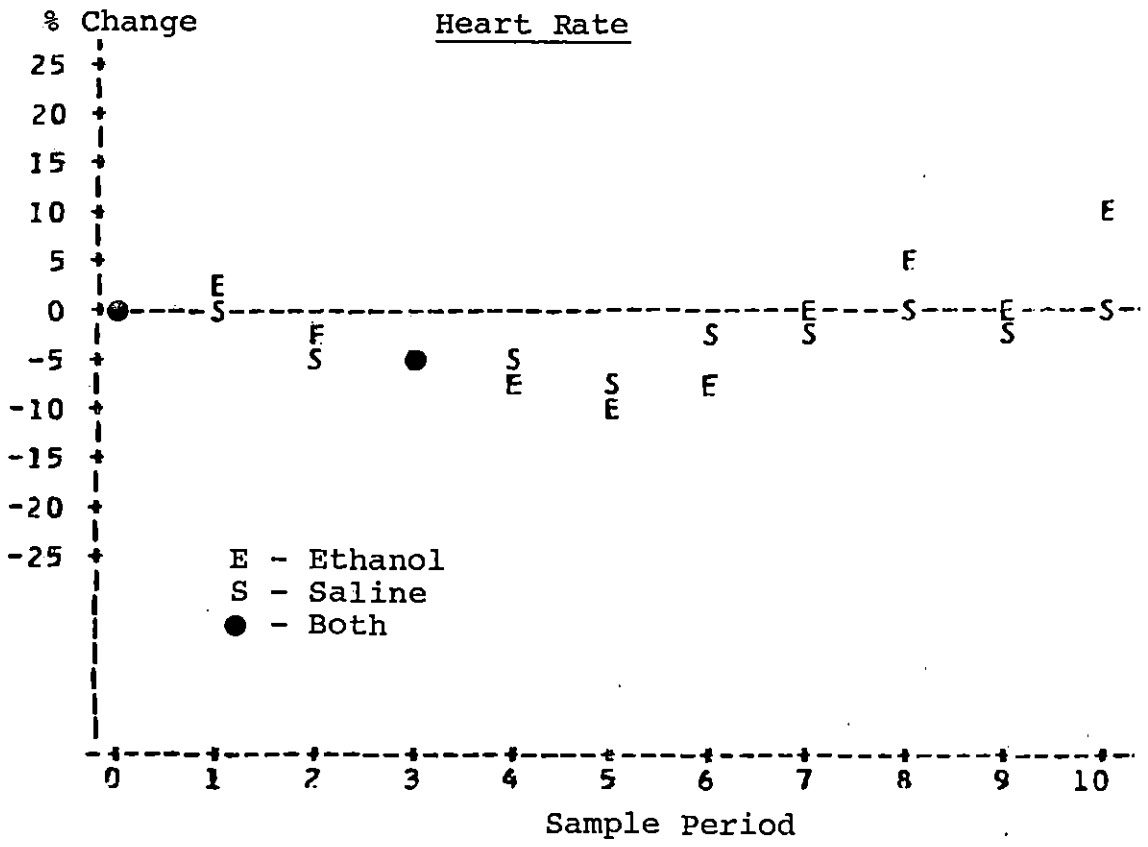
Figure 13. Composite of the percent change in respiratory frequency, airway resistance, tidal volume, and lung compliance for the saline infused treatment group

There is also a large increase in R. The normal increase in f that could be expected with a decreased C_L is suppressed by large increases in R. If f was increased, it would take even more energy since R is increased. It is interesting to note that only after R begins to decrease does f increase in response to decreasing C_L. The response to these changes in R and C_L is not entirely clear, but it is fairly consistent.

The Group II responses are less well-defined. With no apparent increase in R, one would expect an increased f and decreased V_T in response to the decreased C_L. In fact, there is no such pattern. Some of the problem may be due to the low number (n=3) of recordings available for calculation of R and C_L in Group II.

Cardiovascular Effects

An assessment of some of the cardiovascular effects of the ethanol treatment was provided by measurement of heart rate, cardiac output, and arterial blood pressures. Figure 14 shows that the heart rate (HR) changed very little over the experimental period with no differences between the two experimental groups. This would be expected at these low BEC levels. Nakano and Kessinger (1972) showed that doses of ethanol less than 100 mg/dL given intravenously to dogs would cause moderate increase in HR, but the bulk of the



T0 values:
E 137 ± 15 beats/min
S 157 ± 10 beats/min

Figure 14. Percent change in heart rate (HR)

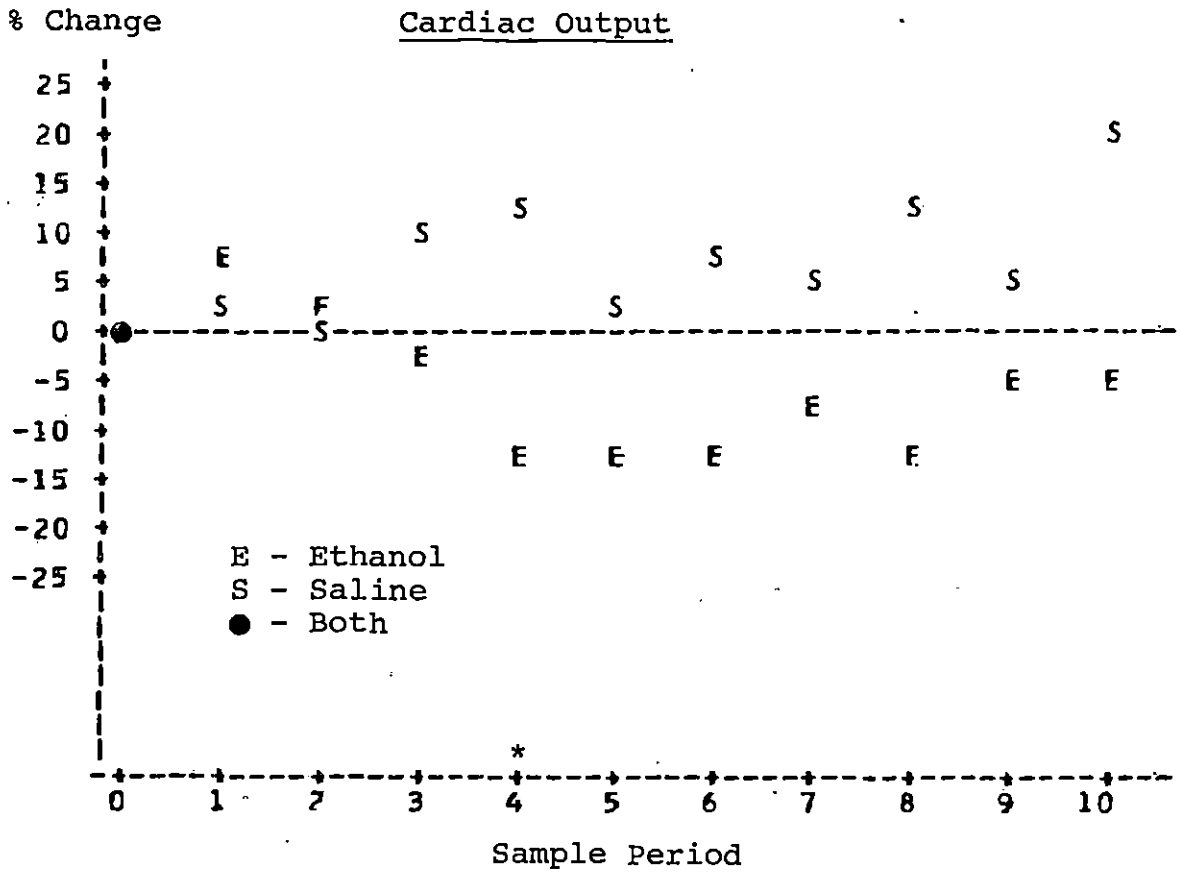
work they reported dealt with much higher ethanol levels. Those higher levels lead to decreases in HR.

The plot of cardiac output ($\dot{Q}$) in Figure 15 shows that the saline infused dogs have a slight tendency towards an increased $\dot{Q}$ over the experimental period, while the ethanol treated animals show a trend towards a decreased $\dot{Q}$ after an initial increase. Since this is not associated with any reduction in heart rate, it is logical to assume a reduction in stroke volume.

As can be seen in Figure 16, systolic arterial blood pressure (SAP) shows only a slight increase in both groups during the experiment. The increase in diastolic arterial blood pressures (DAP)(Figure 17), was slightly greater. However, there is a trend for the ethanol treated group to show slightly larger increases in systolic and diastolic pressures. The significance of the changes is uncertain. Doekel et al. (1978) reported no changes in either $\dot{Q}$ or SAP during intravenous injection of ethanol in dogs. Because of the small magnitude of the changes noted here, these results can neither confirm or refute their findings.

Ventilation-Perfusion

Ventilation-perfusion relationships illustrate how blood flow is matched to lung ventilation. Any changes in this relationship can be assessed by measuring shifts in the $\dot{V}_A$ to



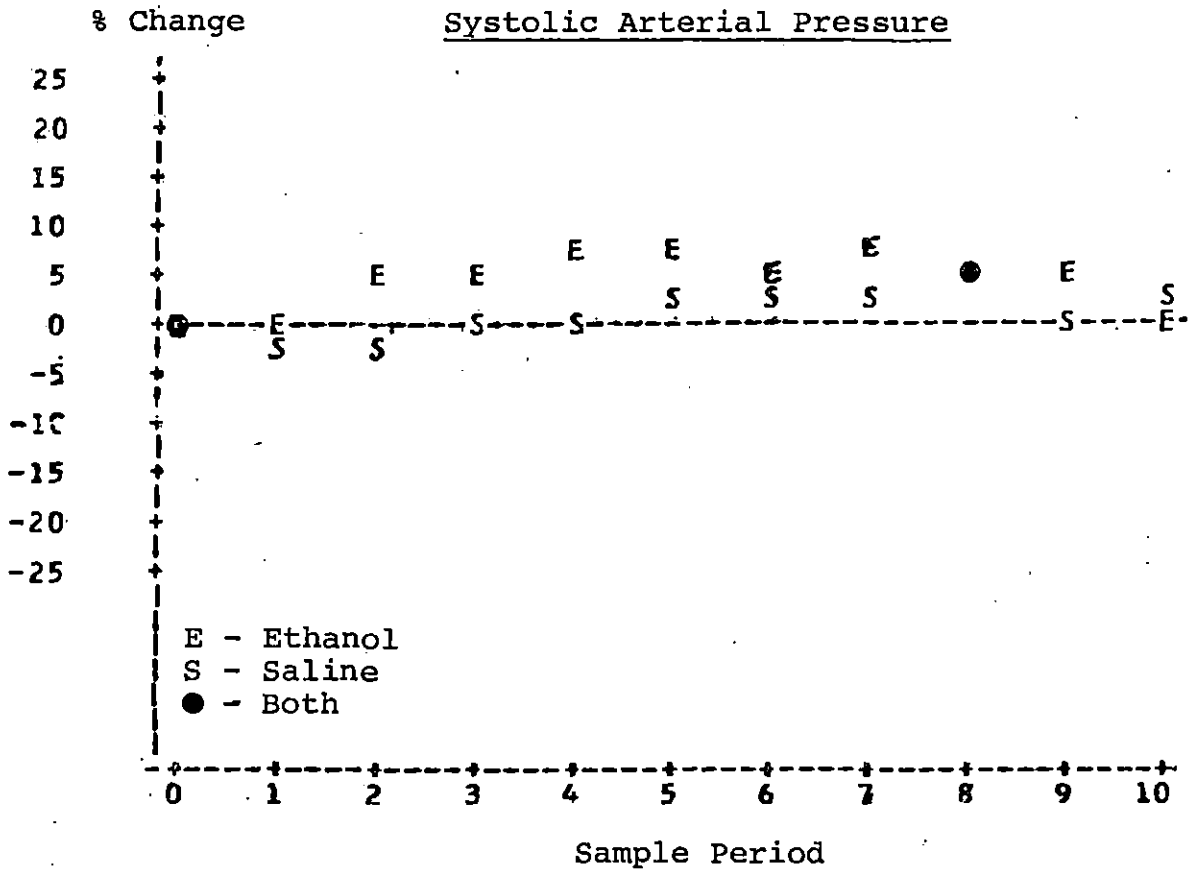
T0 values:

E 5.340 ± 0.786 L/min

S 4.623 ± 0.600 L/min

*p<.01.

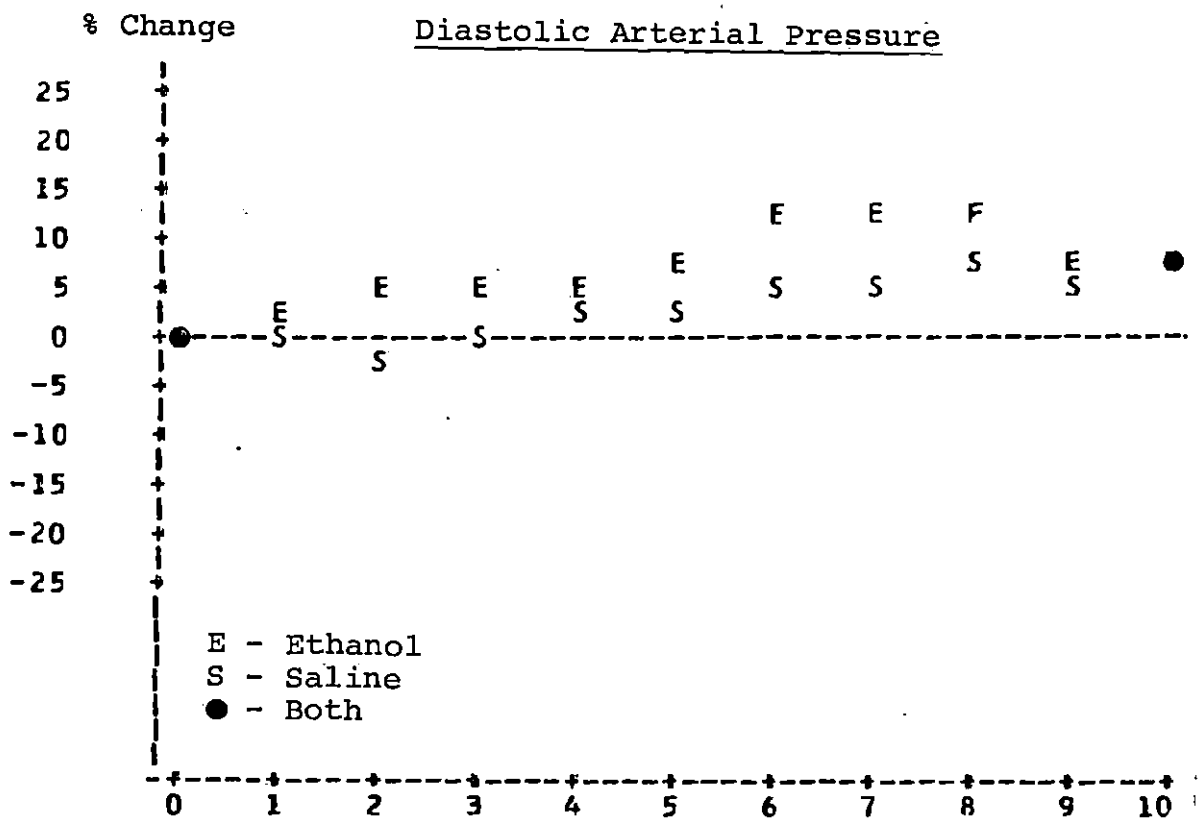
Figure 15. Percent change in cardiac output ($\dot{Q}$)



T0 values:

E 143 ± 3 mm Hg
S 147 ± 7 mm Hg

Figure 16. Percent change in systolic arterial blood pressure (SAP)



T0 values:

E 111 ± 3 mm Hg

S 120 ± 2 mm Hg

Figure 17. Diastolic arterial blood pressure (DAP)

$\dot{Q}$ ratio ($\dot{V}A/\dot{Q}$) or the physiological shunt ($\dot{Q}s/\dot{Q}t$).

Figure 18 shows how $\dot{V}A/\dot{Q}$ changes over the experimental period. Although both groups show a generally increasing $\dot{V}A/\dot{Q}$, it is evident that the ethanol treated group shows a much larger increase. There are statistically significant differences between the two groups at several sample periods. This increased $\dot{V}A/\dot{Q}$ is the result of the increased $\dot{V}_A$ and decreased $\dot{Q}$ already discussed. Either of these changes would tend to increase $\dot{V}A/\dot{Q}$, together, they cause a very clear change. It is impossible to determine if this change in $\dot{V}A/\dot{Q}$ for the total lung is an accurate reflection of the regional changes in $\dot{V}A/\dot{Q}$. There is a good possibility that there are substantial shifts in the regional $\dot{V}A/\dot{Q}$ ratios based on the evidence provided by V_{ds} and FRC.

Increased V_{ds} indicates that more of the ventilation is not being used for gas exchange. The increase in FRC indicates that there is more air left in the lung after a normal expiration. This would mean that the animal is breathing off the "top" of the lung, where blood flow does not match ventilation as well.

Further evidence for this theory is provided by the plot of $\dot{Q}s/\dot{Q}t$ in Figure 19. There is a general increase in $\dot{Q}s/\dot{Q}t$ in both experimental groups. It is apparent that there is little difference between the two groups. It is interesting to note that the Group I dogs were consistently

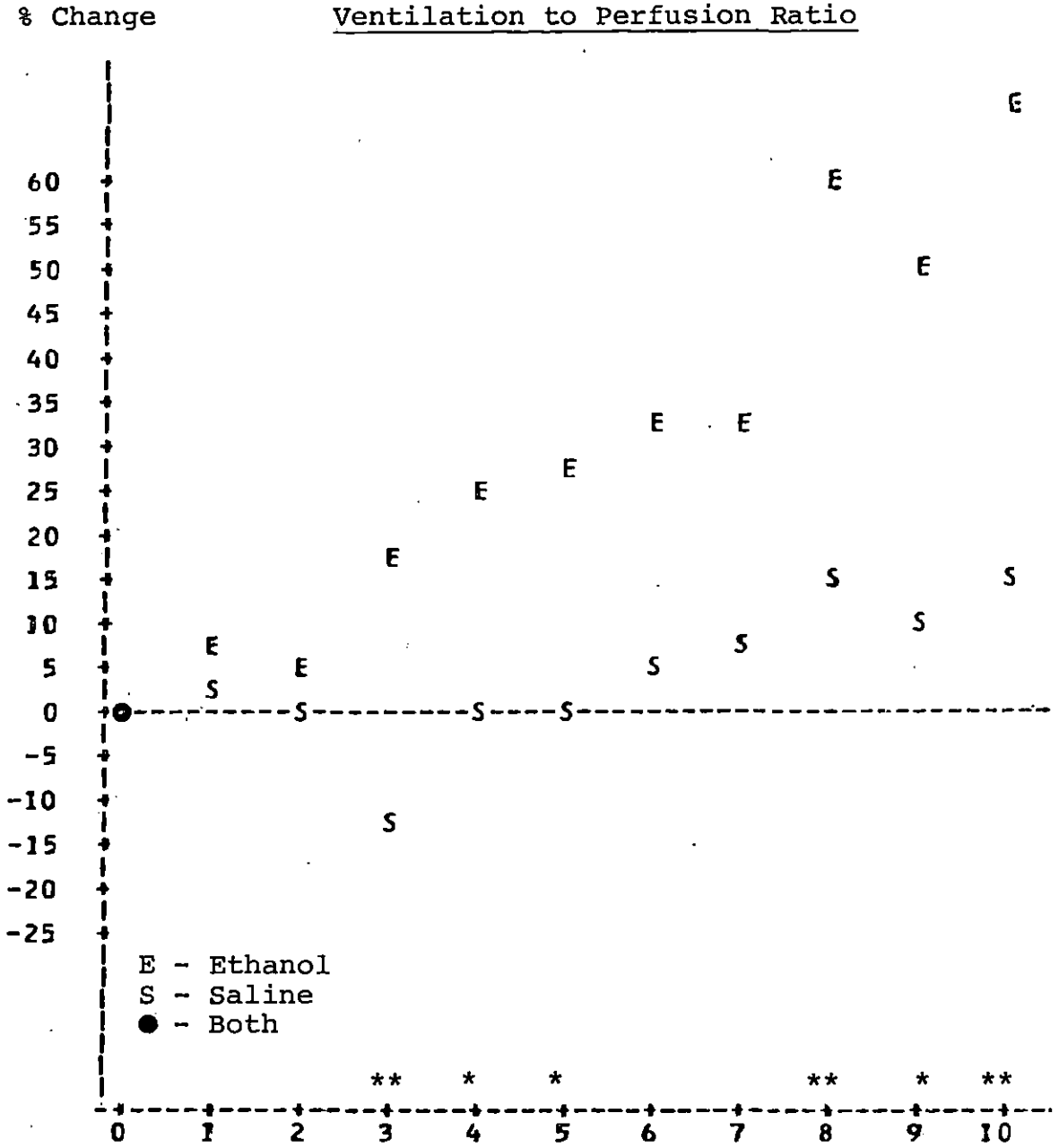
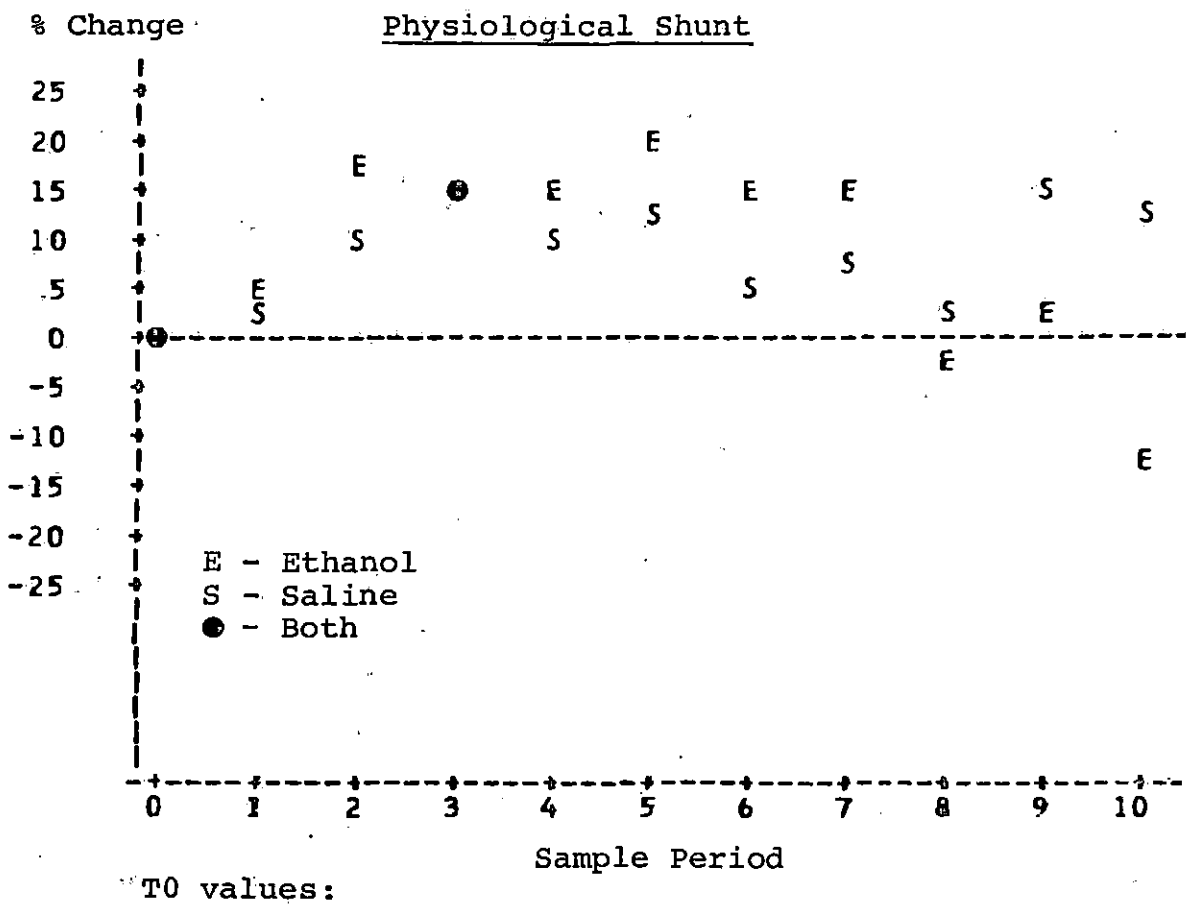


Figure 18. Percent change in the ventilation to perfusion ratio ($\dot{V}A/\dot{Q}$)



T0 values:

E 0.376 ± 0.046

S 0.256 ± 0.029

Figure 19. Percent change in physiological shunt ($\dot{Q}s/\dot{Q}t$)

above the Group II animals. This difference is not large and certainly not statistically significant, but the trend could certainly be physiologically significant.

An increased $\dot{Q}s/\dot{Q}t$ would indicate an increase in the amount of blood that passes through the lung without being oxygenated, or being less oxygenated. Such a shift could possibly be caused by changes in regional shunt relationships. Prolonged dorsal recumbency tends to decrease the ventilation to the dependent portions of the lung. Blood passing through these portions of the lung would be poorly oxygenated. Evidence supporting the possibility of a change in ventilation rather than a change in blood flow is provided by the changes in $\dot{Q}s/\dot{Q}t$ after T7. The reduced shunt seen corresponds to the increased $\dot{V}_A$ already discussed. This increased ventilation would tend to ventilate the entire lung more evenly, reducing any existing shunt. The evidence presented tends to support a change in regional ventilation. Reduced $\dot{Q}$ would tend to intensify the consequences of this shift.

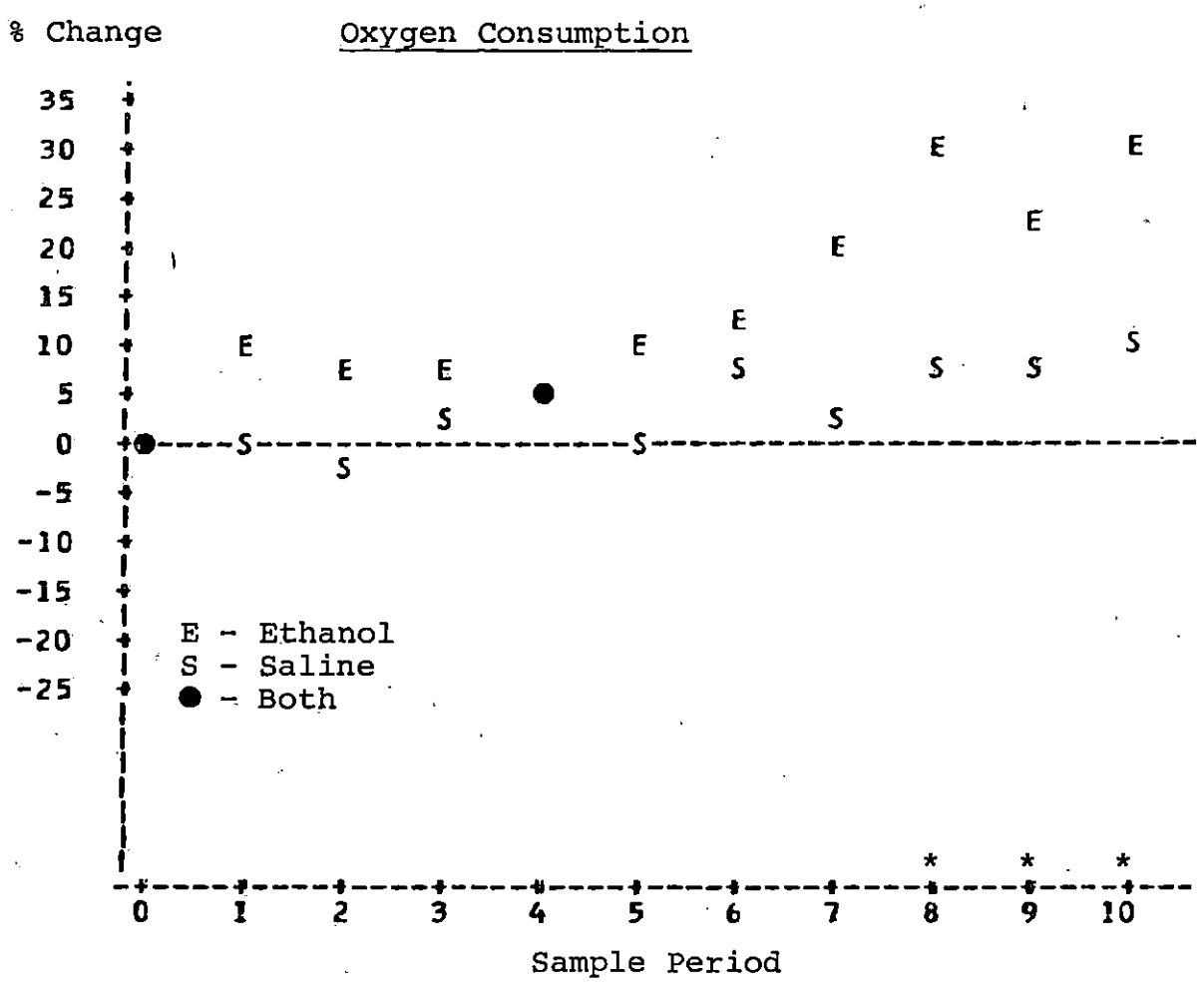
Basal Metabolism

The only measurement of metabolic rate available in this experiment is rate of oxygen uptake ($\dot{V}O_2$). This can be used along with $\dot{V}_{CO_2}$ to calculate the respiratory quotient ($RQ = \dot{V}CO_2/\dot{V}O_2$). These measurements determine how an animal's

metabolism or metabolic rate responds to a treatment.

Figure 20 shows that $\dot{V}O_2$ increases over the course of the experiment in both groups. The values indicate a significant trend for a difference between the two groups at the last three sample periods. This difference is puzzling. The most likely explanation is that the increased $\dot{V}O_2$ is due to the increased $\dot{V}_A$ and f also seen during these time periods. In other words, is the increase $\dot{V}O_2$ due to the increased work of breathing? This may be a reasonable explanation considering the increased R shown during this period. Whether this response is specifically due to the ethanol treatment is unclear. Higgins (1917) measured the $\dot{V}O_2$ in human subjects and reported inconsistent increases in $\dot{V}O_2$ in response to an oral dose of alcohol. Johnstone and Rier (1973) reported values that indicate only a slight response to an intravenous dose of alcohol.

Figure 21 shows that RQ changes very little in the Group II animals. The Group I animals tend to show a consistent decrease in RQ from the control values. The two groups show a significant trend for a difference at T6 and a statistically significant difference at T7. Thereafter, the values return to approximately control levels. This trend for reduced RQ has been reported in humans by Higgins (1917). Johnstone and Rier (1973) reported significant reduction of RQ in human subjects given a moderate intravenous dose of alcohol. This



T0 values:

E 0.133 ± 0.014 L/min

S 0.166 ± 0.020 L/min

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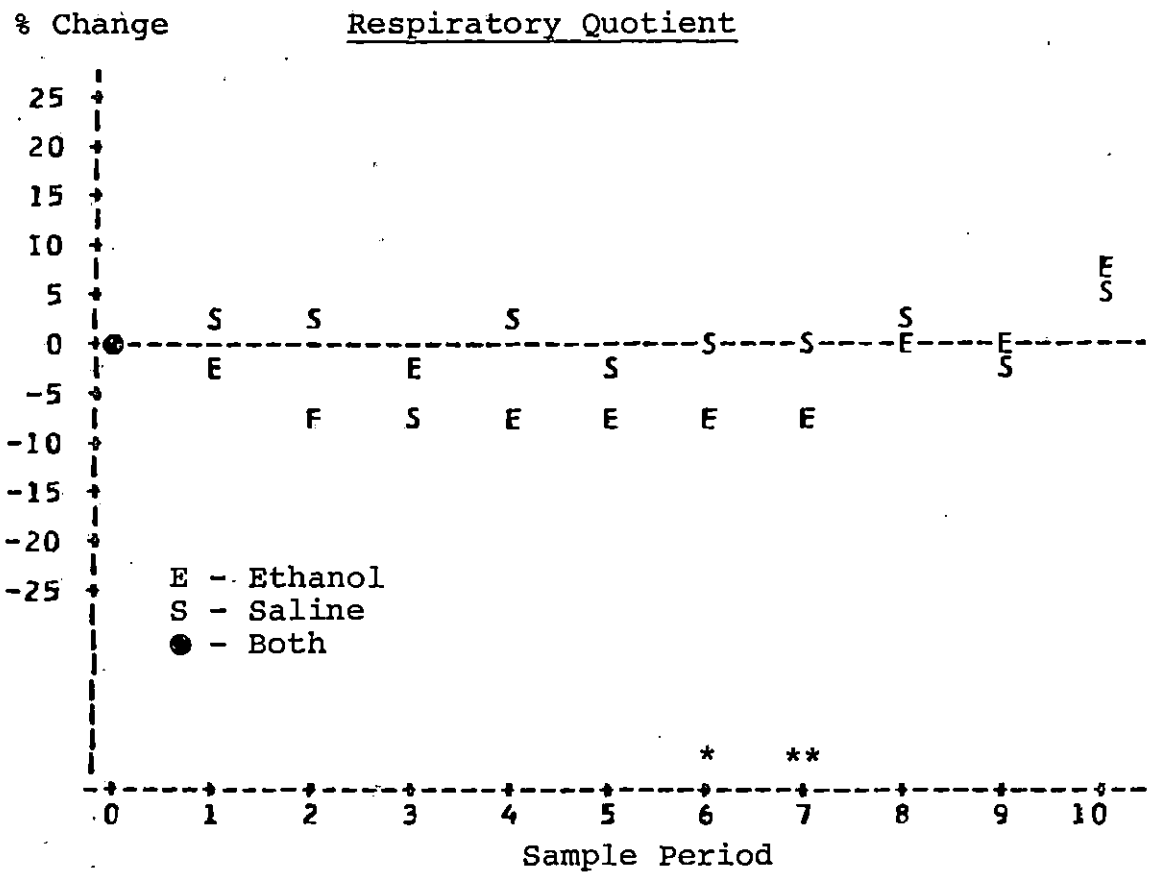
*$p<0.1$.

Figure 20. Percent change in oxygen consumption ($\dot{V}O_2$)



T0 values:

E 0.571 ± 0.048

S 0.625 ± 0.061

*p<.1.

**p<.05.

Figure 21. Percent change in respiratory quotient (RQ)

reduction of RQ may be due to the use of ethanol as an energy source rather than the normal carbohydrate or fat sources.

Blood Gas Parameters

Analysis on anaerobic arterial and mixed venous blood samples yields values for the respective blood pH, PCO_2, and PO_2 values. The hemoglobin saturation (Sat) can be calculated from a nomogram using the values for pH and PO_2. These measurements provide information on the acid-base equilibrium (pH), how well CO_2 is being removed from the blood (PCO_2), and oxygen delivered to the body (PO_2 and Sat).

Blood pH

As seen in Figures 22 and 23, both arterial and mixed venous pH values tend to increase over the experimental period. This increase becomes most marked in the latter part of the experiment. It appears that the Group I animals show a slightly reduced tendency toward increased pH compared to the group II animals. The large increases toward the end of the experiment are probably due to the increased ventilation, producing a respiratory alkalosis.

There is no evidence of any acidosis that has been reported by others. Johnstone and Witt (1972) reported a mild acidosis in patients admitted for treatment of severe

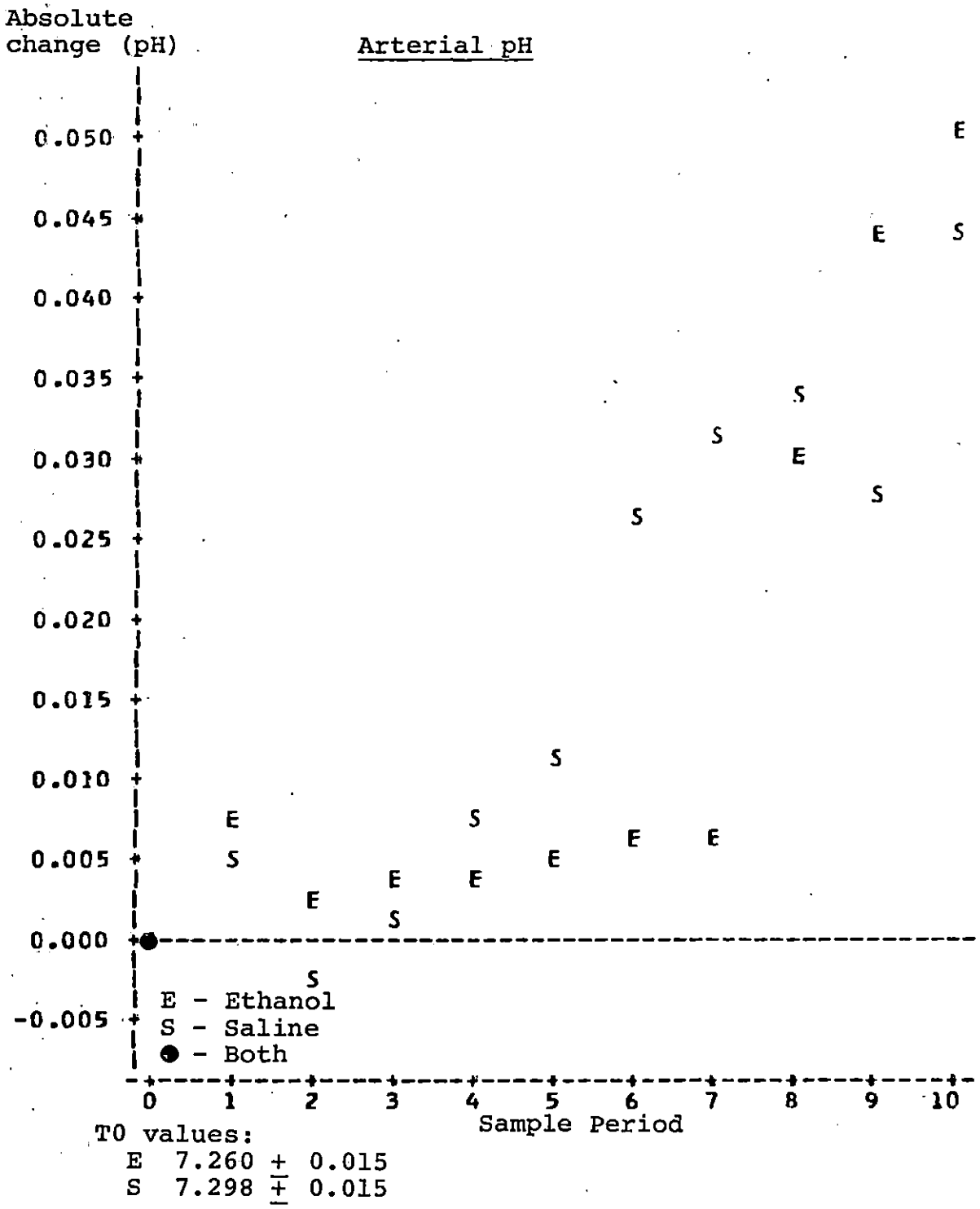


Figure 22. Absolute change in arterial pH (apH)

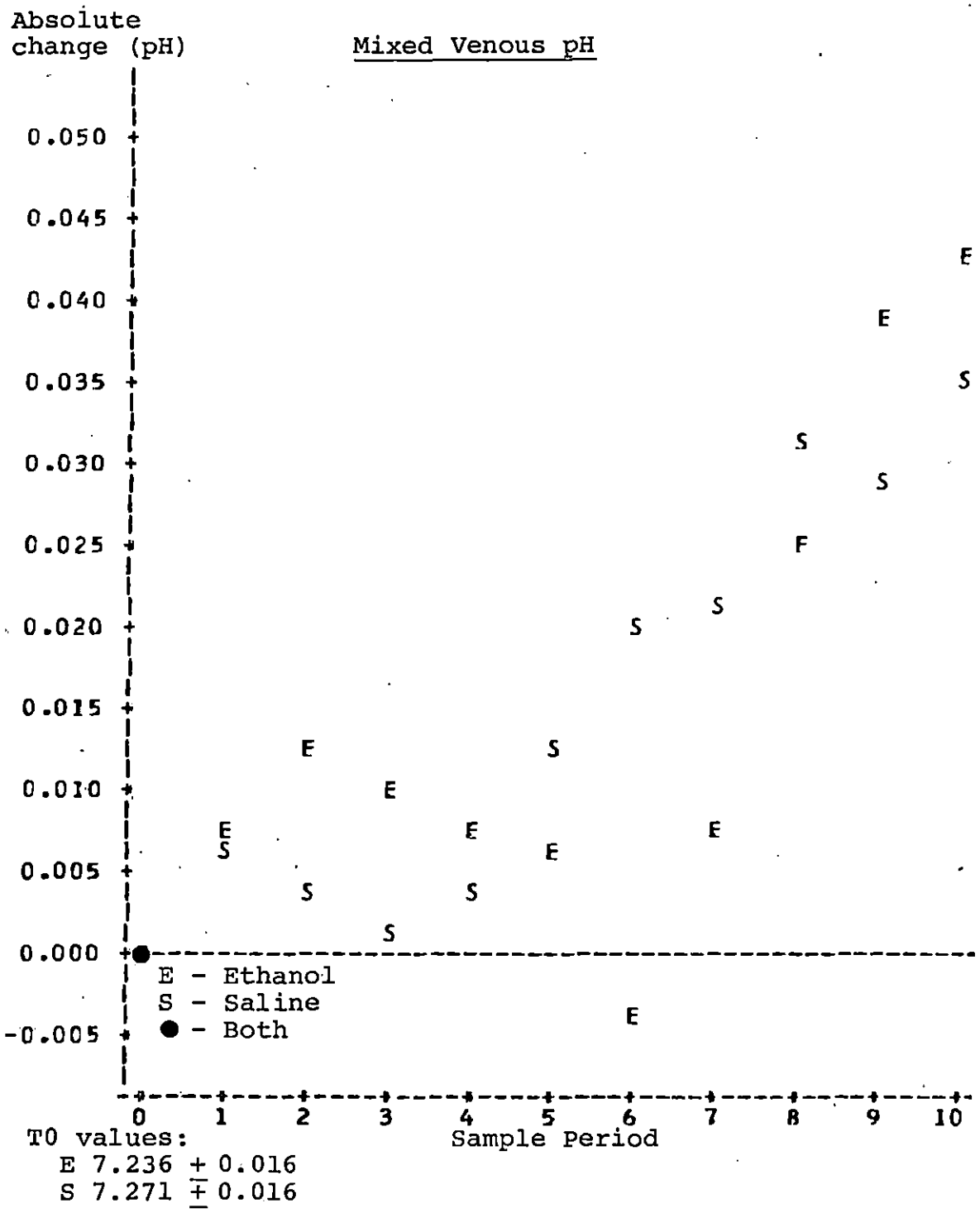


Figure 23. Absolute change in mixed venous pH ($\bar{v}$pH)

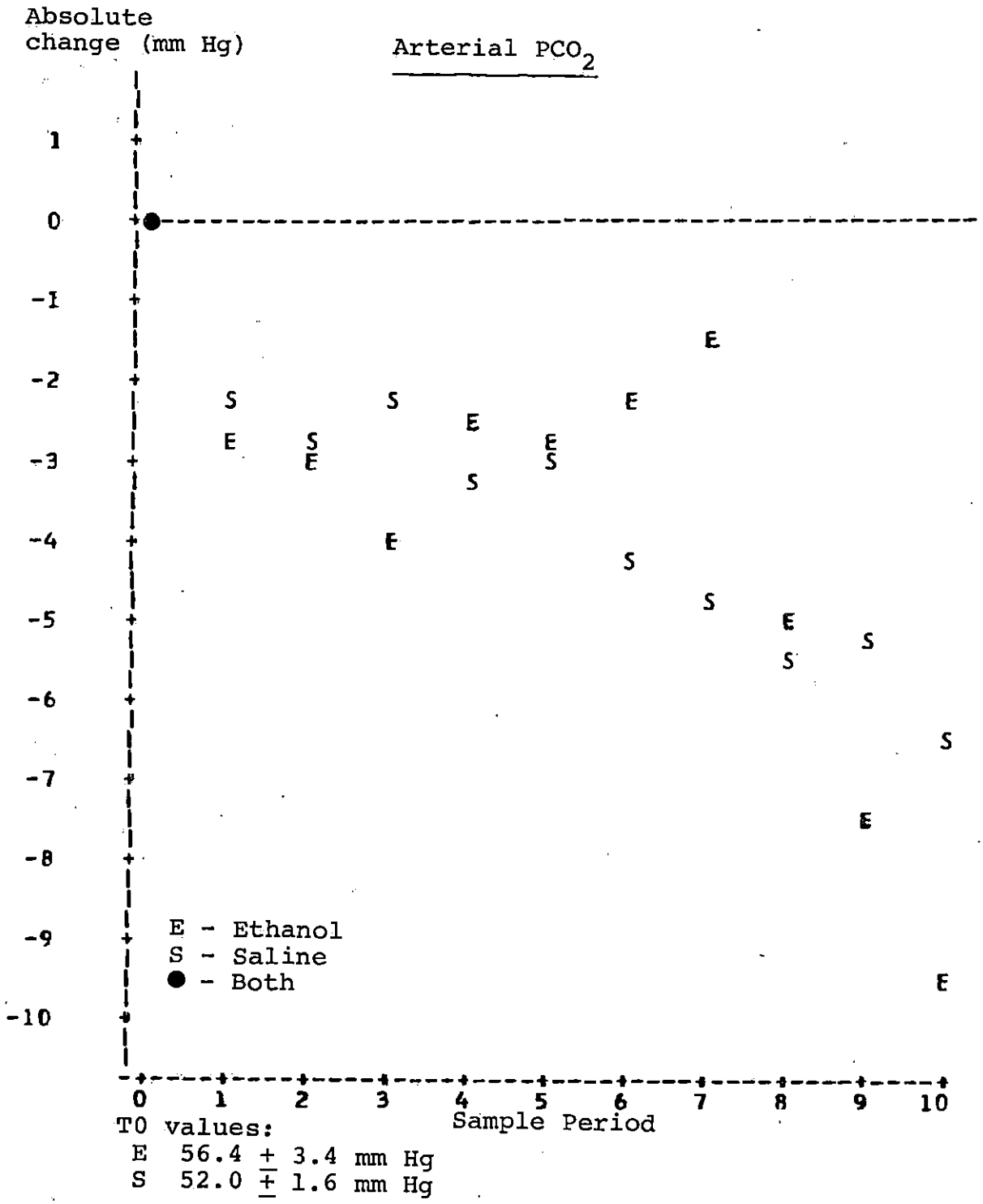
intoxication (with BEC over 250 mg/dL). Sahn et al. (1979) also reported a mild acidosis of metabolic origin in humans given a moderate oral dose of alcohol. This dose resulted in a maximum BEC of 140 mg/dL. It may be that the low BEC used in this study was simply not sufficient to cause any similar acidosis.

Blood PCO_2

As would be expected with the increase in the pH values, there was also a decrease in both the arterial and mixed venous PCO_2 as seen in Figures 24 and 25. There is little evidence of any consistent difference between the two groups. The largest decreases, seen after T6, are readily explained by the increased ventilation also seen during these periods. The increased ventilation would tend to "blow-off" CO_2. This reduction of CO_2 levels is the primary cause of the increased pH values.

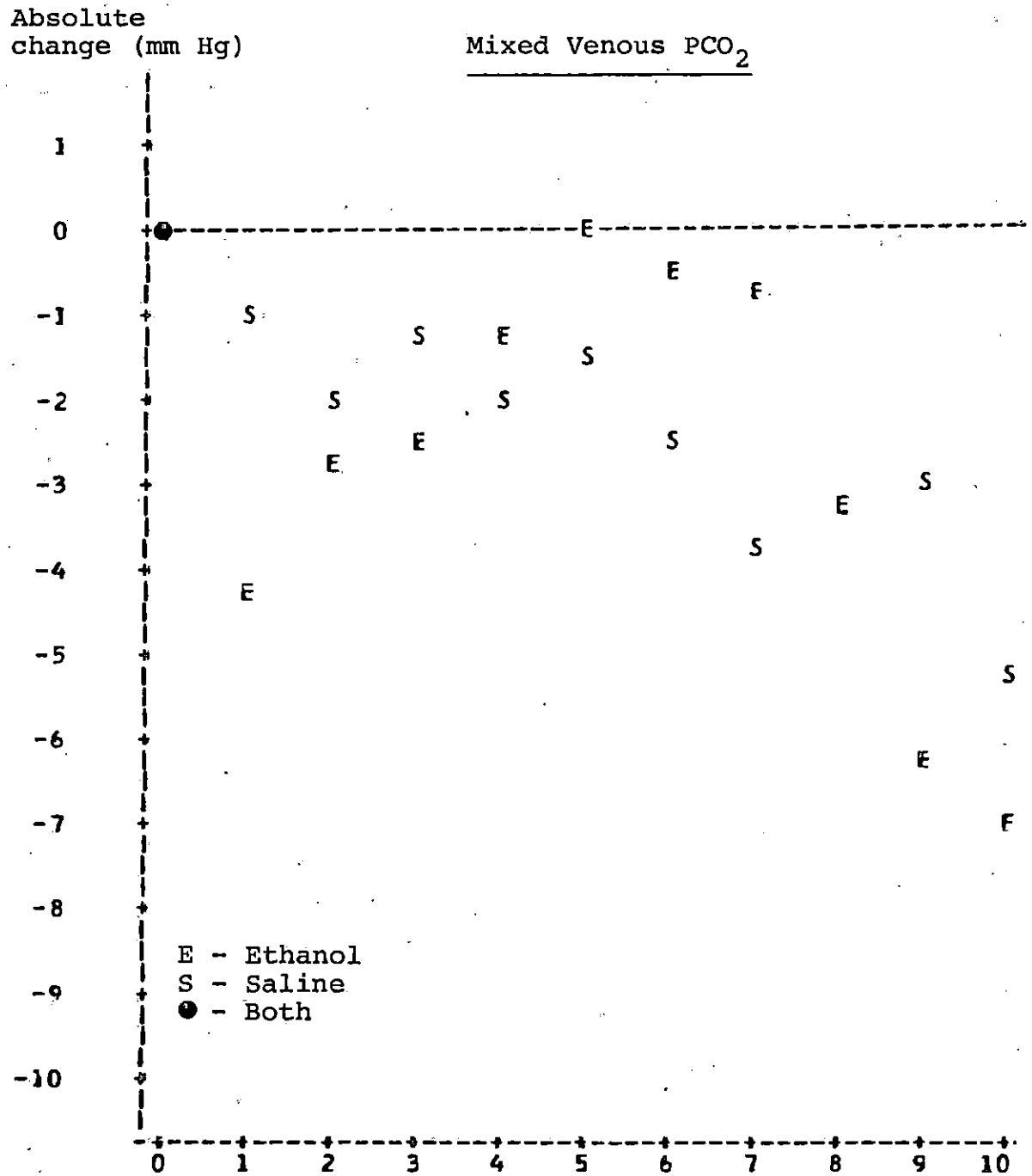
Blood PO_2

Both groups showed decreased arterial (PaO_2); Figure 26, and mixed venous ($P\bar{v}O_2$); Figure 27, PO_2 values. The Group II animals demonstrate steady, though variable reduction in PaO_2 over the entire experimental period. The Group I animals show a statistically greater decrease at T4. The maximum decrease in PaO_2 occurs at T5 in the Group I animals, and thereafter there is a reduction in this decrease. This change



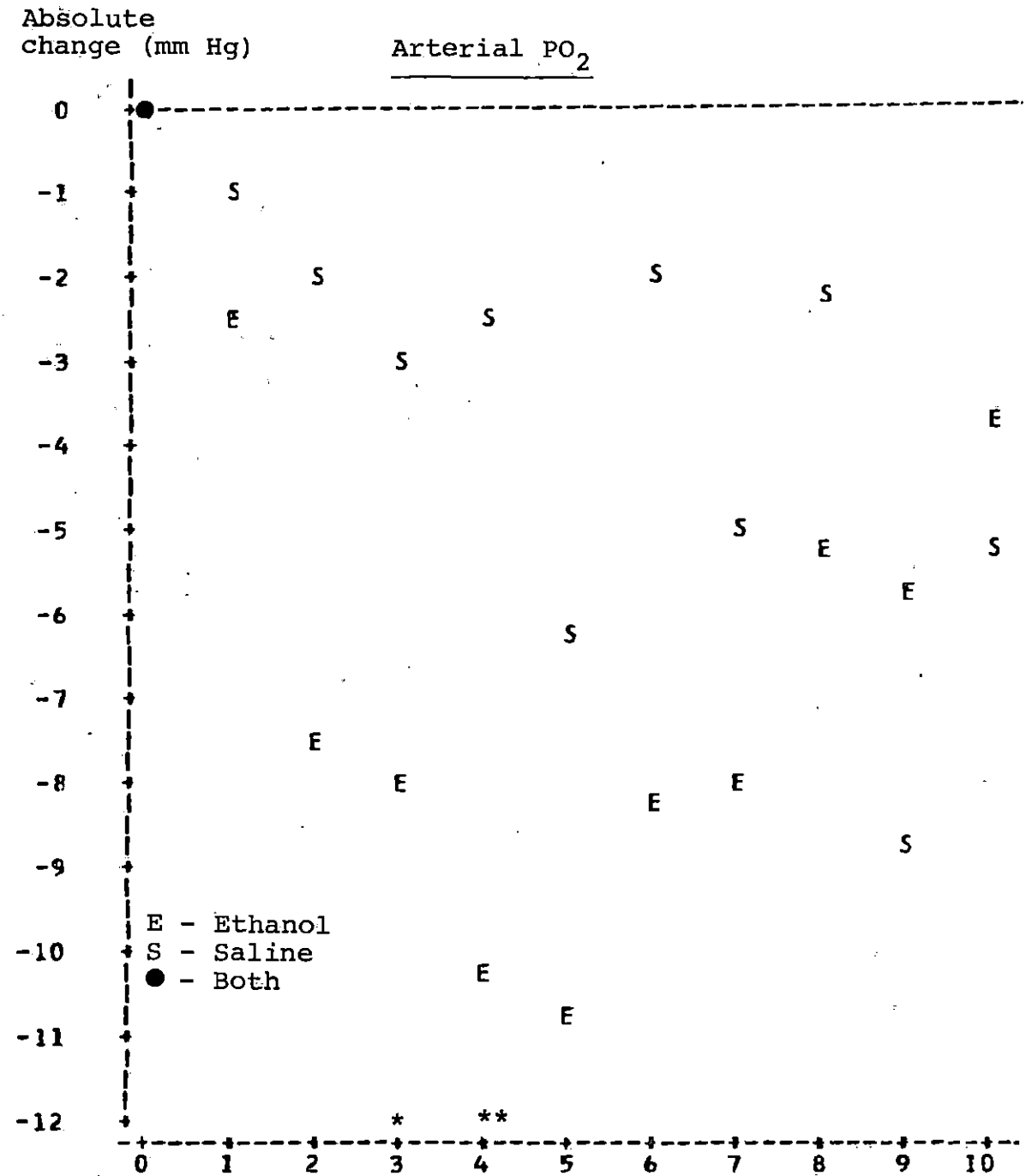
T0 values:
E 56.4 ± 3.4 mm Hg
S 52.0 ± 1.6 mm Hg

Figure 24. Absolute change in arterial PCO_2 ($PaCO_2$)



T0 values:
E 65.2 ± 3.7 mm Hg
S 60.2 ± 1.9 mm Hg

Figure 25. Absolute change in mixed venous PCO_2 ($P\bar{v}CO_2$)



To values:
E 86.9 ± 2.7 mm Hg
S 92.2 ± 3.9 mm Hg

*$p \leq .1$.
**$p \leq .05$.

Figure 26. Absolute change in arterial PO_2 (PaO_2)

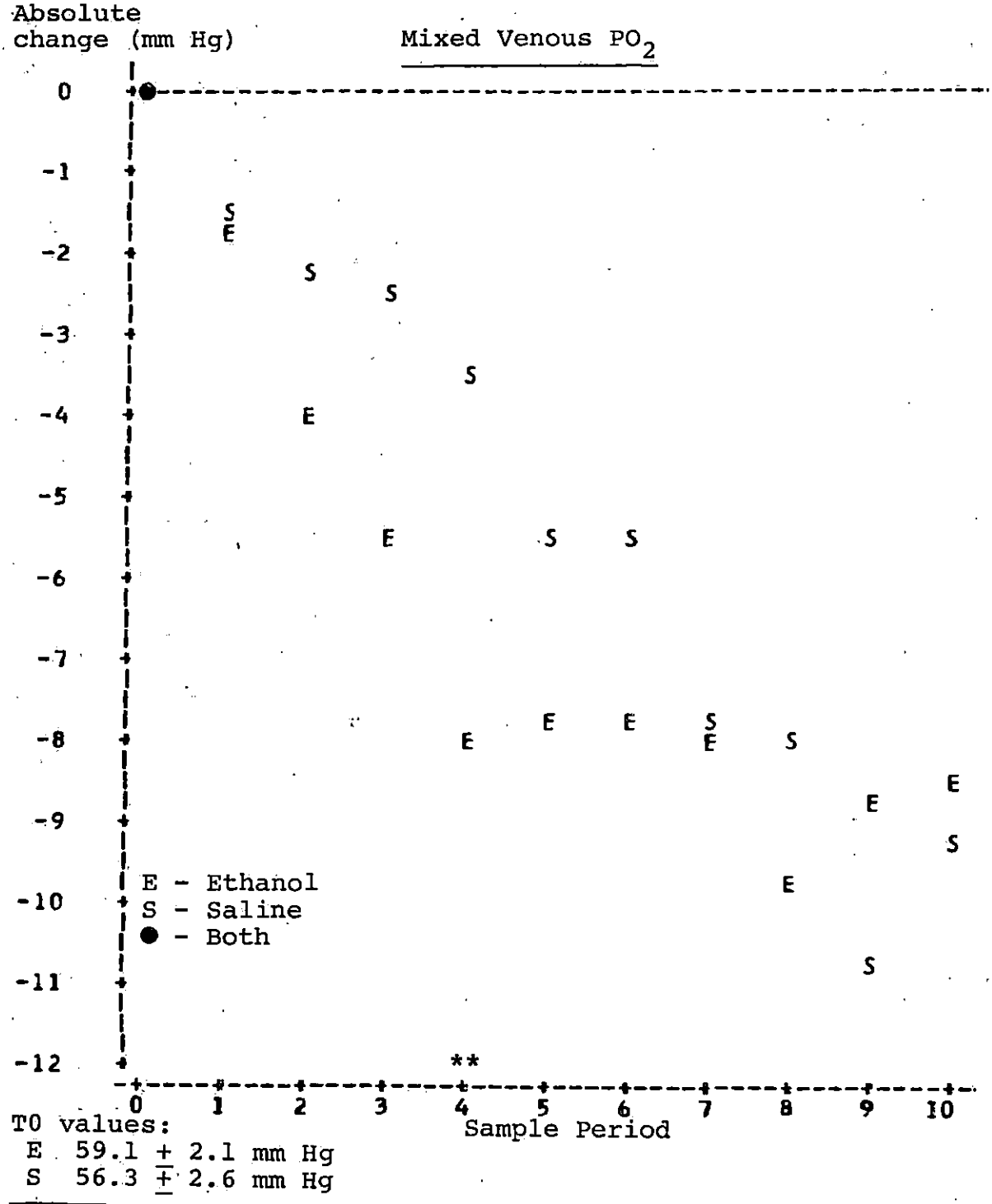


Figure 27. Absolute change in mixed venous PO_2 ($P\bar{v}O_2$)

correlates well with the BEC. The large variability seen in the Group II response does not allow any differences between the two groups to be clearly seen. The fairly consistent values for the Group I animals do indicate that such a difference may possible exist.

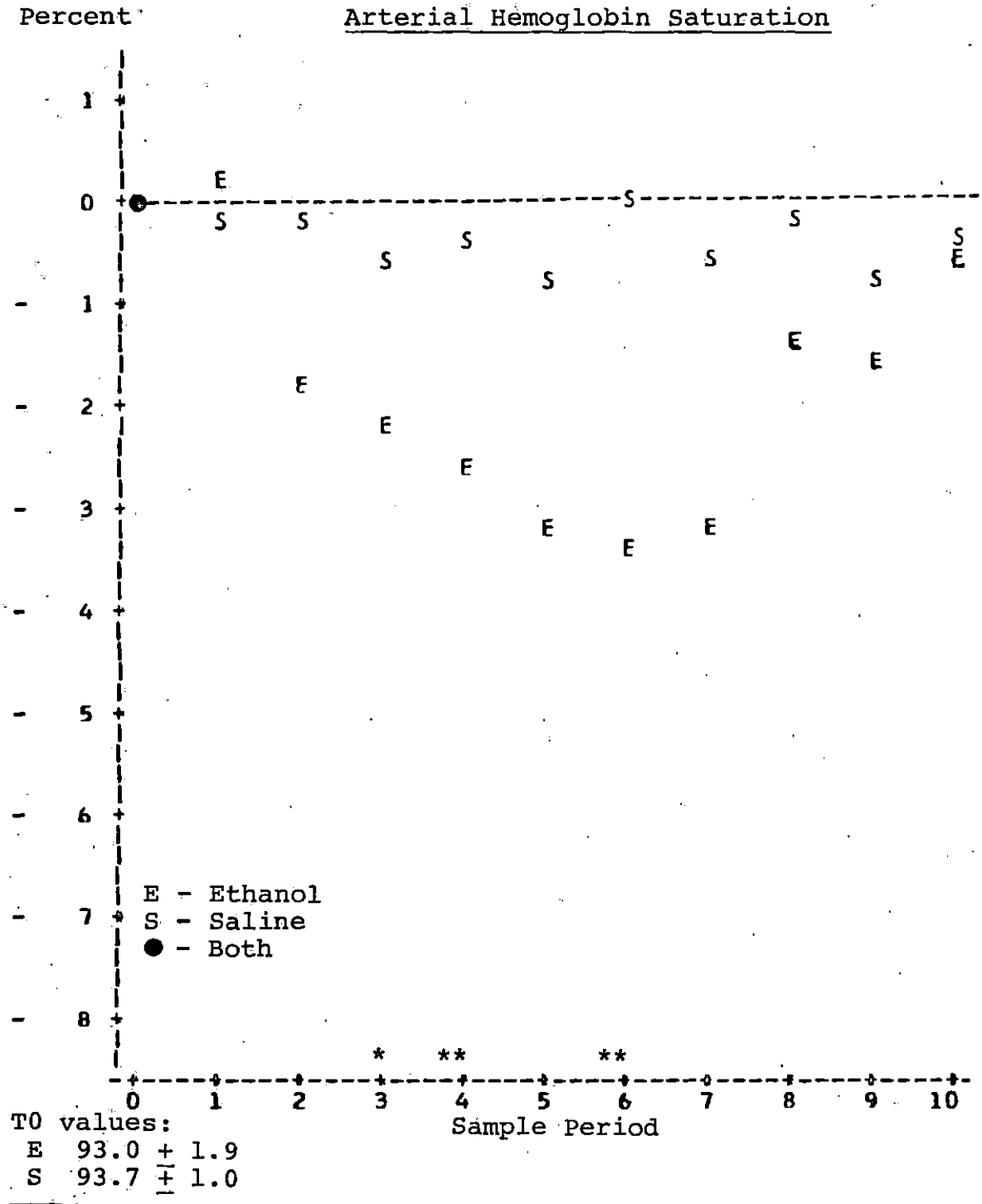
Even though the $P\bar{v}O_2$ values shown in Figure 27 show a statistical difference at T4, there is very little evidence of any consistent difference between the two groups.

It is surprising to have any depression of either PaO_2 or $P\bar{v}O_2$ values in light of the evidence for increased $\dot{V}_A$. The fact that there are decreases adds even more evidence to the theory of regional changes in $\dot{V}A/\dot{Q}$.

Blood saturation

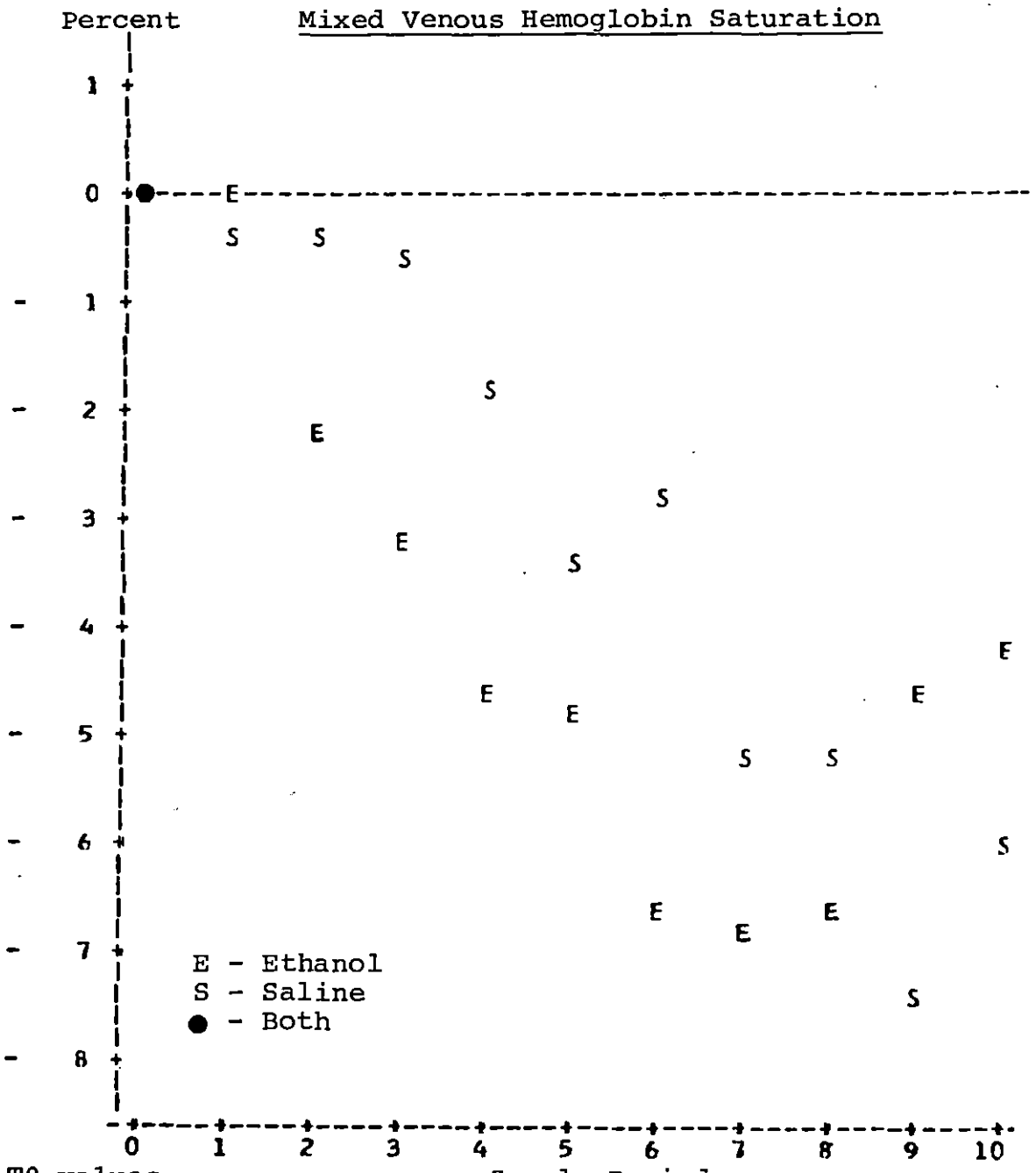
The plot of arterial hemoglobin saturation (aSat) in Figure 28 shows that there is a decrease in Group I aSat that correlates very well with the plot of BEC. Both peak at T6. There is only a slight decrease in aSat for Group II and the two groups are statistically different at several points.

As seen in Figure 29, there is a steady decrease in mixed venous hemoglobin saturation ($\bar{v}$Sat) in both groups. In contrast to the plot for aSat, there is less indication of any differences between treatment groups here. It is of interest that the values for Group I are consistently below those shown



*$p \leq .01$.
**$p \leq .05$.

Figure 28. Percent change in arterial hemoglobin saturation (aSat)



T0 values:
E 79.6 ± 1.4
S 78.9 ± 1.8

Figure 29. Percent change in venous hemoglobin saturation ($\bar{v}$Sat)

for the Group II animals until T9.

Since hemoglobin saturation depends on pH, and PO_2, it is reasonable to assume that the relative increases in pH and PO_2 seen after T5 are related to the increase in aSat after T6. It is also reasonable to assume a relationship between the increased $\dot{V}_A$ and increased pH and pO_2. It is interesting to speculate that the decreased aSat was the cause of the increase in $\dot{V}_A$. On the other hand, if BEC had been maintained at T6, there is the possibility that $\dot{V}_A$ would not have increased and aSat would have continued to fall.

Possible mechanisms to account for the decrease in aSat, seen in the ethanol treated group, could involve nearly all of the measured parameters pH, PCO_2, and V_T. The easiest explanation involves the regional ventilation-perfusion relationships. If blood does not pass by ventilated capillaries, then it will not be oxygenated. These minor shifts in regional $\dot{V}A/\dot{Q}$ may be reflected in the total lung $\dot{V}A/\dot{Q}$, or they may not. The increases in V_{ds} and FRC as well as $\dot{Q}s/\dot{Q}t$ shifts indicate that shifts in $\dot{V}A/\dot{Q}$ are occurring, but the exact mechanism remains unclear.

SUMMARY

This project measured changes in respiratory, cardiovascular, ventilation-perfusion, metabolic, and blood gas parameters caused by treatment with a moderate dose of ethanol.

There was an increase on $\dot{V}_A$ due mainly to an increase in f. Increases observed in V_{ds} and FRC were closely linked with BEC. Increases in R also correlated well with BEC. There were no changes in V_T, C_L, or peak airflows that could be attributed to the ethanol treatment.

Cardiovascular responses produced by treatment by ethanol include a slight decrease in $\dot{Q}$ with no change in HR. Systolic and diastolic arterial pressures showed slightly higher increases in the ethanol treated group.

The large increases in $\dot{V}A/\dot{Q}$ can be attributed to the changes in both $\dot{V}_A$ and $\dot{Q}$. The existence of regional changes in $\dot{V}A/\dot{Q}$ cannot be proven or disproven by the data presented, but the consistent trends seen in V_{ds}, FRC, and $\dot{Q}s/\dot{Q}t$ tend to support that hypothesis.

The increased $\dot{V}O_2$ due to ethanol treatment is most likely caused by the increased work of breathing, especially considering the increase in R. There was a significant reduction of RQ, but the significance of this change, though supported by the literature, is uncertain.

Blood gas parameters indicate no definite metabolic acidosis, but the common respiratory alkalosis observed is generally suppressed until BEC began to decline in the Group I animals.

The changes in pH were correlated with decreases in PCO_2. Decreases in PO_2 and hemoglobin saturation indicate some type of hypoxia that correlates well with the BEC and could well be a consequence of the hypothesized shifts in regional $\dot{V}A/\dot{Q}$ relationship.

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APPENDIX

Table A1. Average blood ethanol concentration (BEC)

	Sample Period										
	T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
BEC	0 ±0	16[a] ± 9	26 ± 5	36 ±12	40 ± 7	41 ± 6	48 ± 4	45 ± 4	43 ± 3	41 ± 4	37 ± 4
n	8	5	5	3	3	5	7	8	6	6	8

[a] mg/dL ± S.E.M.

Table A2. Changes in the ventilatory parameters. Includes: alveolar ventilation ($\dot{V}_A$), tidal volume (V_T) and respiratory frequency (f)

Group	n	Sample Period										
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = $\dot{V}_A$												
Ethanol	8	1.658[a] ±0.224	10.1[b] ±4.7	3.8 ±6.3	10.0 ±7.5	1.95 ±5.7	6.3 ±8.7	8.1 ±6.9	15.5 ±11.7	34.6 ±9.2	31.3 ±11.5	53.1 ±6.3
Saline	8	2.215 ±0.268	2.3 ±4.6	0.1 ±7.9	-4.1 ±7.1	8.5 ±8.7	0.3 ±8.4	11.2 ±9.2	6.4 ± 8.1	16.5 ±12.1	6.2 ± 9.6	22.8 ±16.8
Parameter = V_T												
Ethanol	8	0.366[c] ±0.040	-3.0[b] ±3.9	2.0 ±6.7	4.7 ±8.9	6.6 ±7.5	9.2 ±6.7	13.6 ±11.3	12.3 ±12.4	9.3 ±11.5	7.1 ± 9.2	6.3 ±10.0
Saline	8	0.348 ±0.021	-2.8 ±2.3	3.6 ±2.1	7.1 ±2.1	6.1 ±1.8	10.8 ±3.6	11.0 ± 3.9	9.7 ± 5.7	10.1 ± 5.7	12.3 ± 5.0	11.2 ± 5.4
Parameter = f												
Ethanol	8	9.3[d] ±0.7	15.8[b] ±7.3	3.4 ±5.6	8.8 ±10.6	0.1 ±10.0	0.9 ±10.6	3.2 ±14.4	14.2 ±18.4	35.2 ±19.6	37.5 ±23.5	51.4 ±17.9
Saline	8	11.7 ± 1.3	2.7 ±4.1	-4.8 ±5.5	-10.2 ±6.4	0.9 ±6.8	-9.7 ±5.9	0.9 ± 7.8	1.6 ±11.0	7.2 ±10.6	-1.1 ±10.3	13.7 ±16.1

[a] L/min ± S.E.M.

[b] Percent change from control ± S.E.M.

[c] L ± S.E.M.

[d] Breaths/min ± S.E.M.

Table A3. Change in lung volumes; includes: physiological dead space (V_{ds}), and functional residual capacity (FRC)

Group	n	Sample Period T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = V_{ds}												
Ethanol	8	0.181[a] ±0.017	-4.4[b] ±3.9	1.4 ±5.4	3.6 ±8.5	7.9 ±7.2	10.4 ± 5.6	12.8 ±11.0	16.8 ±10.2	12.5 ±10.0	11.5 ± 8.4	5.4 ±8.9
Saline	8	0.169 ±0.013	-1.7 ±3.6	0.3 ±3.9	3.8 ±2.8	-0.8 ±4.4	3.8 ± 4.6	1.6 ± 6.0	0.5 ± 6.0	-1.5 ± 6.9	-2.5 ± 6.3	-1.6 ±6.7
Parameter = FRC		A		B		C						
Ethanol	4	1.069[c] ±0.132		7.0[b] ±2.0		-3.0 ±7.0						
Saline	5	1.511 ±0.0148		-10.6 ± 7.5		-13.5 ± 4.0						

[a] L ± S.E.M.

[b] Percent change ± S.E.M.

[c] L ± S.E.M.

Table A4. Changes in lung mechanics parameters; includes: lung compliance (C_L), airway resistance (R), peak inspiratory flow (PIF)

Group	n	Sample Period T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = C_L												
Ethanol	5	0.062[a] ±0.012	-1.0[b] ±4.6	-3.4 ±3.8	-1.6 ±3.9	-7.5 ±9.4	-7.2 ±3.7	-6.1 ±4.4	-9.5 ±2.1	-11.0 ± 5.8	-11.7 ± 4.0	-18.4 ± 3.2
Saline	3	0.101 ±0.012	-4.7 ±10.1	-11.6 ± 6.3	-17.3 ±13.0	-19.2 ± 7.5	-8.2 ±2.8	-11.6 ±11.0	-13.4 ±11.0	-18.3 ± 9.8	-14.6 ±10.3	-22.3 ± 5.6
Parameter = R												
Ethanol	5	7.058[c] ±0.880	7.4[b] ± 8.6	3.9 ±9.6	18.6 ± 5.7	20.2 ±26.9	33.7 ± 9.5	26.9 ± 8.9	25.2 ±10.4	25.7 ± 8.9	21.5 ± 9.2	18.7 ±13.2
Saline	3	7.584 ±2.276	-15.5 ±14.0	1.3 ±5.2	4.9 ± 7.2	-4.3 ±14.2	-13.2 ±26.3	4.6 ± 6.8	-7.6 ±21.5	-8.4 ±21.1	8.9 ±18.7	10.6 ±12.8
Parameter = PIF												
Ethanol	8	0.368[d] ±0.022	3.5[b] ± 4.6	10.9 ± 6.1	9.8 ± 7.4	14.2 ±17.4	14.9 ±12.7	13.1 ± 4.7	16.3 ± 5.7	13.9 ± 5.8	18.5 ± 5.3	19.2 ± 5.5
Saline	8	0.429 ±0.014	-0.5 ± 2.0	6.1 ± 2.4	11.5 ± 3.4	13.3 ± 2.6	17.3 ± 4.7	16.6 ± 4.4	15.1 ± 5.2	17.8 ± 6.2	15.8 ± 5.9	19.8 ± 7.5

[a] L/cm H_2O.

[b] Percent change from control ± S.E.M.

[c] cm H_2O/L/sec.

[d] L/sec ± S.E.M.

Table A5. Changes in cardiovascular parameters, includes: cardiac output ($\dot{Q}$), heart rate (HR), systolic arterial pressure (SAP), and diastolic arterial pressure (DAP)

Group	n	Sample Period										
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = $\dot{Q}$												
Ethanol	8	5.340[a] ±0.786	2.9[b] ±10.1	-3.5 ± 3.0	-5.0 ± 7.7	-6.9 ±11.7	-9.6 ± 9.7	-7.2 ± 9.4	-0.8 ± 9.6	5.0 ±13.7	-0.1 ±11.7	9.1 ± 7.3
Saline	8	4.623 ±0.600	-0.5 ± 5.0	-3.9 ± 5.6	-5.2 ± 7.3	-4.5 ± 9.0	-7.8 ± 5.2	-2.7 ± 7.5	-1.3 ±11.7	-1.1 ±15.3	-2.4 ±15.7	0.6 ±17.8
Parameter = HR												
Ethanol	8	137[c] ± 15	2.9[b] ± 3.4	-3.5 ± 3.5	-5.0 ± 3.3	-6.9 ± 4.3	-9.6 ± 6.2	-7.2 ± 6.6	-0.8 ± 6.8	5.0 ± 7.8	-0.1 ± 7.1	9.1 ± 7.4
Saline	8	157 ± 10	-0.5 ± 3.9	-3.9 ± 2.6	-5.2 ± 4.3	-4.5 ± 4.9	-7.8 ± 4.5	-2.7 ± 7.1	-1.3 ± 3.8	-1.1 ± 4.0	-2.4 ± 8.6	0.6 ± 8.2
Parameter = SAP												
Ethanol	8	143[d] ± 3	0.6[b] ± 1.3	4.4 ± 2.9	5.9 ± 4.8	8.0 ± 5.2	6.5 ± 5.4	5.7 ± 4.4	6.5 ± 2.3	5.2 ± 2.8	4.1 ± 3.0	-0.3 ± 3.4
Saline	8	147 ± 3	-1.3 ± 0.8	-1.6 ± 0.7	0.9 ± 1.6	0.4 ± 1.5	2.0 ± 1.5	2.4 ± 3.0	1.7 ± 3.3	3.8 ± 2.3	0.8 ± 4.5	3.3 ± 3.3
Parameter = DAP												
Ethanol	8	111[e] ± 3	1.3[b] ± 2.1	3.8 ± 2.6	3.8 ± 3.1	6.2 ± 3.4	7.5 ± 3.5	13.5 ± 2.6	11.8 ± 2.5	12.6 ± 4.2	7.0 ± 2.9	7.9 ± 3.7
Saline	8	120 ± 3	-1.3 ± 1.2	-3.2 ± 1.2	0.5 ± 1.7	2.7 ± 1.4	3.3 ± 1.3	5.4 ± 2.5	5.5 ± 2.8	6.4 ± 2.6	4.2 ± 3.6	8.8 ± 2.3

[a] L/min ± S.E.M.

[b] Percent change from control ± S.E.M.

[c] Beats/min ± S.E.M.

[d] mm Hg ± S.E.M.

[e] mm Hg ± S.E.M.

Table A6. Change in ventilation-perfusion parameters, includes; ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$), physiological shunt ($\dot{Q}_s/\dot{Q}_t$)

Group	n	Sample Period									
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = $\dot{V}_A/\dot{Q}$												
Ethanol	8	0.336[a] ±0.048	7.5[b] ±10.7	4.9 ± 7.8	18.0 ±12.2	25.4 ±12.7	27.2 ±13.6	31.6 ±13.0	31.4 ±12.2	59.6 ±13.7	49.6 ±16.1	68.3 ±16.0
Saline	8	0.526 ±0.080	1.5 ± 7.3	-0.4 ± 6.2	-13.3 ± 4.5	-1.1 ± 7.5	-0.4 ± 7.4	5.6 ± 7.4	7.9 ±10.4	14.3 ±15.9	9.7 ±13.3	15.2 ±16.4
Parameter = $\dot{Q}_s/\dot{Q}_t$												
Ethanol	8	0.376[c] ±0.046	6.1[b] ±10.9	17.1 ±10.1	15.2 ±12.4	14.6 ±11.3	20.9 ±17.7	15.4 ±20.3	14.6 ±19.5	-3.6 ±15.3	1.7 ±15.9	-11.8 ±10.8
Saline	8	0.256 ±0.029	3.0 ± 9.6	10.7 ±11.2	15.2 ± 7.9	10.3 ± 8.2	12.7 ±10.2	4.1 ±10.0	8.6 ±13.7	1.9 ±13.9	13.9 ±13.3	11.9 ±18.9

[a] Ratio ± S.E.M.

[b] Percent change from control ± S.E.M.

[c] Ratio ± S.E.M.

Table A7. Changes in metabolic parameters, includes: respiratory exchange ratio (RQ), and oxygen consumption ($\dot{V}O_2$)

Group	n	Sample Period										
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = RQ												
Ethanol	8	0.571[a] ±0.048	-2.3[b] ± 4.0	-7.4 ± 3.0	-1.8 ± 5.3	-8.2 ± 3.5	-7.0 ± 4.1	-8.7 ± 2.5	-8.1 ± 2.2	0.5 ± 4.6	0.6 ± 2.3	8.1 ± 3.2
Saline	8	0.625 ±0.061	2.4 ± 6.1	3.3 ± 8.3	-7.6 ± 5.4	1.3 ± 4.2	-2.0 ± 3.7	1.2 ± 4.2	-0.4 ± 2.8	3.7 ± 3.8	-2.5 ± 5.4	4.9 ± 5.1
Parameter = $\dot{V}O_2$												
Ethanol	8	0.133[c] ±0.14	10.8[b] ± 5.7	8.3 ± 5.1	8.6 ± 4.9	5.7 ± 5.4	9.8 ± 7.0	13.7 ± 5.9	20.2 ± 9.6	28.8 ± 6.6	22.2 ± 6.5	31.2 ± 7.5
Saline	8	0.166 ±0.020	0.3 ± 5.0	-1.6 ± 5.8	2.4 ± 4.7	4.1 ± 5.2	0.3 ± 4.3	7.0 ± 6.0	3.3 ± 6.1	8.0 ± 8.6	6.3 ± 5.0	9.6 ± 9.4

[a] Ratio = S.E.M.

[b] Percent change from control ± S.E.M.

[c] L/min ± S.E.M.

Table A8. Changes in arterial pH (apH) and mixed venous pH ($\bar{v}$pH)

Group	n	Sample Period									
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter apH												
Ethanol	8	7.260[a] ±0.015	0.007[b] ±0.005	0.002 ±0.005	0.003 ±0.005	0.004 ±0.009	0.005 ±0.012	0.006 ±0.015	0.006 ±0.018	0.030 ±0.016	0.044 ±0.019	0.050 ±0.017
Saline	8	7.298 ±0.018	0.005 ±0.066	-0.003 ±0.011	0.001 ±0.005	0.008 ±0.007	0.011 ±0.009	0.027 ±0.009	0.031 ±0.014	0.034 ±0.020	0.027 ±0.015	0.044 ±0.019
Parameter = $\bar{v}$pH												
Ethanol	8	7.236[a] ±0.016	0.008[b] ±0.007	0.013 ±0.006	0.010 ±0.008	0.007 ±0.009	0.006 ±0.009	-0.003 ±0.016	0.008 ±0.017	0.025 ±0.018	0.039 ±0.018	0.043 ±0.018
Saline	8	7.271 ±0.016	0.007 ±0.006	0.004 ±0.005	0.001 ±0.005	0.003 ±0.006	0.012 ±0.006	0.020 ±0.008	0.022 ±0.010	0.031 ±0.017	0.029 ±0.018	0.035 ±0.018

[a] pH units ± S.E.M.

[b] Absolute change from control ± S.E.M.

Table A9. Changes in the partial pressure of arterial ($PaCO_2$) and mixed venous ($P\bar{v}CO_2$) carbon dioxide

Group	n	Sample Period										
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = $PaCO_2$												
Ethanol	8	56.4[a] ±3.4	-2.6[b] ±1.6	-3.1 ±1.5	-4.1 ±1.8	2.4 ±1.4	-2.8 ±1.9	-2.4 ±4.0	-1.6 ±2.5	-5.1 ±2.3	-7.3 ±2.7	-9.5 ±2.6
Saline	8	52.0 ±1.6	-2.2 ±0.9	-2.8 ±1.3	-2.2 ±0.5	-3.3 ±1.0	-2.9 ±1.2	-4.2 ±1.2	-4.7 ±1.3	-5.6 ±2.1	-5.3 ±1.7	-6.4 ±2.2
Parameter = $P\bar{v}CO_2$												
Ethanol	8	65.2[a] ±3.7	-4.2[b] ±1.5	-2.7 ±1.1	-2.5 ±1.1	-1.2 ±1.3	-0.0 ±2.1	-0.5 ±2.6	-0.7 ±2.8	-3.4 ±2.4	-6.2 ±3.0	-7.1 ±2.4
Saline	8	60.2 ±1.9	-0.9 ±6.9	-1.9 ±1.2	-1.2 ±1.1	-2.0 ±1.4	-1.6 ±1.4	-2.5 ±1.4	-3.7 ±2.1	-3.3 ±2.4	-3.1 ±2.7	-5.4 ±2.8

[a] mm Hg ± S.E.M.

[b] Absolute change from control in mm Hg ± S.E.M.

Table A10. Changes in the partial pressures of arterial (PaO_2) and mixed venous ($\bar{P}vO_2$) oxygen

Group	n	Sample Period									
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = PaO_2												
Ethanol	8	86.9[a]	-2.5[b]	-7.5	-8.1	-10.2	-10.8	-8.3	-8.0	-5.1	-5.7	-3.8
		±2.7	±3.1	±2.6	±2.4	±2.4	±3.8	±5.5	±5.3	±5.0	±4.7	±3.6
Saline	8	92.2	-1.0	-2.0	-3.0	-2.5	-6.1	-2.1	-5.0	-2.3	-8.8	-5.2
		±3.9	±2.1	±2.7	±0.7	±1.9	±2.6	±2.8	±2.7	±3.8	±3.2	±3.5
Parameter = $\bar{P}vO_2$												
Ethanol	8	59.1[a]	-1.6[b]	-4.1	-5.5	-7.9	-7.8	-7.8	-8.1	-9.8	-8.8	-8.5
		±2.1	±0.4	±0.8	±0.7	±1.3	±1.6	±1.2	±1.6	±1.5	±1.8	±1.7
Saline	8	56.3	-1.5	-2.2	-2.6	-3.4	-.56	-.56	-7.7	-7.9	-10.7	-9.2
		±2.6	±0.6	±1.6	±1.8	±1.6	±1.3	±1.5	±1.5	±1.8	±1.6	±2.0

[a] mm Hg ± S.E.M.

[b] Absolute change from control in mm Hg ± S.E.M.

Figure All. Changes in arterial (aSat) and mixed venous ($\bar{v}$Sat) percent hemoglobin saturation

Group	n	Sample Period									
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Parameter = aSat												
Ethanol	8	0.930[a] ±0.019	.001[b] ± .007	-.017 ± .008	-.022 ± .008	-.025 ± .007	-.031 ± .011	-.034 ± .014	-.033 ± .014	-.014 ± .013	-.016 ± .013	-.005 + .009
Saline	8	0.937 ±0.010	-.003 ± .005	-.002 ± .007	-.005 ± .003	-.004 ± .005	-.007 ± .009	-.000 ± .006	-.006 ± .011	-.001 ± .011	-.009 ± .009	-.004 ± .010
Parameter = $\bar{v}$Sat												
Ethanol	8	0.796[a] ±0.014	.000[b] ± .009	-.023 ± .014	-.031 ± .012	-.045 ± .015	-.049 ± .013	-.065 ± .018	-.069 ± .015	-.066 ± .023	-.046 ± .017	-.041 ± .009
Saline	8	0.789 ±0.018	-.004 ± .006	-.004 ± .011	-.005 ± .012	-.019 ± .017	-.034 ± .014	-.029 ± .014	-.053 ± .020	-.051 ± .025	-.074 ± .018	-.060 ± .030

[a]Percent saturation/100 ± S.E.M.

[b]Absolute change from control ± S.E.M.