3-5

Effects of oxygen breathing on the pulmonary and cardiovascular systems in dogs

Mohammad Taufiq Taiyoob

A Thesis Submitted to the
Graduate Faculty in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE

Major: Biomedical Engineering

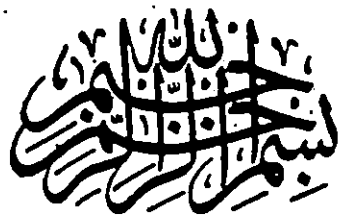
Iowa State University
Ames, Iowa

1984

TABLE OF CONTENTS

DEDICATION

TO MY PARENTS



In the name of Allah, the Beneficent, the Merciful.

We have enjoined on man
Kindness to his parents:
In pain did his mother
Bear him, and in pain
Did she give him birth.
The carrying of the (child)
To his weaning is
(A period of) thirty months.
At length, when he reaches
The age of full strength
And attains forty years,
He says, "O my Lord!
Grant me that I may be
Grateful for Thy favour
Which Thou hast bestowed
Upon me, and upon both
My parents, and that I
May work righteousness
Such as Thou mayest approve;
And be gracious to me
In my issue. Truly
Have I turned to Thee
And truly do I bow
(To Thee) in Islam."

وَوَصَّيْنَا الْإِنسَانَ بِوَالِدَيْهِ إِحْسَانًا ۖ
حَمَلَتْهُ أُمُّهُ كُرْهًا وَوَضَعَتْهُ كُرْهًا ۖ
وَحَمْلُهُ وَفِصَالُهُ ثَلَاثُونَ شَهْرًا ۖ
حَتَّىٰ إِذَا بَلَغَ أَشُدَّهُ
وَبَلَغَ أَرْبَعِينَ سَنَةً ۙ
قَالَ رَبِّ أَوْزِعْنِي
أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي
أَنْعَمْتَ عَلَيَّ وَعَلَىٰ وَالِدَيَّ
وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ
وَأَصْلِحْ لِي فِي ذُرِّيَّتِي ۖ
إِنِّي تُبْتُ إِلَيْكَ
وَإِنِّي مِنَ الْمُسْلِمِينَ ○

LIST OF ABBREVIATIONS

ACONT	Arterial blood oxygen content
ACO2	Arterial blood carbon-dioxide tension
AOXY	Arterial blood oxygen tension
APH	Arterial blood pH
AS	Arterial blood hemoglobin oxygen saturation
CARABF	Carotid artery blood flow
CARVO2	Cerebral oxygen consumption
FAVDO	Arterial to femoral vein blood oxygen extraction
FCONT	Femoral vein blood oxygen content
FCO2	Femoral vein blood carbon-dioxide tension
FEMABF	Femoral artery blood flow
FEMVO2	Hindlimb oxygen consumption
FOXY	Femoral vein blood oxygen tension
FPH	Femoral vein blood pH
FS	Femoral vein blood hemoglobin oxygen saturation
GENVO2	General (total) oxygen consumption
JAVDO	Arterial to jugular vein blood oxygen extraction
JCONT	Jugular vein blood oxygen content
JCO2	Jugular vein blood carbon-dioxide tension
JOXY	Jugular vein blood oxygen tension
JPH	Jugular vein blood pH
JS	Jugular vein blood hemoglobin oxygen saturation
MINVOL	Minute volume or minute ventilation

OXYDEL	Oxygen delivery or oxygen transport
PAVDO	Arterial to pulmonary artery blood oxygen extraction
PCONT	Pulmonary artery blood oxygen content
PCO2	Pulmonary artery blood carbon-dioxide tension
POXY	Pulmonary artery blood oxygen tension
PPH	Pulmonary artery blood pH
PS	Pulmonary artery blood hemoglobin oxygen saturation
PULAP	Pulmonary arterial pressure
PVR	Pulmonary vascular resistance
RESPR	Respiratory rate or respiratory frequency
SVR	Systemic vascular resistance
SYSAP	Systemic arterial pressure
TIDVOL	Tidal volume
TOTLCO	Total (general) cardiac output

INTRODUCTION

Shortly after isolating oxygen in 1774, Priestley is reported to have written: From the greater strength and vivacity of the flame of a candle, in this pure air, it may be conjectured, that it might be peculiarly salutary to the lungs in certain morbid cases.....but, perhaps, we may also infer from these experiments, that though pure dephlogisticated air (oxygen) might be very useful as a "medicine", it might not be so proper for us in the usual healthy state of the body: for, as a candle burns out much faster in dephlogisticated than in common air, so we might, as may be said, "live out too fast", and the animal powers be soon exhausted in this pure kind of air. A moralist, at least, may say, that the air which nature has provided for us is as good as we deserve.....the feeling of it to my lungs was not sensibly different from that of common air; but I fancied that my breast felt peculiarly light and easy for some time afterwards. Who can tell but that, in time, this pure air, may become a fashionable article in luxury (Welch 1982).

Oxygen is the most popular medical gas in the world. Its therapeutic and the harmful effects can be traced back as far as the pioneers of the study of respiratory gases.

Commonly, oxygen is widely used on a short and long term basis. Usually, long term users of oxygen therapy are patients with chronic obstructive pulmonary disease, and patients presented with clinical symptoms that could only be relieved with oxygen. Low flow (low

concentration) oxygen is usually used in a long term situation.

Higher oxygen concentration is usually used in a short term oxygen therapy. It is administered to patients presented with any acute pathological situation that cause immediate oxyhemoglobin desaturation, such as hyaline membrane disease of the newborn, methemoglobin anemia, cyanide and carbon monoxide poisoning, acute pulmonary edema, asthma attacks, respiratory allergies, hydro-, hemo-, and pneumothorax, acute onset of shortness of breath, and congestive heart failure with pulmonary edema.

In all cases, the main objective of oxygen therapy is to correct arterial blood hypoxemia. Oxygen does not cure the underlying pathological situation, but it merely helps alleviate the symptoms of arterial hypoxemia.

On the other hand, administration of oxygen to subjects with normal arterial blood oxygen tension will increase the arterial blood oxygen tension unnecessarily, but will also cause an adverse effects on the other systems, such as increase vascular resistances, reduce cardiac output and arterial blood flows, depress neuro-oxygen sensors, increase respiratory air flow resistance, induce vasoconstrictions, restrict oxygen delivery to the tissues, and alter peripheral, regional and total oxygen consumptions (Reinstorff and Fenner 1972, Harkema et al. 1982, Eggers et al. 1962, Haneda et al. 1983, Kety and Schmidt 1948, Welch et al. 1977, Andersen and Hillestad 1970, Smith and Ledingham 1972, Cassuto and Farhi 1979, Grave et al. 1970, Allison et al. 1979, Bergofsky and Bertun 1966,

Hughes et al. 1979, Shearer et al. 1970, Whitehorn et al. 1946, and Berclay et al. 1979). Yet, there has been little investigation of the possible effects of oxygen on total, and cerebral oxygen consumptions.

This research was undertaken to explore the effects of short term (one hour) oxygen therapy on total, cerebral, and hindlimb oxygen consumptions in normal resting healthy dogs. The Fick equation was used in this study to address the following questions.

1. What oxygen concentration will most effect the oxygen uptake.

2. How do the changes in either cardiac output or oxygen extraction, or both, influence the changes in oxygen uptake during oxygen breathing.

3. What are the other variables that could affect cardiac output and tissue oxygen extractions during oxygen breathing.

In this study, 16 dogs were clinically studied on room air and then during oxygen breathing. Cardiac output, arterial blood flows, vascular pressures, blood gas analysis, and respiratory parameters were determined.

By evaluating the effects of short term oxygen breathing on total, cerebral, and hindlimb oxygen consumptions, an understanding of the effects of oxygen at the cellular level might be gained.

LITERATURE REVIEW

Ventilatory Responses During Hyperoxia

The administration of 100% oxygen to patients with chronic obstructive pulmonary disease (COPD) during acute respiratory failure resulted in an early decrease in minute ventilation by 18% compared to control values. Both tidal volume and respiratory frequency decreased, this initial decrease in minute ventilation was followed by a slow increase after 15 minutes of oxygen breathing, minute ventilation rose to 93% of the control values (Aubier et al. 1980). They also reported that there was a small difference between minute ventilation on normoxia and that at hyperoxia. Arterial blood oxygen tension increased to 225 Torr, arterial blood carbon-dioxide tension increased by 23 Torr on hyperoxia. There was no significant correlation between the changes in minute ventilation and arterial blood carbon-dioxide tension.

In patients with COPD, resting minute ventilation and mean inspiratory flow decreased after 6 months of 24 hours low flow oxygen (liter flow of oxygen to keep the arterial blood oxygen tension between 60 to 80 Torr) therapy, indicating a reduction in central ventilatory drive. Also the ventilatory responses to carbon-dioxide were depressed, and were associated with a significant increase in arterial blood carbon-dioxide tension (Fleetham et al. 1980). In asthmatic patients, minute ventilation on normoxia was 10.2 l/min, but on hyperoxia it decreased to 8.4 l/min, indicating that hyperoxia is a

ventilatory depressant (Freedman et al. 1983).

Reinstorff and Fenner (1972) reported that in neonatal subjects up to 72 hours of age, a brief exposure to hyperoxia for 8 to 15 seconds duration resulted in an over all mean ventilatory reduction of 15.65%. They also found that infants weighing above 2000 grams showed greater ventilatory reduction of 20.12% and in infants weighing less than 2000 grams, the ventilatory reduction was only 11.69%. There was a statistically significant difference between these two groups.

After breathing 100% oxygen at two atmospheres for 5 hours, airway resistance increased by 30%, thoracic gas volume increased by 25%, and specific airways conductance fell by 41%. However, under the same ambient pressure of two atmospheres on normoxia, there were no respiratory changes (Dewar et al. 1972). These workers further showed that there were no changes in vital capacity, or FEV(1 s)/FVC with either normoxia or hyperoxia at the same atmospheric conditions.

Oxygen therapy had no effect on sleep quality (Fleetham et al. 1982). Nocturnal low flow oxygen (2 l/min by nasal prong) had no apparent effect upon sleep quality in patients with cystic fibrosis and in patients with severe but stable COPD (Spier et al. 1984). They further reported that during normoxia breathing in COPD patients arousals from sleep were associated with periods of arterial blood desaturation. However relief of the hypoxemia with supplemental nocturnal low flow oxygen increased the arterial blood saturation, but it had no effect on arousal frequency (Fleetham et al. 1982, and Spier et al. 1984).

An hyperoxic pulmonary syndrome similar to adult respiratory distress syndrome was produced when normal rats were exposed to hyperoxia (100%) for 48 hours. Similarly, when rats with emphysematous lungs were exposed to hyperoxia, there was a reduction in quasi-static compliance and carbon-monoxide diffusing capacity similar to those in normal lungs under hyperoxia (Harkema et al. 1982). They also pointed out that emphysematous lungs under hyperoxia showed a reduction in forced expiration volumes and flow rates.

Airway resistance decreases in hypoxemic patients with COPD when breathing 30% oxygen. Also patients with hypoxemic COPD demonstrated an increase in air flow rates and a decrease in density dependence of flow while breathing 30% oxygen (Libby et al. 1981). Harkema et al. (1982) reported decrease in air flow rates in emphysematous rats lungs. Libby et al. (1981) also reported that subjects with normal lungs showed no changes in air flow rates or density dependence while breathing 30% oxygen. Miyamura et al. (1976) have shown that the slopes of the minute ventilation to alveolar arterial carbon-dioxide tension lines during positive and negative work increased in normoxia as compared with those on rest, but this effect was less evident in hyperoxia breathing.

After being exposed to hyperoxia (95 to 98%) for 54.6 hours, dogs died with respiratory failure; the lungs on autopsy were dark red, hemorrhagic, edematous, and congested (Smith et al. 1963). They observed an increase in respiratory rate at the time near death, intrapleural pressure increased, and lung compliance dropped.

Arterial Blood Gases During Hyperoxia

In patients with chronic obstructive pulmonary disease the lowest mean arterial oxygen saturation occured during rapid eye movement (REM) sleep (Fleetham et al. 1982). The minimum arterial oxygen saturation occurred during REM sleep and averaged 79.4% on normoxia, but with nocturnal low flow oxygen (2 l/min) therapy this improved to 92.7% (Spier et al. 1984). They further reported that transcutaneous carbon-dioxide tension was 5.1 Torr during REM sleep on nocturnal low flow oxygen therapy, where as it was 5.6 Torr on falling sleep while breathing room air.

Arterial blood oxygen tension varied widely from 30 to 600 Torr according to oxygen fraction of inspired gas. In the "coma" group, the jugular vein blood oxygen tension increased slightly with the increase in arterial blood oxygen tension, whereas the comparable values of jugular vein blood oxygen tension in a "brain death" group were extremely high (Minami et al. 1973).

The curve of oxyhemoglobin dissociation during 20 minutes inhalation of a 95% oxygen shifts to the left (Ivanov and Chebotarev 1980). They also mentioned that this shift of the curve of oxyhemoglobin dissociation indicates an increase in the hemoglobin affinity for oxygen and restricts oxygen release to the tissues.

Cassuto and Farhi (1979) studied the effects of hyperoxia (100%) at one and three atmospheric pressures on the circulatory system. Their investigation revealed that exposure to hyperoxia caused a

sustained rise in arterial oxygen tension. Oxygen uptake during hyperoxia at one atmospheric pressure was the same as in control conditions. These workers also noticed an immediate rise in right heart oxygen tension, while the right heart to arterial carbon-dioxide tension difference rose indicating gradual fall in cardiac output, this phenomenon was accompanied by an increase in lactic acidosis, implying that some tissues were becoming hypoxic in the presence of arterial hyperoxia. Dewar et al. (1972) reported no changes in alveolar to arterial oxygen difference in patients breathing 100% oxygen at two atmospheric pressure for 5 hours.

When neonates and two week old beagle puppies were exposed to 80 to 90% oxygen, no significant difference between the mean arterial carbon-dioxide tension of the two groups (40.6 Torr on hyperoxia; vs. 39.7 Torr on normoxia) was observed (Grave et al. 1970). Irnell and Nordgren (1966) reported that in patients with bronchial asthma, the oxygen saturation in the brachial artery was 96.4% on normoxia, and it was 99.6% during hyperoxia breathing. Inhalation of high oxygen mixture (85 to 100%) produced a slight but significant increase in arterial oxygen content (a 1.4 Vol% increase) with no change in the carbon-dioxide content and tension or the pH of arterial blood (Kety and Schmidt 1948, and Grave et al. 1970).

Vascular Pressures During Hyperoxia

Short term (over night) oxygen therapy in patients with COPD lowered mean sleeping pulmonary arterial pressure and eliminated transient arterial hypoxemia (Fletcher and Levin 1984). These authors also reported the effect of long term (eight weeks) home oxygen therapy in patients with COPD, the mean pulmonary artery pressures during sleep were lower then the baseline normoxia values. These patients also exhibited lower pulmonary vascular resistance.

High oxygen breathing for 10 minutes decreased the airway impedence (from 78 to 57 dynes.sec/(cm^5), and pulmonary arterial resistance in patients with pulmonary hypertension. Pulmonary artery pressures in patients with pulmonary venous hypertension and with normotensive pulmonary system were not affected in ten minutes on hyperoxia (Haneda et al. 1983). Wright et al. (1983) reported that oxygen breathing had no effect at rest, but during exercise the pulmonary artery and pulmonary artery wedge pressures were lowered in patients with more severe COPD. During oxygen breathing, the mean pulmonary arterial pressure was 11 Torr as compared with 12 Torr on room air. Hyperoxia exposure for 20 minutes at rest in patients with severe COPD did affect the pulmonary artery pressure (Irnell and Nordgren 1966, Tammivaara-Hilty 1973, and Wright et al. 1983).

Hyperoxia (87 to 90%) breathing for 7 days at normobaric pressure, in rats, caused pulmonary hypertension, increased pulmonary vascular resistance and remodelled the walls of pulmonary precapillary

arteries (Jones et al. 1983, and Moran and Wolfe 1978). Moran and Wolfe (1978) discovered that pulmonary arteriolar resistance increased from 183 to 791 dynes.sec/(cm^5) after 70 hours on 95% oxygen in dogs. Perivascular pulmonary edema was evident at post-mortem.

Inhalation of high oxygen mixture (85 to 100%) produced a moderate increase in cerebrovascular resistance (from 1.7 to 2.2 resistance units) which indicates vasoconstriction in the brain vessels as the probable cause for the reduction in cerebral blood flow (Kety and Schmidt 1948). These workers reported a significant increase in systolic, diastolic, and in mean arterial pressure.

Blood pressure was not affected in the experiment at 55 to 70% of maximal aerobic activity in man during oxygen breathing. However, there was a reduction in blood flow by 11% to exercising limb without any change in blood pressure during hyperoxia, indicating an increase in resistance to blood flow in the exercising limb (Welch et al. 1977).

Statistically significant increase in peripheral vascular resistance, and mean arterial pressure occurred during 30 minutes on hyperoxia and persisted for 40 minutes after hyperoxia period ended (Eggers et al. 1962). Andersen and Hillestad (1970) reported vasoconstriction and blood pressure rise followed 20 minutes oxygen breathing. Oxygen (100%) ventilation at two atmospheres caused a 70% increase in systemic vascular resistance and a rise in left ventricular end diastolic pressure (Smith and Ledingham 1972). Dewar et al. (1972) reported no changes in blood pressure in man exposed to 90% oxygen at two atmospheric pressure for 5 hours.

Hemodyamic Responses During Hyperoxia

It was found that the mean pulmonary lobar blood flow was 62.7 ml/min at arterial blood oxygen tension of 354 Torr; 69.2 ml/min at normoxia; and 31.2 ml/min at hypoxia. These differences between the blood flow values were statistically significant (Allison et al. 1979). They suggested that pulmonary blood flow was greater during normoxic breathing; either hypoxic or hyperoxic breathing both caused a decrease in blood flow.

Eggers et al. (1962) reported no changes in central blood volume, but they indicated that a marked increase in pulmonary blood volume occurred in patients exposed to hyperoxia for 30 minutes duration. The effects of long term (8 weeks) oxygen therapy in COPD patients showed an increase in cardiac output during sleep (Fletcher and Levin 1984).

Hyperoxia decreases regional blood flow, the effect is being most marked in the brain, less so in the bowel and least obvious in the hindlimb (Bergofsky and Bertun 1966). Vasoconstrictive action on the cerebral vasculature is the result of a direct action of oxygen. The extreme degree of retinal vasoconstriction in the premature infants exposed to oxygen suggest a direct constrictive action of oxygen at this age (Grave et al. 1970). They also demonstrated that neonates and two weeks old beagle puppies during exposure to 80 to 90% oxygen at normobaric pressure had mean values for cerebral and retinal blood flow 20% less than those of the control group on normobaric normoxia.

Hyperoxia studies at arterial blood oxygen tension above 200 Torr produced no significant effects upon liver blood flow (Hughes et

al. 1979). Inhalation of high oxygen mixtures produced a significant decrease of 13% in mean cerebral blood flow, probably due to vasoconstriction in the brain vessels (Kety and Schmidt 1948). Leg blood flow was reduced by 11% during exercise while breathing 100% oxygen (Welch et al. 1977), but the actual oxygen delivery (product of blood flow and oxygen extraction) was not significantly different.

After inhalation of either normoxia or 100% oxygen for at least 30 minutes and following the 45 seconds occlusion of actual total circumflex coronary artery, transmural myocardial blood flow was determined (Rivas et al. 1980). They reported that on normoxia, mean regional myocardial blood flows to non-ischemic, intermediate, and ischemic regions were 0.92, 0.51, and 0.10 ml/min.g, respectively. However, during hyperoxia; mean regional myocardial blood flows were significantly diminished in non-ischemic, intermediate, and ischemic regions. Rivas et al. (1980) concluded that transmural blood flow to each layer was uniformly reduced in all regions and that hyperoxia (100% oxygen) further reduced myocardial blood flow to ischemic regions. Moran and Wolfe (1978) reported that dogs exposed to 95% oxygen for 70 hours had a significantly increased myocardial perfusion to all three layer of the ventricular wall at 24 and 48 hours.

Total renal blood flow reduced by 25% at an arterial oxygen tension above 100 Torr, but the glomerular filtration rate, and the effective renal plasma flow remained constant (Shearer et al. 1970).

Andersen and Hillestad (1970) concluded that breathing 100% oxygen at one atmospheric pressure for 20 minutes in healthy subjects produced

consistent cardiac output depression and vasoconstriction. These authors concluded that such adverse hemodynamic effects abolish the expected rise in general and regional oxygen transport. Rise in right heart to arterial carbon-dioxide tension difference in the presence of hyperoxia indicate a gradual fall in cardiac output (Cassuto and Farhi 1979). Bergofsky and Bertun (1966) reported that hyperoxia decreases the regional blood flow by increasing regional vascular resistance.

Responses to hyperoxia in patients with acute decompensation of COPD was characterized by decrease in cardiac output and an increase in oxygen delivery because of sharp increase in arterial oxygen content (Degaute et al. 1981). Contrary to Degaute et al., Welch et al. (1977) pointed out that hyperoxia breathing did not change oxygen delivery to the leg during exercise.

Although, Degaute et al. (1981) showed specifically that patients with severe hypoxemia (arterial blood oxygen tension of less than 40 Torr) showed no changes in cardiac output to oxygen therapy, but there was a significant increase in oxygen delivery. They also pointed out that patients with moderate hypoxemia (arterial blood oxygen tension between 40 and 60 Torr) when exposed to oxygen therapy showed a significant decrease in cardiac output with out any changes in oxygen delivery.

On the other hand, Dewar et al. (1972) reported no changes in cardiac output in patients exposed to 100% oxygen at two atmospheric pressures for 5 hours. Smith and Ledingham (1972) reported a fall in cardiac output of approximately 30% within four hours of commencing

hyperoxia (100%) ventilation at two atmospheric pressures. They further mentioned that at the end of 8 hours of hyperoxia, there was a rapid restoration of all parameters towards the initial values on normoxia.

Slight but statistically significant decrease in cardiac index and heart rate were observed during 100% oxygen breathing for 30 minutes (Eggers et al. 1962). Irnell and Nordgren (1966) reported that in patients with bronchial asthma, the cardiac output was 4.9 L/min during hyperoxia breathing and 5.9 L/min during normoxia breathing.

Whitehorn et al. (1946) reported that hyperoxia breathing for 60 minutes (one hour) resulted in a decrease in cardiac output as compared with the normoxia values. They further reported that the average decrease after five minutes of oxygen inhalation was 13% and continued to drop until to an average of 19.4% below the normal room air values after 60 minutes. These changes were statistically significant.

Muscular Performance During Hyperoxia

The tension developed by gastrocnemius plantaris muscles decreased by 14% in muscles perfused with hyperoxic blood after 20 minute and it decreased by 35% in muscles perfused by normoxia blood, indicates that hyperoxia maintains muscle tension (Barclay et al. 1979). Breathing 35% oxygen against 6.5 cm of water.s/l inspiratory resistance produced a significant increases in anaerobic threshold, maximum oxygen consumption, peak heart rate and endurance while decreasing the hyperventilatory response to work above anaerobic threshold

(Dressendorfer et al. 1977).

Linnarsson et al. (1974) investigated the effect of hyperoxia in men on muscle performance during submaximal and short term maximal exercise. At submaximal exercise, oxygen deficit, phosphagen depletion and muscle lactate accumulation were inversely related to inspired oxygen tension. Whereas, at maximal exercise oxygen deficit, phosphagen depletion and muscle lactate accumulation were not affected by inspired oxygen tension.

Oxygen Consumption During Hyperoxia

Hyperoxia produced a small increase in hepatic oxygen consumption without any change in liver blood flow (Hughes et al. 1979). In patients with bronchial asthma, the oxygen uptake was 267 ml/min during hyperoxia breathing; and 217 ml/min during resting normoxia breathing (Irnell and Nordgren 1966).

The average oxygen consumption during submaximal exercise was not significantly different between hyperoxia and normoxia. Oxygen consumption during maximal exercise condition was significantly higher in hyperoxia breathing subjects (Welch and Pedersen 1981). Welch et al. (1977) reported that oxygen consumption of the exercising limb was not different during hyperoxia breathing as compared with normoxia, although leg blood flow was reduced by 11% during exercise in oxygen breathing.

Literature Summary

To sum up, the effects of oxygen breathing vary with the duration of exposure and the presence or absence of any underlying lung disease.

Short term oxygen exposure in subjects with lung disease; such as COPD, and asthma, causes 1) an increase in minute ventilation, 2) an increase in arterial blood oxygen tension, 3) an increase in carbon-dioxide tension, 4) a decrease in airway resistance, 5) an increase in air flow rates, 6) a decrease in pulmonary artery pressure, 7) a decrease in pulmonary arterial resistance, 8) an increase in oxygen delivery, and 9) a decrease in cardiac output.

Effects of long term oxygen exposure in patients with underlying lung disease are manifested by 1) a decrease in minute ventilation, 2) an increase in arterial blood oxygen tension, 3) an increase in carbon-dioxide tension, 4) a decrease in mean pulmonary artery pressure and resistance, 5) an increase in pulmonary artery blood flow, 6) a decrease in vasuclar resistance, and 7) an increase in cardiac output.

The effects of short term oxygen breathing in subjects with normal pulmonary system are manifested by 1) a decrease in minute ventilation, 2) an increase in arterial blood oxygen tension, 3) an increase in carbon-dioxide tension, 4) an increase in pulmonary artery blood oxygen tension, 5) an increase in hemoglobin oxygen saturation, 6) a decrease in pulmonary lobar blood flow, 7) an increase in mean arterial blood pressure, 8) an increase in systemic and diastolic pressures, 9) an increase in systemic vascular resistance, 10) generalized peripheral vasoconstriction, 11) a decrease in total cardiac output, 12) cerebral

and retinal vasoconstriction, 13) an increase in cerebrovascular resistance, 14) an increase in resistance to regional blood flow, 15) cause a reduction in regional blood flow to areas such as; brain, hindlimb, retina, myocardium, and kidney.

Long term oxygen exposure in subjects with normal lung caused 1) respiratory failure, 2) increased pulmonary artery pressure and resistance, 3) increased intrapleural pressure, 4) decreased lung compliance, 5) pulmonary congestion, 6) edema, and 7) death.

MATERIALS AND METHODS

Experimental Design

Sixteen adult canine dogs of weight range 24.064 ± 2.614 kg. (13 males, 3 females) were used in this study. These dogs were obtained from Laboratory Animal Resources at Iowa State University, and were fasted over night with only water provided. Most of these dogs were tested for heart worms either before the experiment using Canine Heart Worms Test Kit: Dirotect (Mallinckrodt Inc., Bohemia, New York) or after the experiment on autopsy. Dogs that were positive for heart worms were not used in this study, and if autopsy findings were positive for heart worms then the data gathered were also discarded.

Thirteen dogs were tranquilized intramuscularly in the thigh with 1.21 ± 0.24 ml/kg of Acepromazine Maleate (10mg/ml) (Fort Dodge Laboratories Inc., Fort Dodge, Iowa). Twenty minutes later, these dogs were anesthetized intravenously with 19.16 ± 3.05 ml/kg of Pentobarbital Sodium (50 mg/ml) (Abott Laboratories, Chicago, Illinois). Three dogs that were not given any Acepromazine required 31.33 ± 2.90 ml/kg of Pentobarbital Sodium to induce anesthetic state. Depth of anesthesia was estimated by peripheral signs and continuous recording of respiratory rate and tidal volume. Additional doses of barbiturate 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 60 minutes period on high

concentration of oxygen. Samples were taken initially on room air at time zero (TØ) and at subsequent 1Ø, 15, and 3Ø minutes intervals till 6Ø minutes on hyperoxia (oxygen concentration greater than 2Ø.9% in inspired gas). Blood flow measurements in the carotid and femoral arteries were made every 1Ø minutes. Pulmonary and systemic vascular pressures were recorded every 15 minutes. Arterial and venous blood gases and cardiac output were determined at 3Ø minutes intervals. Total experimental time consisted of 3Ø minutes on normoxia and 6Ø minutes on hyperoxia breathing.

Pulmonary and Systemic Hemodynamics

Once in anesthetized state, dogs were strapped in dorsal recumbency on a surgical table and then intubated using Air-Cuff veterinary endotracheal tube (size 1Ø mm I.D.; Bivona Surgical Inc., Gary, Indiana). Endotracheal tube placement was established by observing bilateral chest expansion. Femoral vein and artery were cannulated for pulmonary arterial and systemic arterial pressure measurement, respectively. Carotid and femoral arteries were used to record blood flow measurement to the brain and hind limb, respectively.

After the dog appeared to be physiologically stabilized, the initial recordings of pressures and blood flows were made on normoxia. The minute respiratory rate and ventilation were computed, also the arterial blood gases and cardiac output curves were obtained at the end of 3Ø minutes on normoxia breathing. Hyperoxia breathing was instituted for 6Ø minutes and recording were made in a similar fashion

as described in normoxia. The dogs were then terminated at the end of experiment.

Respiratory rate was measured by a Fleish NO. Ø pneumotach and Statham differential pressure transducer (model 14890; Statham, Hato Rey, Puerto Rico). Minute volume was recorded on an inline Singer air meter (model DTM-115; American Meter Division. USA). The difference between the initial and final meter reading was the total ventilation inspired by the dog in that period. Tidal volume was then computed knowing the total ventilation divided by total breaths in that time period.

Arterial blood pressure and pulmonary artery blood pressure were recorded with Statham pressure transducers (model P23db and P23gb, respectively). Carotid and femoral arteries blood flow were recorded with blood flow transducers connected to Pulsed Logic Electromagnetic Blood Flowmeter (model BL-61Ø; Biotronix Laboratory, Inc., Kensington, Maryland). This device was used to check the baseline and see if the flow had a positive deflection on the meter, its output was connected to Beckman recorder.

Indocyanine Green dye (Cardio-green dye) dilution technique was employed in recording cardiac output curve on an Soltec Strip Chart Recorder (model 1242; Soltec, Sun Valley, California).

All the pressures, flows, and respiratory rate measurements were recorded on 8 channel Beckman Type R Dynograph (Beckman Instruments Inc., Schiller Park, Illinois). All the channel used in this experiment were calibrated and zeroed for baseline recordings.

Surgical Techniques

Surgical preparation included clipping of hair on the neck and the pelvic area. A single incision on the neck was used to expose the external and the internal jugular veins, and the common carotid artery. External jugular vein was cannulated and the catheter tip was advanced and positioned into the internal jugular vein. This cannula was used to collect the anaerobic venous blood samples. The well exposed carotid artery was used to attach the electromagnetic blood flow transducer (model T-1a or A-2; In Vivo Metric System, Redwood Valley, California).

Another single incision was made on left pelvic region and left femoral artery and vein were exposed. A triple lumen Swan-Ganz flow directed thermodilution catheter (size 7F; American Edwards Laboratories, Irvine, California) connected to Statham pressure transducer, was introduced into the left femoral vein and its tip positioned into the pulmonary artery via right ventricle. The catheter position was confirmed by the characteristic right ventricle and pulmonary artery pressures wave forms. The proximal port of this catheter was used to record pulmonary artery pressure and collect anaerobic mixed venous blood samples for blood gases analysis. The distal port was used to inject cardio-green dye into the right ventricle for the cardiac output determination.

Similarly, left femoral artery was cannulated using single lumen Swan-Ganz flow directed monitoring catheter (size 8F) connected to Statham pressure transducer. Its tip was directed into the left

ventricle via mitral valve, and then the catheter was pulled back and positioned just outside the left ventricle into the ascending aortic arch. The catheter positioned was confirmed by the characteristic left ventricle and systemic arterial pressures wave forms. This catheter was used to record systemic arterial pressure, to collect anaerobic arterial blood samples for blood gases analysis, and to aspirate blood at a constant speed by an Infra-Red Densitometer to detect the cardio-green dye concentration in the arterial blood for the measurement of cardiac ouput.

A single incision over the right pelvic region was made to expose the right femoral artery and vein. Right femoral vein was cannulated indirectly via one of the side branches, catheter tip was positioned into the patent femoral vein. This catheter was used only for collections of femoral anaerobic venous blood for blood gas analysis. Electromagnetic blood flow transducer was attached to right femoral artery in a similar fashion as described for carotid artery.

All blood vessels were ligated cranially to the cannulation site. Area around the blood flow transducers was kept moist using saline soaked gauze pads. All cannulas were maintained patent by periodically flushing with 1Ø USP units/ml of heparinized saline.

Normoxia Measurements and Recordings

Normoxia recordings or measurements were designated at time zero (TØ). All dogs were allowed 3Ø minutes for physiological stabilization after the surgical procedures and before starting the actual experiment.

During this waiting period, dogs were heparinized using 100 USP units/kg of Heparin (1000 USP units/ml) (Lypho Medical Inc., Chicago, Illinois). Also hemoglobin determination was done by aspirating 20 microliter blood sample and mixing with 5 ml reagent Cyanmethemoglobin solution containing 250 mg Potassium Cyanide per liter (Fisher Scientific Company, Orangeburg, New York). We used Spectronic 70 (Bausch & Lomb, Rochester, New York), setting wave length at 540 nanometer. The absorbance values were converted to give hemoglobin values in gram/100 ml of blood.

All the pressure transducers, and blood flow meters were checked for baseline zero initially and before every measurement during the experiment. Respiratory rate and minute ventilations were recorded during the entire experimental period. Vascular pressure measurements were recorded continuously, but values were calculated at 15 minutes interval. Similarly, blood flows were recorded through out the experimental period but measurements were taken at every 10 minute interval. Each artery was occluded completely to get zero blood flow recordings prior to each blood flow measurement.

At the end of 30 minutes on normoxia, arterial blood from the aorta, mixed venous blood from the pulmonary artery, and venous blood samples from the internal jugular and femoral veins were drawn in 3 cc pre-heparinized syringes and stored in an ice beaker at 0 degree C. These blood samples were analyzed using pH/Blood Gases Analyzer (model IL 513; Instrumentation Laboratory, Lexington, Massachusetts). Cardiac output curve was obtained at the end of normoxia period. 0.2 mg/kg of

Indocyanine Green (Cardio-Green) dye (2.5 mg/ml) (Hynson, Westcott, & Dunning, Baltimore, Maryland) was injected into right ventrical and simultaneouly blood was aspirated at a constant speed into Infra-Red Densitometer (model 103-IR; Gilford Instrumentation Laboratories, Inc., Oberlin, Ohio), it detected the concentration of dye in the blood and plotted the dye concentration curve on Soltec strip chart recorder as a function of time. With the measurement of cardiac output curve the normoxia period ended.

Hyperoxia Measurements

Three types of hyperoxic gases were used. 40, 60, and 100% oxygen balanced with nitrogen. Inspired hyperoxic gas was analyzed using nitrogen gas analyzer, and collected in reservoir bags. We used Nitrogen Analyzer (model 47302A; Hewlett Packard, Waltham, Massachusetts). Nitrogen gas concentration in our hyperoxic gases were 60, 40, and 0% respectively. Five dogs were treated on 40%, other five on 60%, and the remaining six were treated with 100% oxygen. Only one treatment was administered per dog, and the following measurements were recorded.

Respiratory rate, and total ventilation were recorded for the entire period of 60 minutes on hyperoxic breathing. Pressures and blood flow measurements were recorded in a similar fashion as described during normoxic breathing. Blood gases and cardiac output curve were determined at 30 minutes interval, and at the end of 60 minutes on hyperoxia another cardiac output curve was obtained. With this

observation completed, hyperoxia was terminated and dogs were switched to normoxic breathing using one way valve on pneumotach.

Before terminating the dogs, blood flow transducers were calibrated. We surgical cut the artery distal to blood flow transducer and allowed the blood to flow in a time regulated fashion into a graduated cylinder. The blood flow (ml/min) was used to calibrate the blood flow transducer.

We injected 1.0cc/10 lbs plus 1.0cc more of Euthanasia Solution (Fort Dodge Laboratories, Fort Dodge, Iowa) into the pulmonary artery. Dogs were observed till no respiration and blood pressure was present. The thoracic cavity was entered and heart was exposed and checked for heart worms. If negative for heart worms, then the data collected were saved.

Data Analysis

Data were divided into four groups.

Group 2 represent the measurements recorded on 40% oxygen breathing, group 3 represent the measurements recorded on 60% oxygen breathing, group 4 represent the measurements recorded on 100% oxygen breathing, and group 5 represent the values of groups 2, 3, and 4 combined.

The mean values in groups 2, 3, 4, and 5 during oxygen breathing are compared with their respective groups normoxia values. In addition, on some instances, with in the group, mean values are compared with the normoxia values with respect to time.

Treatment 21 represents 40% oxygen mode, and normoxia values. Treatment 22 represents 40% oxygen mode, and hyperoxia values. Treatment 31 represents 60% oxygen mode, and normoxia values, treatment 32 represents 60% oxygen mode, and hyperoxia values. Similarly, treatment 41 represents 100% oxygen mode with normoxia values, treatment 42 represents 100% oxygen mode with hyperoxia values. Treatment AIR and OXY represent values on normoxia and hyperoxia, respectively for groups 2, 3, and 4 combined.

In order to correct for some of the inherent variability between animals, the data were normalized by determining the deviation of each parameter from the control room air, Time zero; TØ, values. All parameters values are presented with their mean, standard deviations, minimum and maximum values, according to groups and treatments.

All figures presented were plotted by the computer with the Statistical Analysis System (SAS). All data that are presented in figure form in the text is also presented in the table form in the Appendix.

An analysis of variance was conducted on the values at each sample period to test for a treatment difference. A p- value of less than Ø.Ø5 was taken to indicate a statistically significant difference between the experimental groups. A p- value greater than Ø.Ø5 but less than Ø.1Ø was taken to indicate a significant trend for a difference between the groups.

RESULTS AND DISCUSSION

Respiratory Parameters

Minute ventilation is defined as the product of one minute respiratory rate and tidal volume. A change in minute ventilation is influenced by changes in respiratory frequency, tidal volume, or both.

Mean values of respiratory parameters during normoxia and hyperoxia for groups 2, 3, and 4 are given in Table A1, and plotted in Figures 1, 3, and 5. Group 2 (40% oxygen) and group 3 (60% oxygen) showed an increase of 7.5% and 18.1% respectively in respiratory frequency during oxygen breathing when compared with normoxia values. Group 4 (100% oxygen) showed a very slight increase in respiratory frequency, and tidal volume increased by 3.2% during hyperoxia. Whereas, groups 2 and 3 showed a decrease in tidal volume during oxygen breathing. Group 5 (40%, 60%, and 100% oxygen combined) showed an overall 3.1% increase in minute ventilation when compared with normoxia breathing. Both tidal volume and respiratory frequency increased. Table A2, and Figures 2, 4, and 6 summarize the mean values of minute ventilation in this group. None of the changes in respiratory parameters in all four groups were statistically significant.

Aubier et al. (1980) have reported an increase in minute volume after 15 minutes of 100% oxygen breathing in COPD patients. Whereas, in asthmatic patients, in newborn, and in COPD patients on long term oxygen therapy, hyperoxia caused a reduction in minute volume (Freedman et al. 1983, Reinstorff and Fenner 1972, and Fleetham et al. 1980).

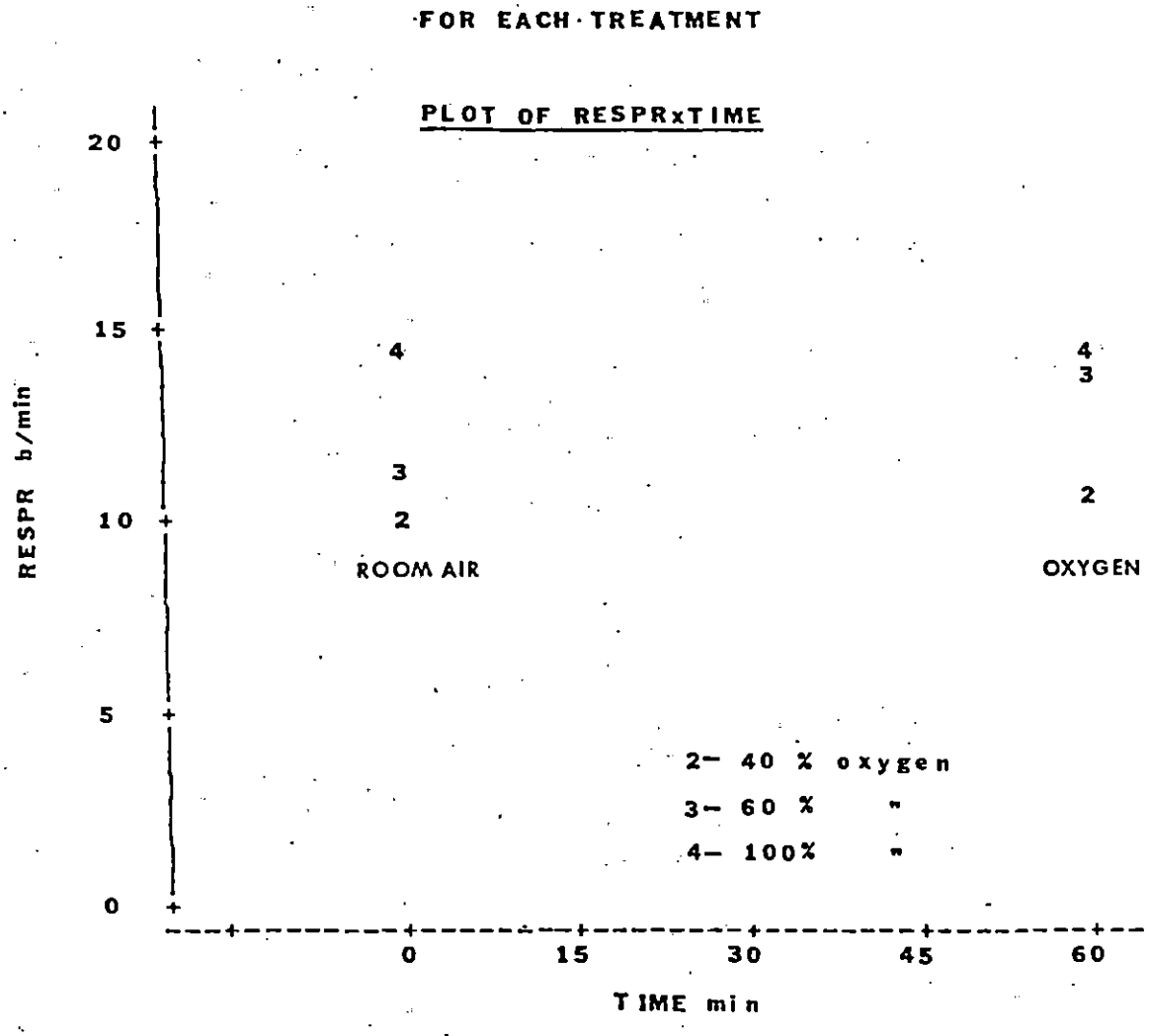


Figure 1. Mean values of respiratory frequency by treatment

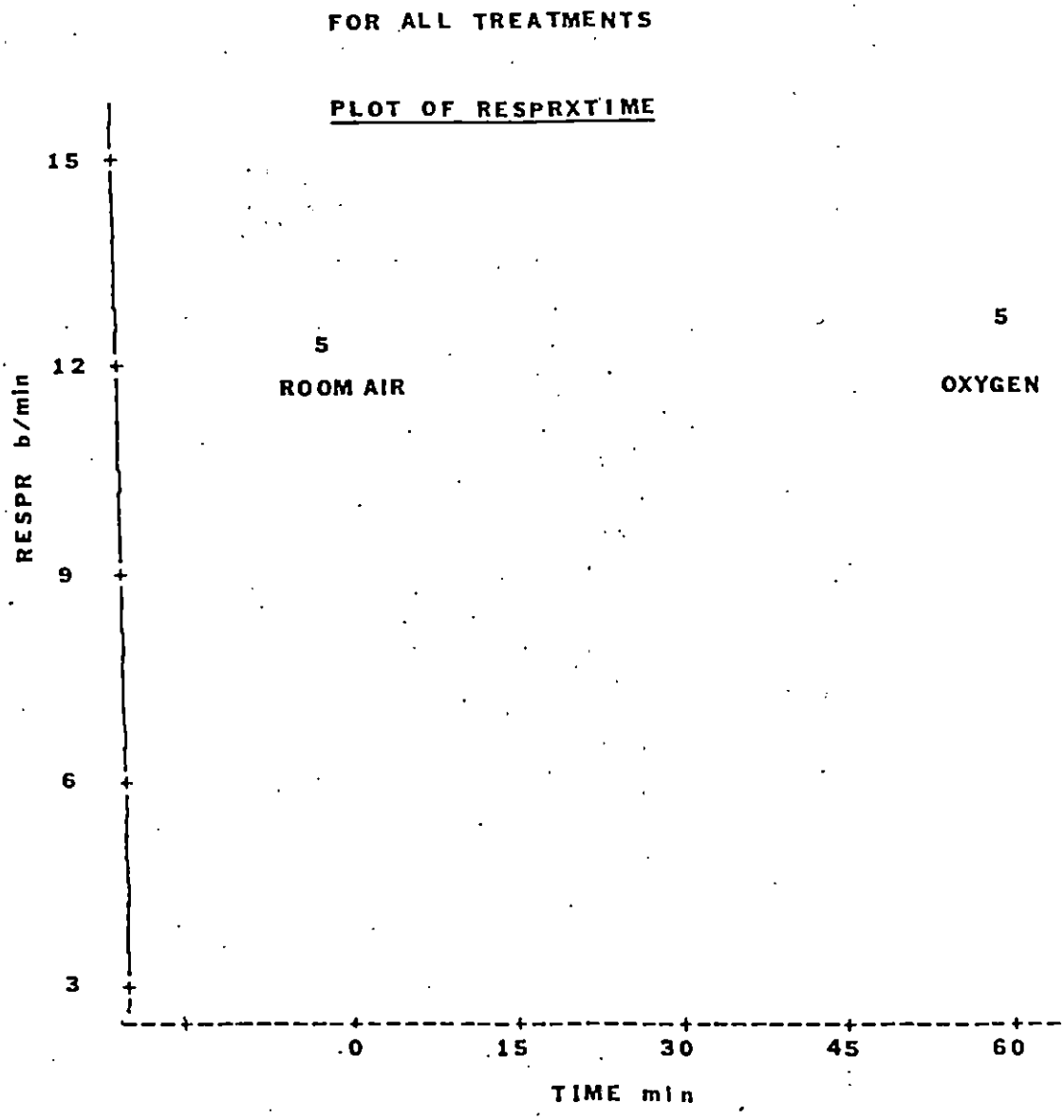


Figure 2. Mean values of respiratory frequency for all treatments

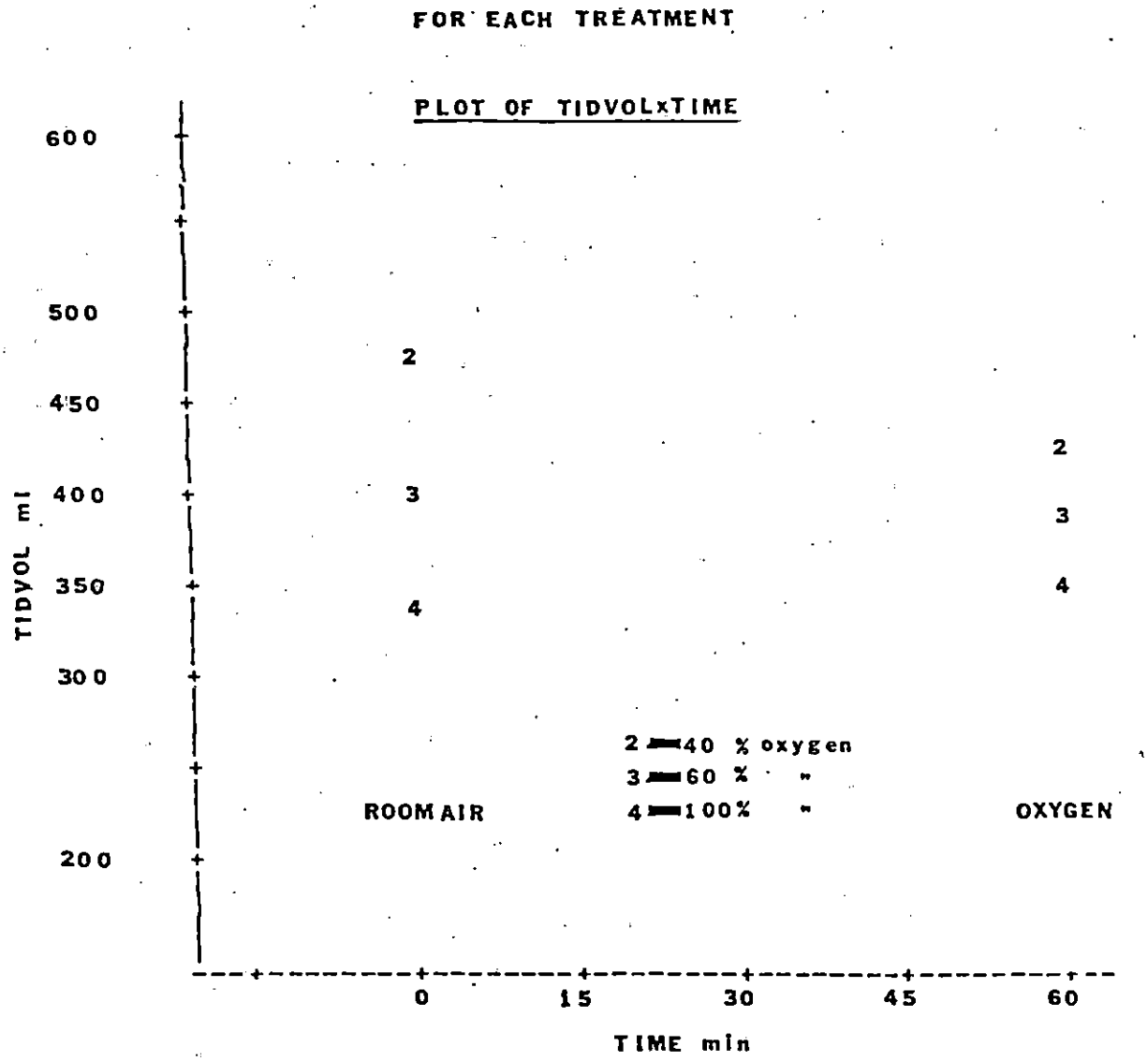


Figure 3. Mean values of tidal volume by treatment

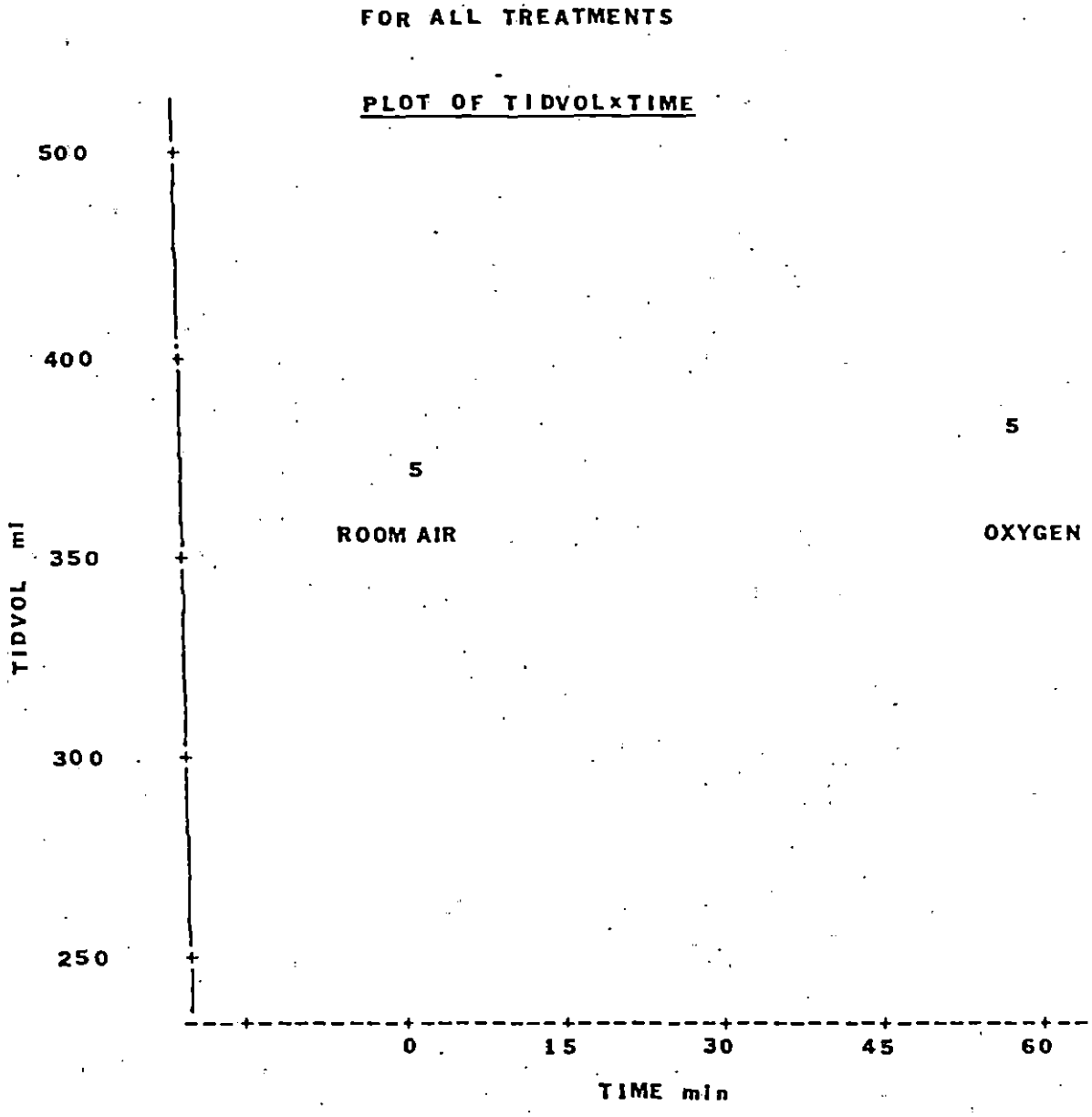


Figure 4. Mean values of tidal volume for all treatments

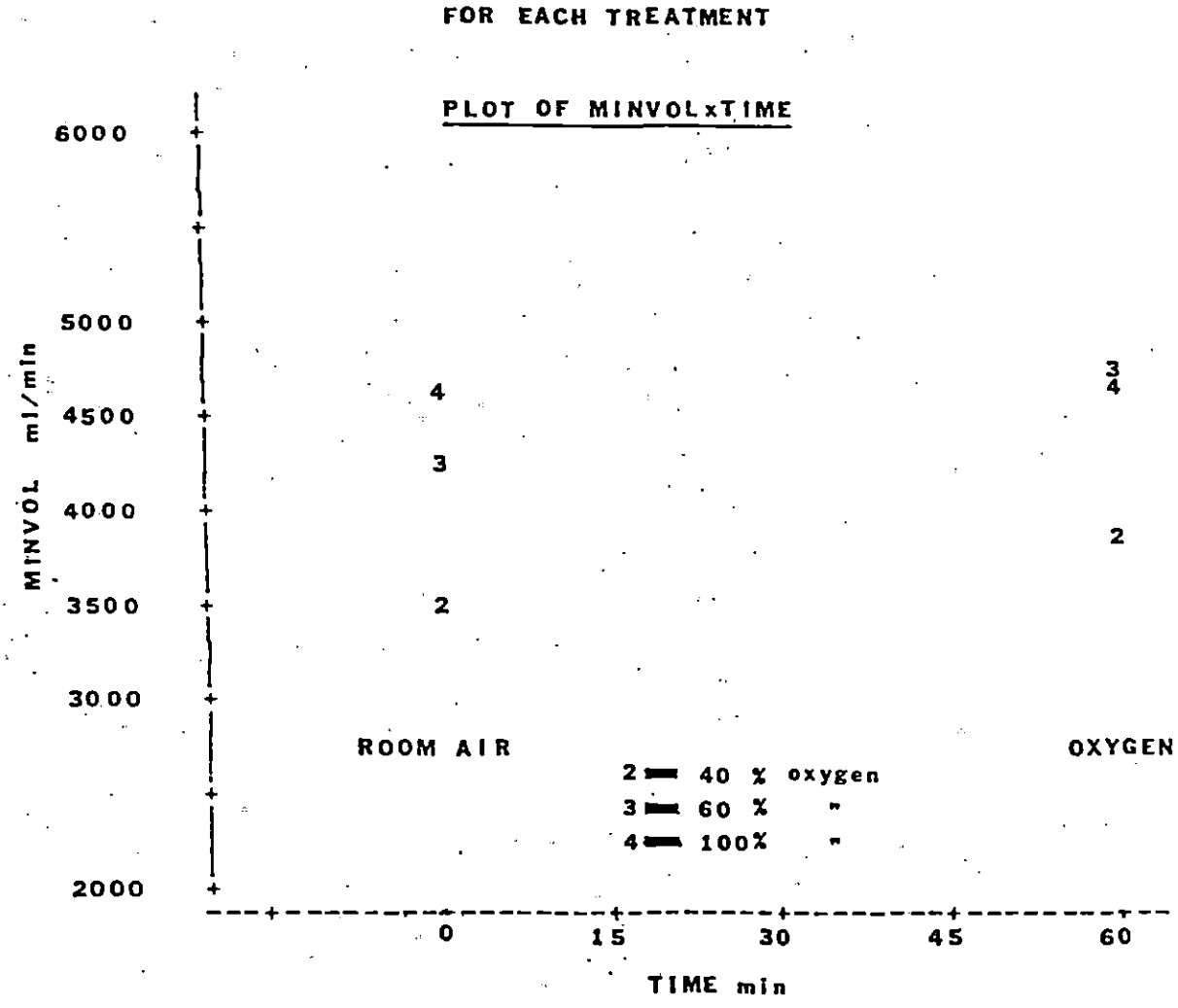


Figure 5. Mean values of minute ventilation for each treatment

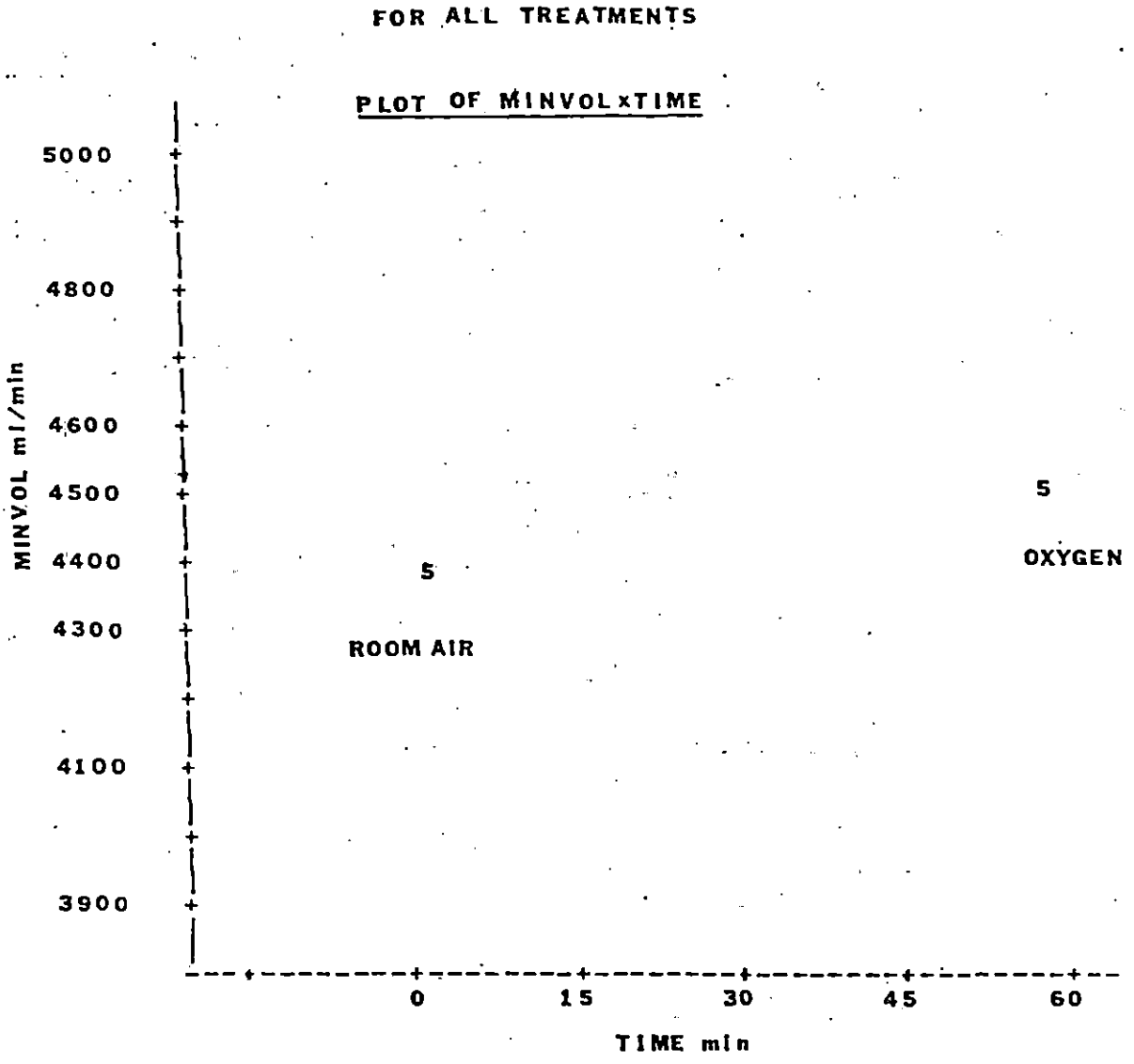


Figure 6. Mean values of minute ventilation for all treatments

Blood Gases

Tables A3, A4, A5, and A6, and Figures 7 through 22 represent the mean values of pH, arterial carbon-dioxide and oxygen tensions, and blood hemoglobin oxygen saturation for arterial, pulmonary artery, jugular and femoral veins for all four groups.

Groups 2, 3, 4, and 5 showed a slight decrease in blood pH with slight increase in blood carbon-dioxide tension during hyperoxia. These changes were not statistically significant. Aubier et al. (1980) reported an increase in blood carbon-dioxide tension by 23 Torr after 15 minutes of 100% oxygen breathing in patients with COPD. COPD patients on long term oxygen therapy also showed a significant increase in arterial blood carbon-dioxide tension (Fleetham et al. 1980). Grave et al. (1970) reported no significant difference between the mean arterial carbon-dioxide tension of the neonates and two weeks old puppies exposed to 80 to 90% oxygen. Inhalation of 85 to 100% oxygen produced no changes in carbon-dioxide tension or the pH of the arterial blood (Kety and Schmidt 1948, and Grave et al. 1970).

Groups 2, 3, 4, and 5 showed a statistically significant increase in arterial blood oxygen tension during hyperoxic breathing, it increased by 103%, 156%, 387%, and 247%. Aubier et al. (1980) reported an increase in arterial blood oxygen tension to 225 Torr on 100% oxygen breathing in patients with COPD. Also Cassuto and Farhi (1979) reported that exposure to hyperoxia caused a sustained rise in arterial oxygen tension.

For pulmonary artery blood oxygen tension, group 5 showed a statistically significant rise of 13%. Whereas, groups 2, and 3 showed a non significant rise of 12.9% and 10%, respectively during hyperoxic breathing. An increase of 13.3% in group 4 shows a significant trend. Cassuto and Farhi (1979) noticed an immediate rise in right heart (mixed venous blood) oxygen tension during 100% oxygen breathing.

Jugular vein blood oxygen tension increased by 18.9%, 17%, 20.4%, and 18.7% in groups 2, 3, 4, and 5, respectively during hyperoxic breathing. In groups 2 and 5, these changes were statistically significant when compared with their respective groups room air values. Changes in group 3 were not significant, changes in group 4, show a significant trend. Minami et al. (1973) reported that the jugular vein blood oxygen tension increased slightly in the "coma" group, but in the "brain death" group it increased significantly during hyperoxia.

Femoral vein blood oxygen tension increased by 11.5%, 11.5%, 15.5%, and 12.5% in groups 2, 3, 4, and 5, respectively during hyperoxia. Only, changes in group 5 were statistically significant.

Arterial blood hemoglobin oxygen saturation in groups 2, 3, 4, and 5 increased by 4.6%, 5%, 3.4%, and 4.2%, respectively during oxygen inhalation, and these changes were highly statistically significant. Spier et al. (1984) reported an increase in arterial blood hemoglobin oxygen saturation to 92.7% during nocturnal hyperoxic breathing, compared to 79.4% during nocturnal normoxic breathing. In asthmatic patients oxygen saturation in brachial artery rose to 99.6% during hyperoxia when comparing with 96.4% on normoxia.

Pulmonary artery, jugular and femoral veins blood hemoglobin oxygen saturation increased in all four groups. Groups 4 and 5 showed an increase of 5% and 4.1%, respectively, in pulmonary artery blood oxygen saturation during hyperoxia, and these changes show a significant trend. The jugular vein blood oxygen saturation increased by 5.6% in group 4, indicating a significant trend, and an increase of 4.6% in group 5 represent a statistically significant difference. Changes in femoral vein blood oxygen saturation in groups 4 and 5 show a significant trend.

A rise in blood carbon-dioxide tension and a fall in blood pH would cause a shift of the oxyhemoglobin dissociation curve to the right which facilitates the unloading of oxygen (the Bohr effect). Ivanov and Chebotarev (1980) mentioned that 20 minutes inhalation of oxygen shift the curve of oxyhemoglobin to the left, thus increasing the hemoglobin affinity for oxygen. In our situation, oxyhemoglobin curve will shift to the right because of an increase in arterial blood carbon-dioxide tension, and a fall in pH value during hyperoxia.

We also noticed a rise in minute ventilation by 3.1% with a slight increase in blood carbon-dioxide tension during hyperoxia, these conditions indicate the presence of mild respiratory acidosis. One would assume that increase in minute ventilation is due to an increase in blood carbon-dioxide tension during hyperoxia. It is also possible that an increase in alveolar oxygen tension during hyperoxia will wash out nitrogen from the lungs, leading to alveolar collapse, poor ventilation, and poor gas exchange in the lungs.

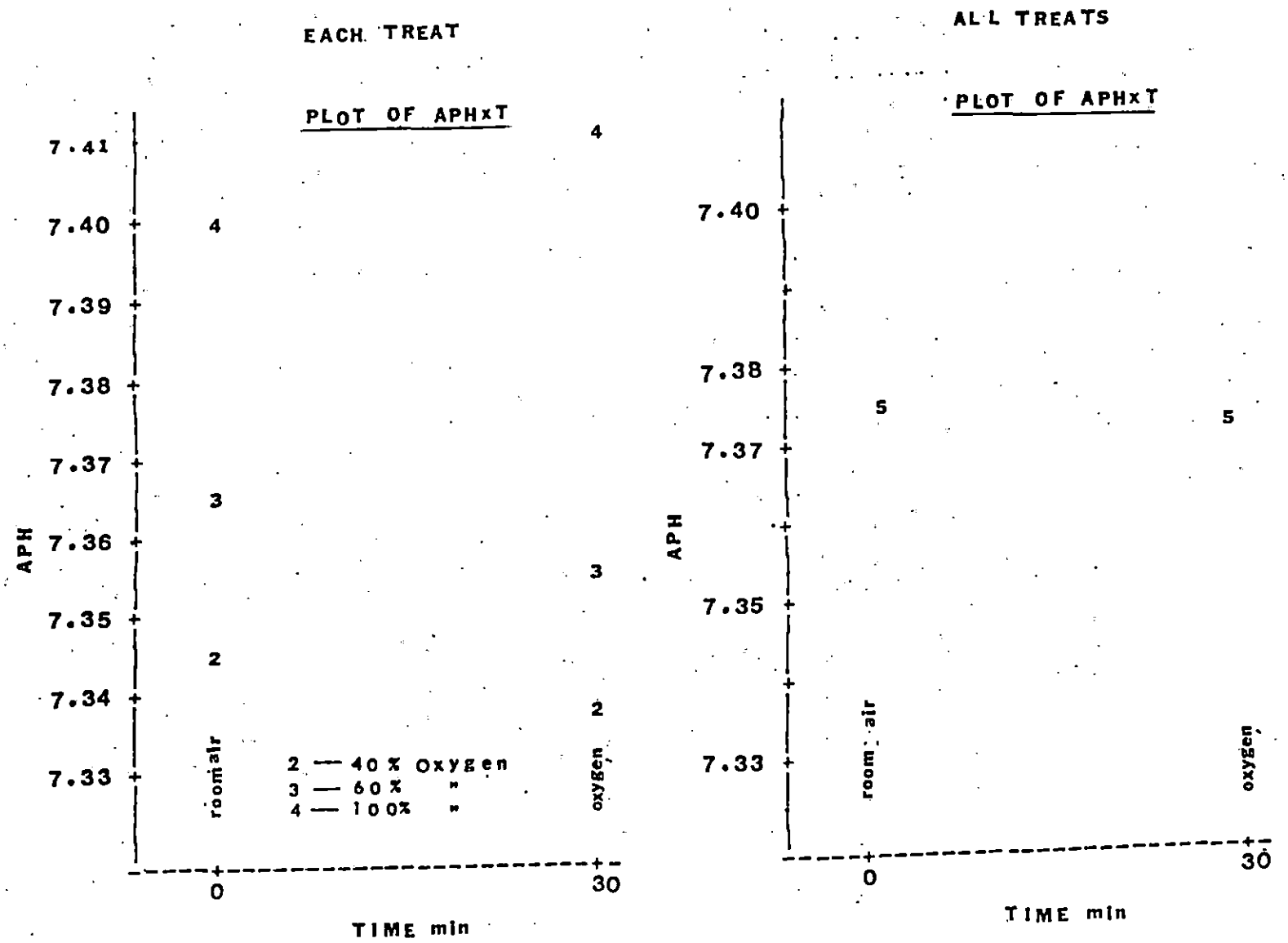


Figure 7 a & b. Mean values of arterial blood pH for each and all treatments

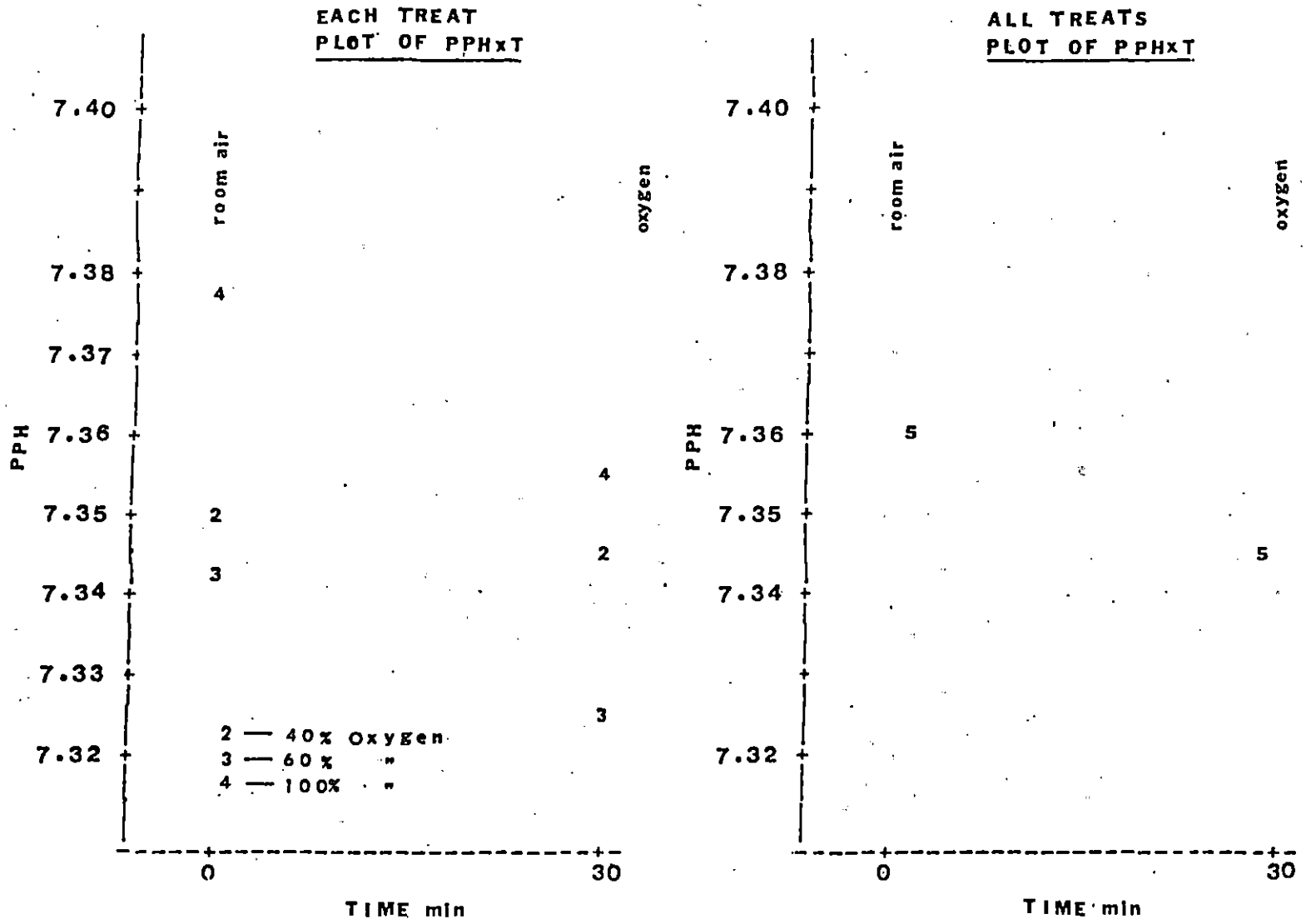


Figure 8 a & b. Mean values of pulmonary artery blood pH for each and all treatments

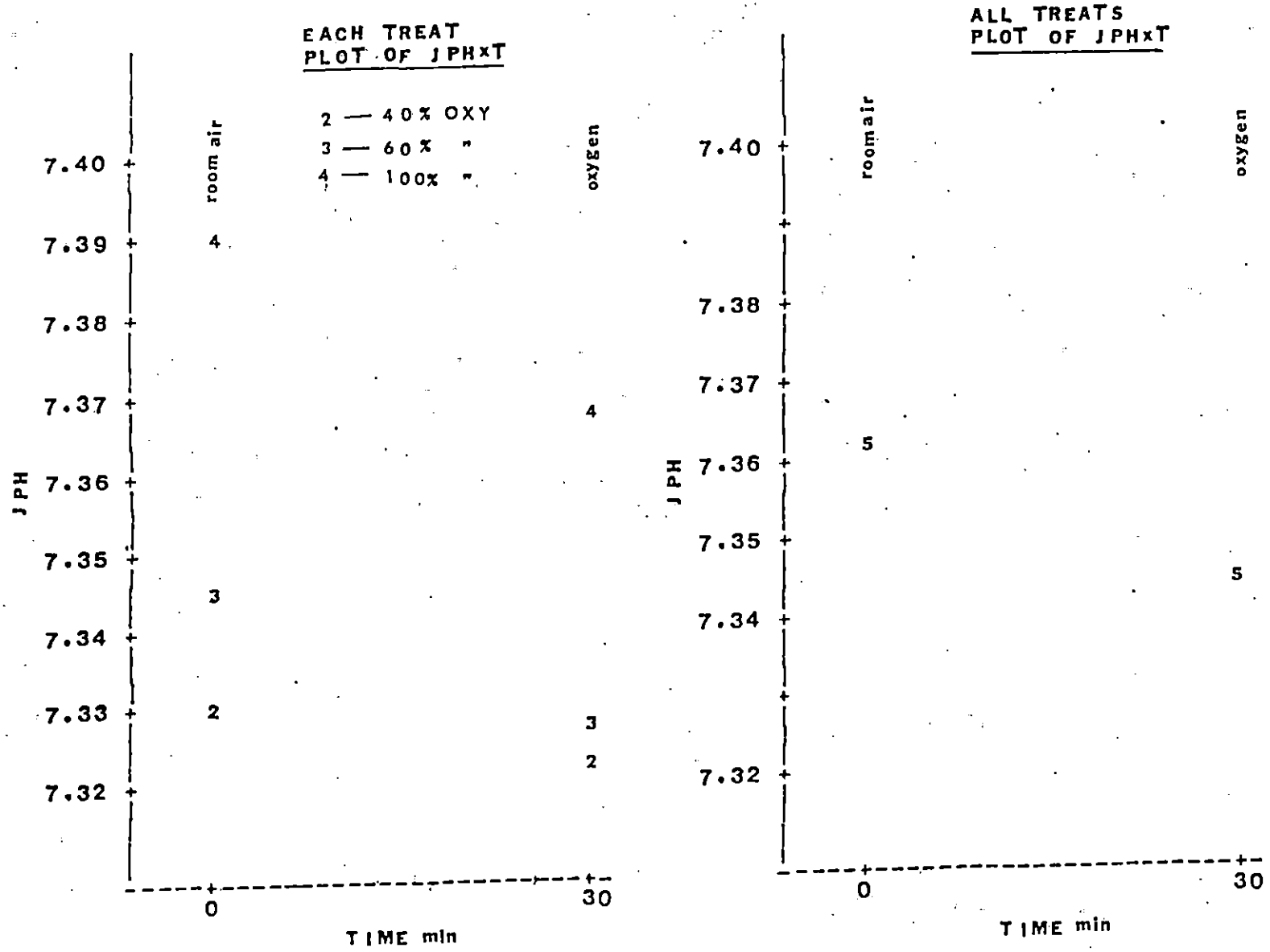


Figure 9 a & b. Mean values of jugular vein blood pH for each and all treatments

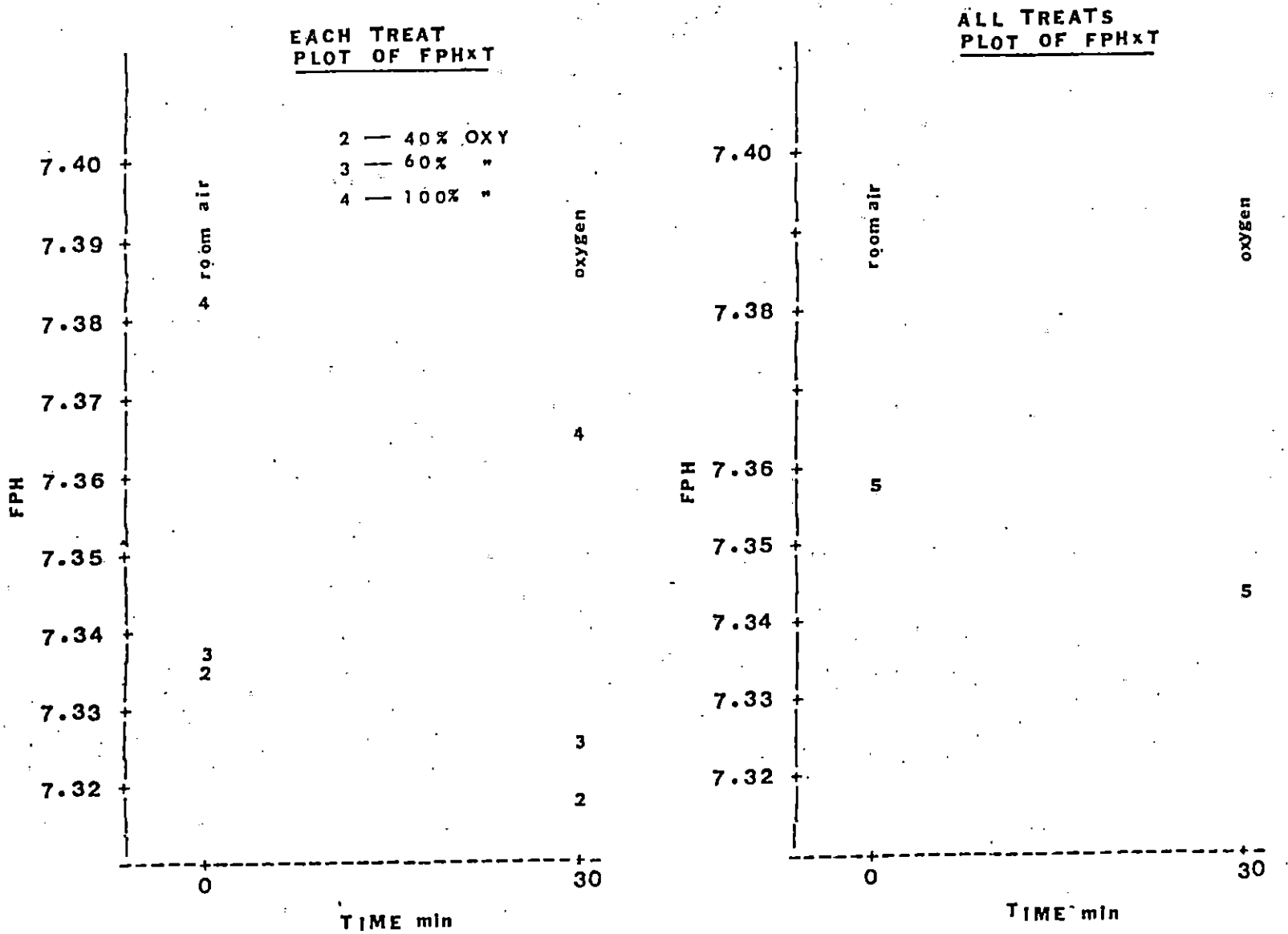


Figure 10 a & b. Mean values of femoral vein blood pH for each and all treatments

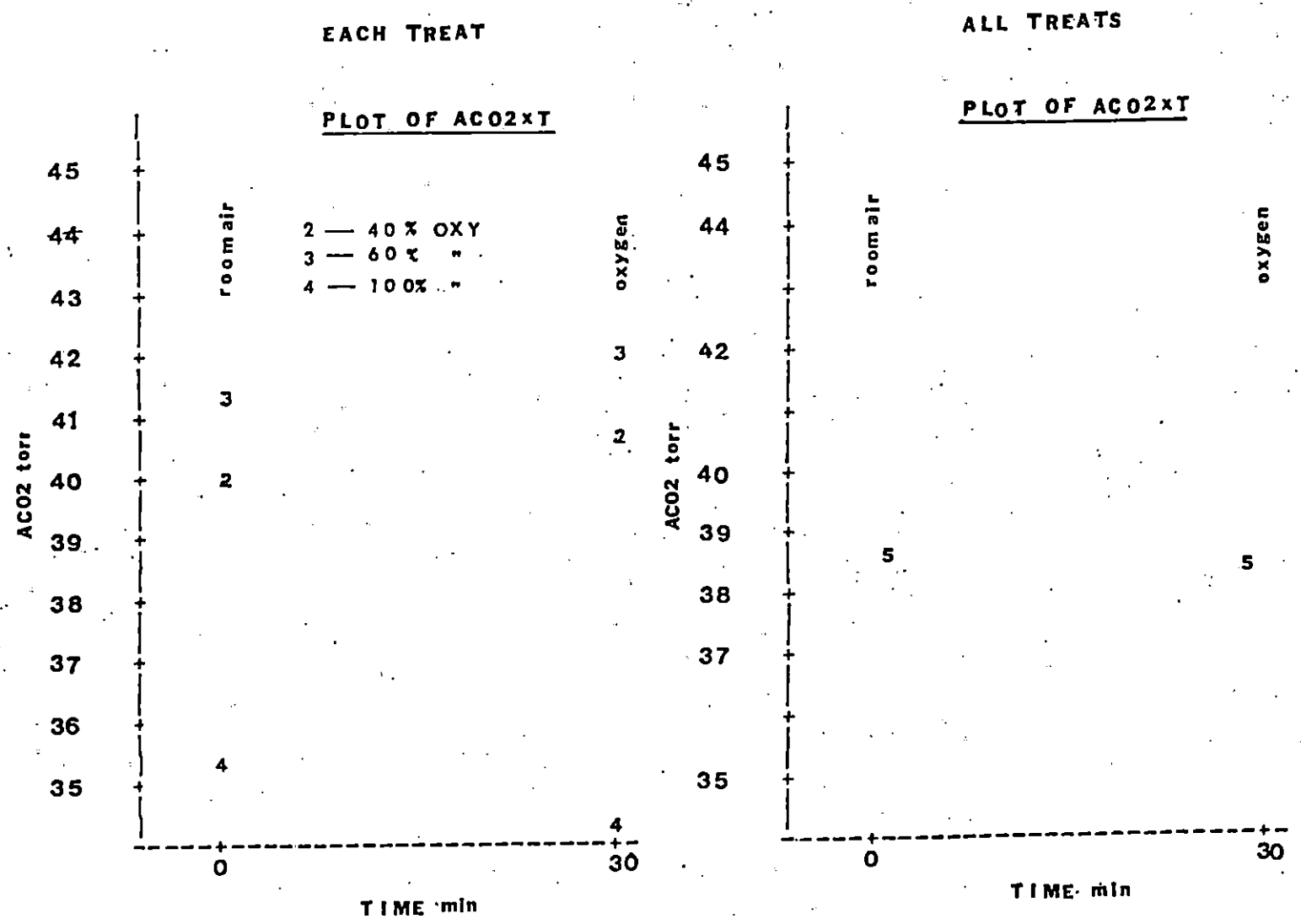


Figure 11 a & b. Mean values of arterial blood carbon-dioxide tension for each and all treatments

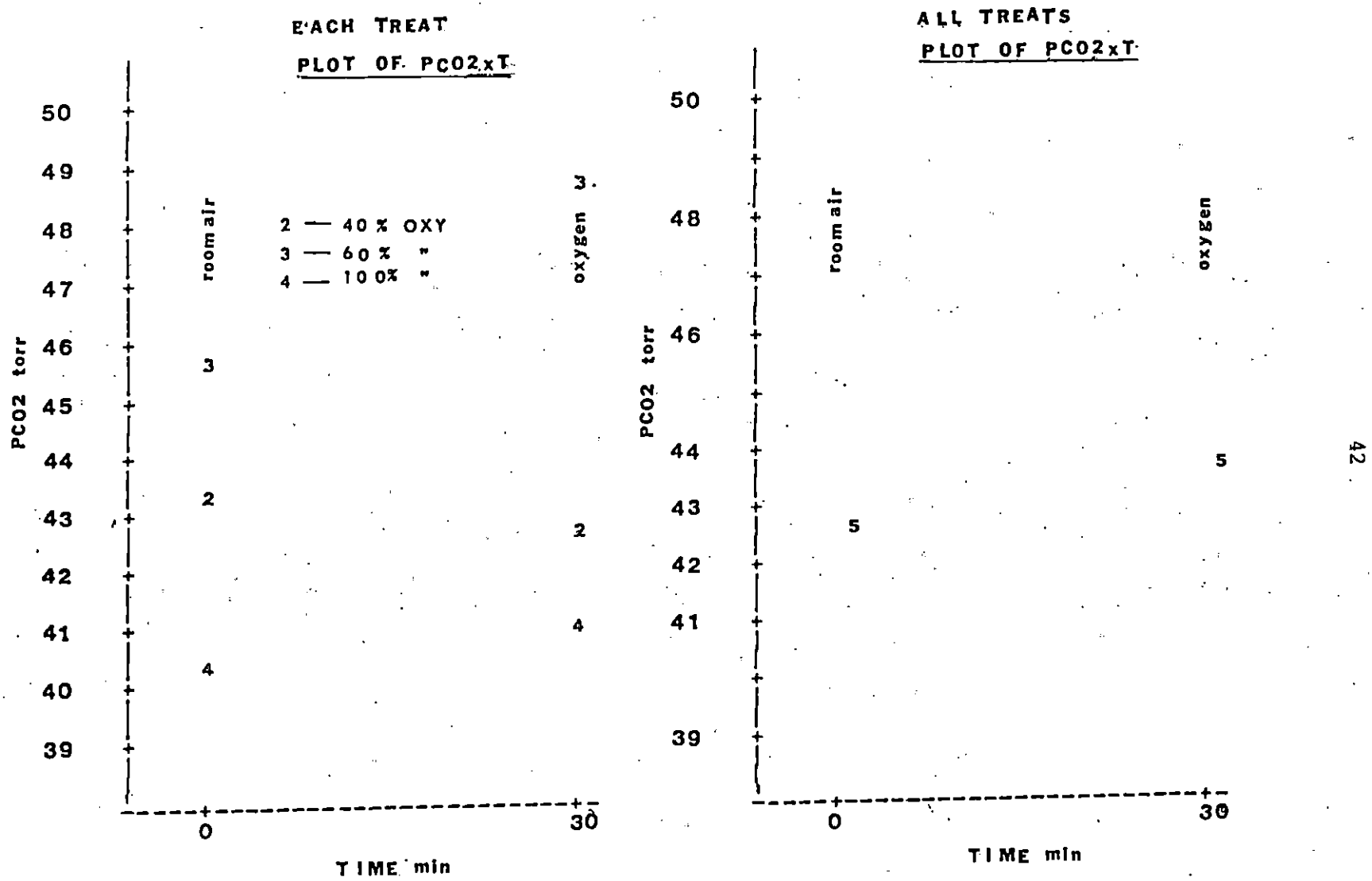


Figure 12 a & b. Mean values of pulmonary artery blood carbon-dioxide tension for each and all treatments

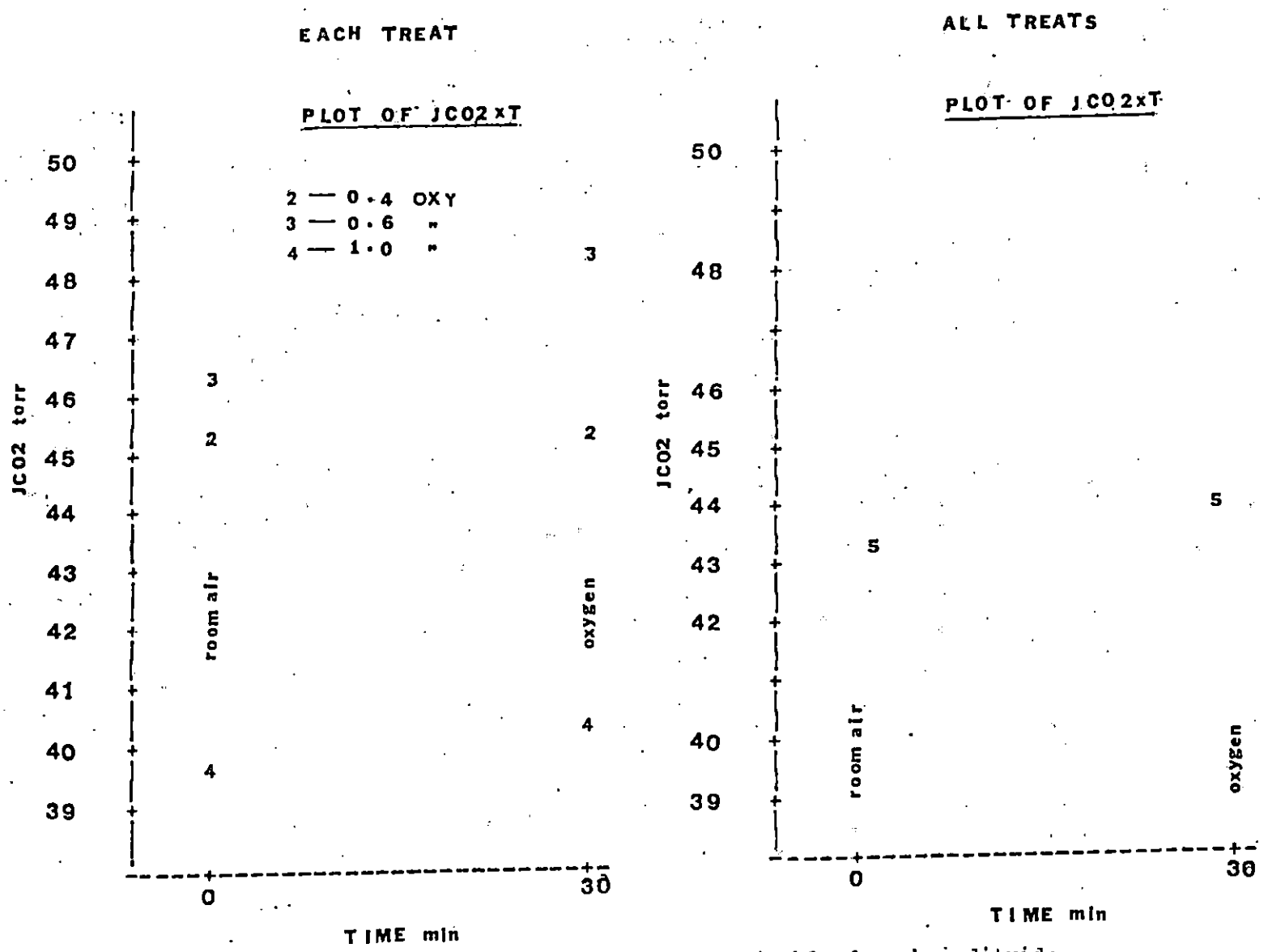


Figure 13 a & b. Mean values of jugular vein blood carbon-dioxide tension for each and all treatments

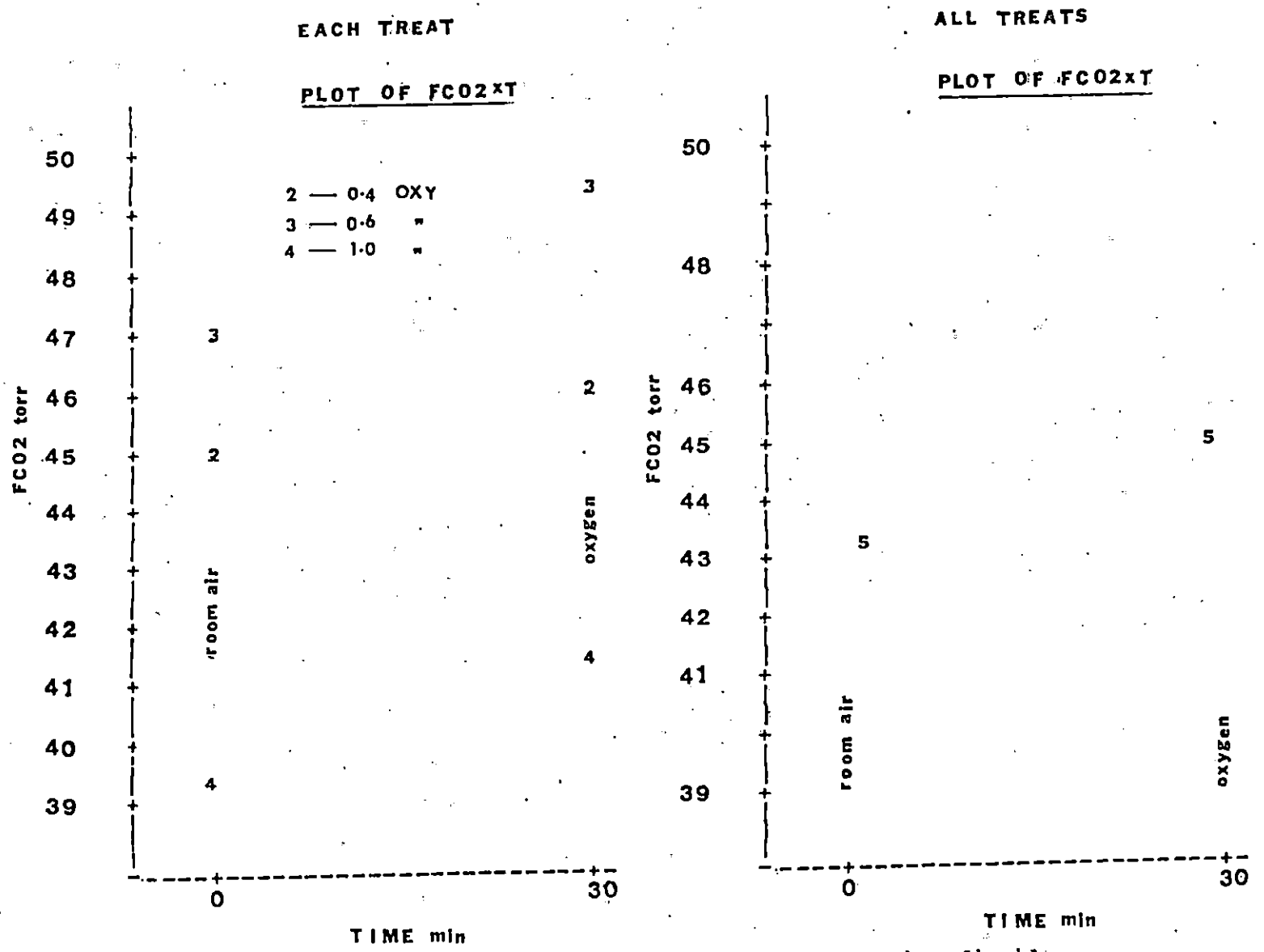


Figure 14 a & b. Mean values of femoral vein blood carbon-dioxide tension for each and all treatments

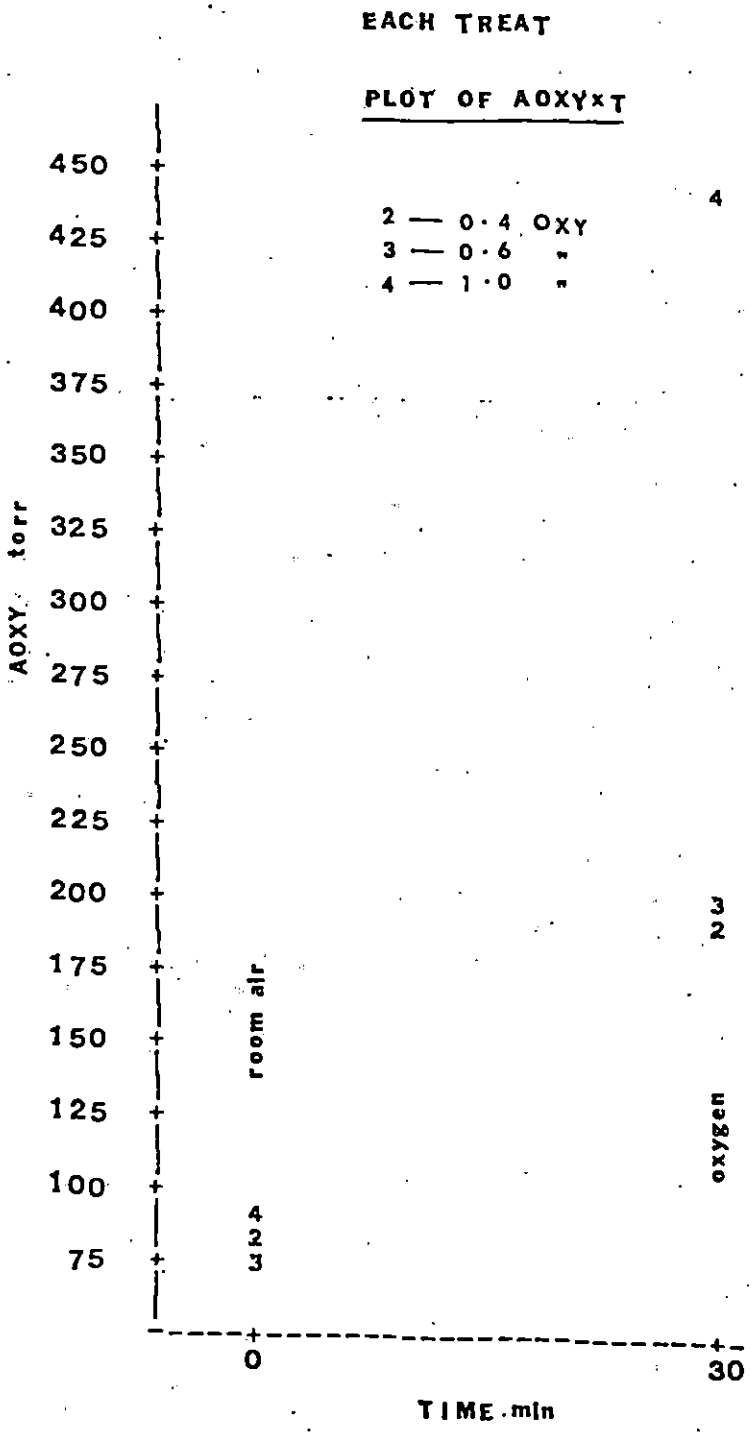


Figure 15 a. Mean values of arterial blood oxygen tension for each treatment

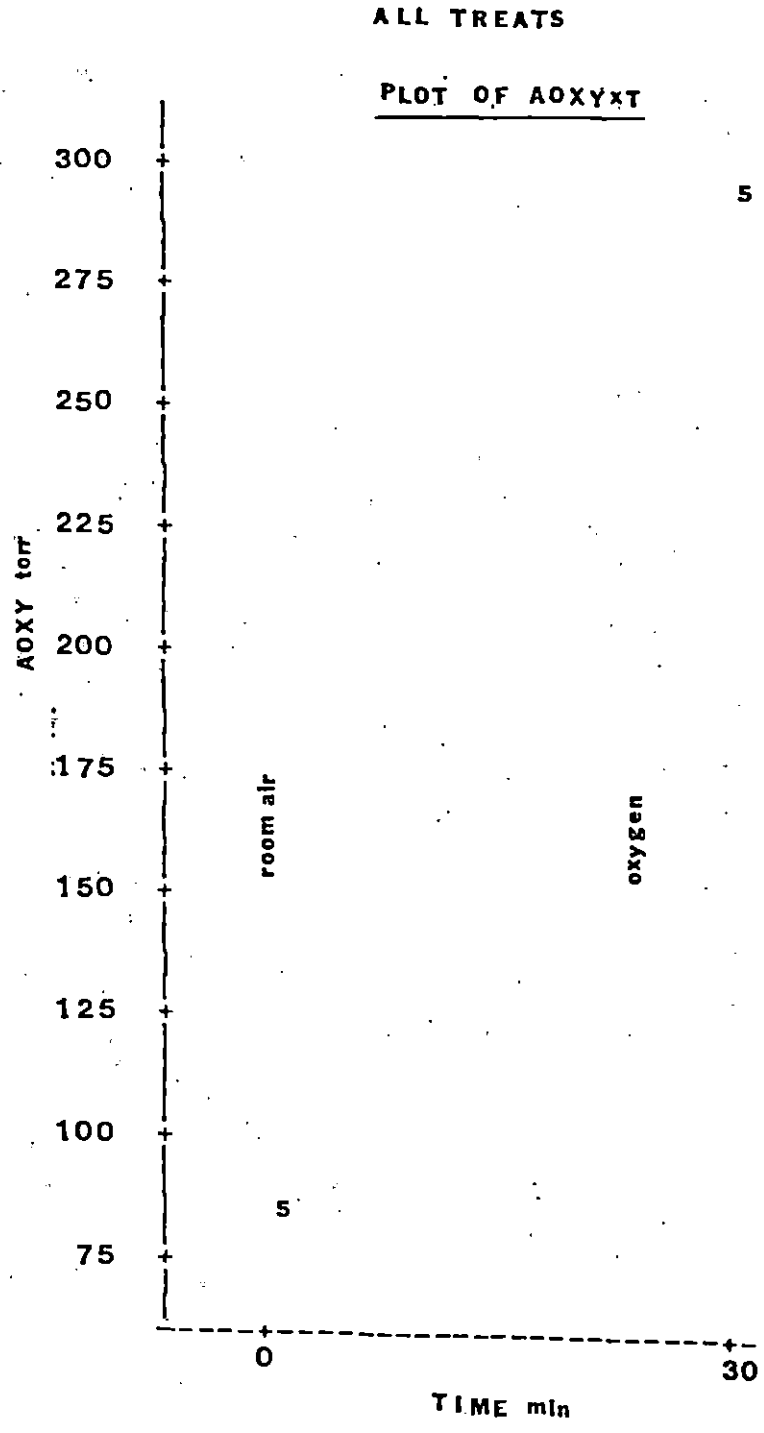


Figure 15 b. Mean values of arterial blood oxygen tension for all treatments

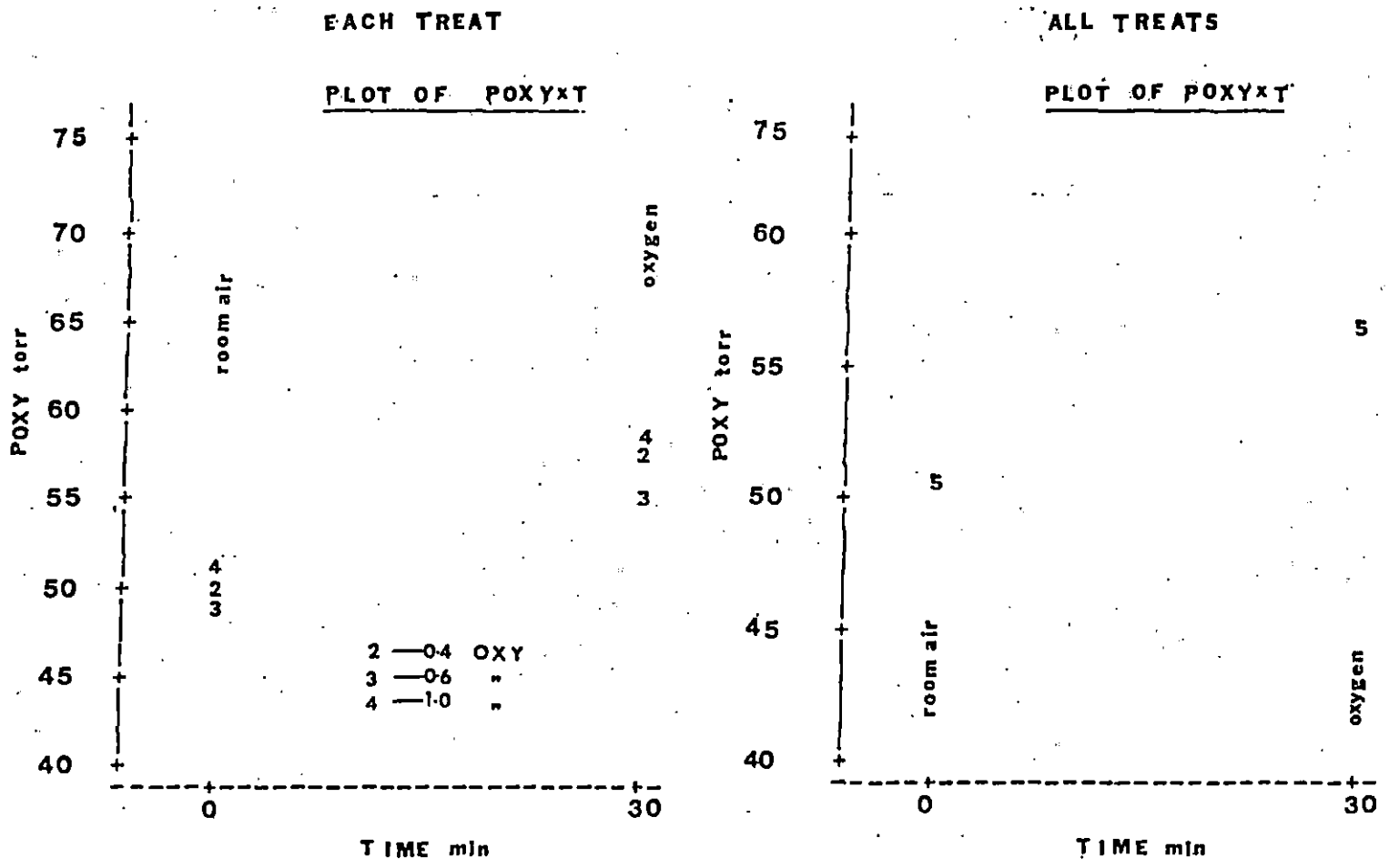


Figure 16 a & b. Mean values of pulmonary artery blood oxygen tension for each and all treatments

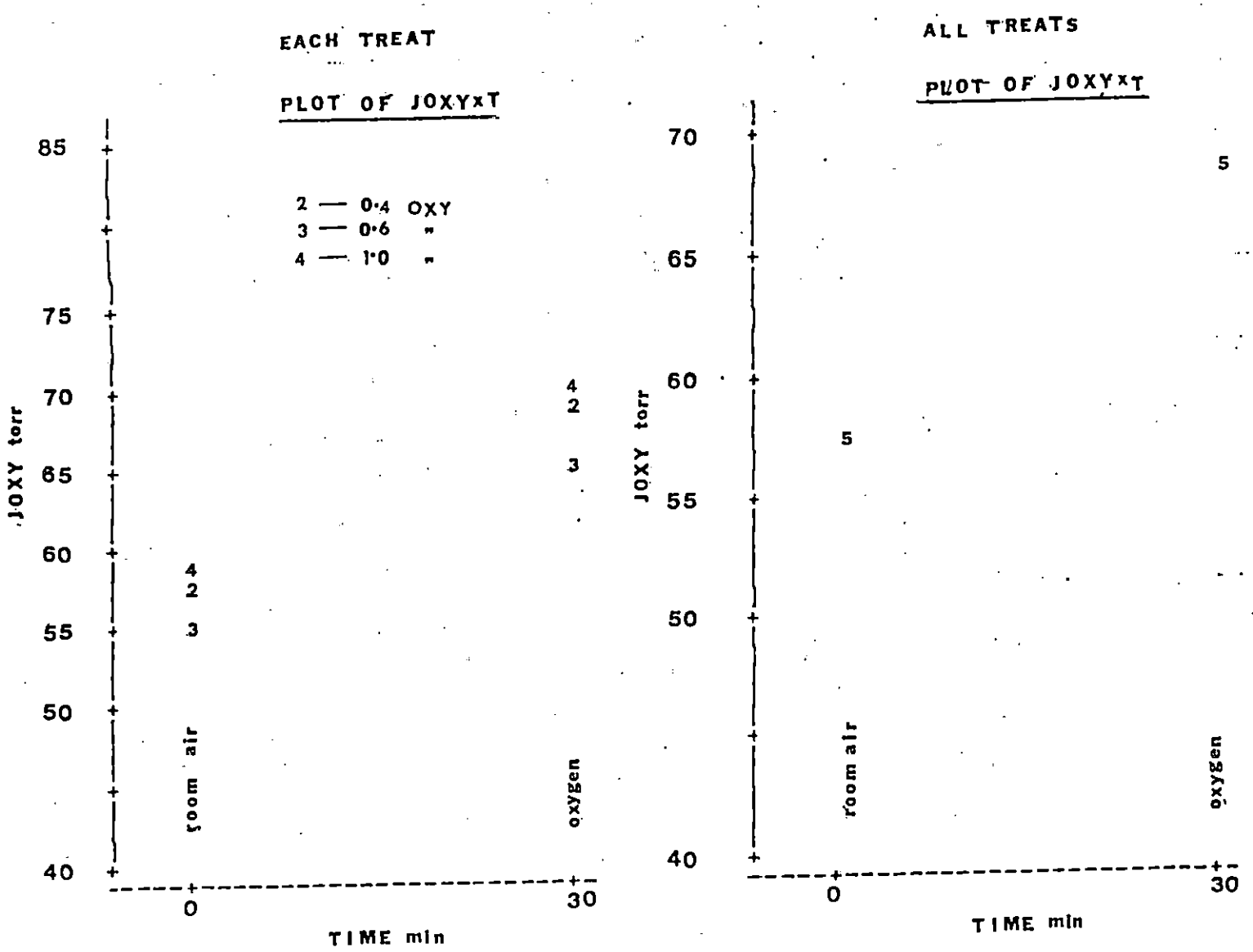


Figure 17 a & b. Mean values of jugular vein blood oxygen tension for each and all treatments

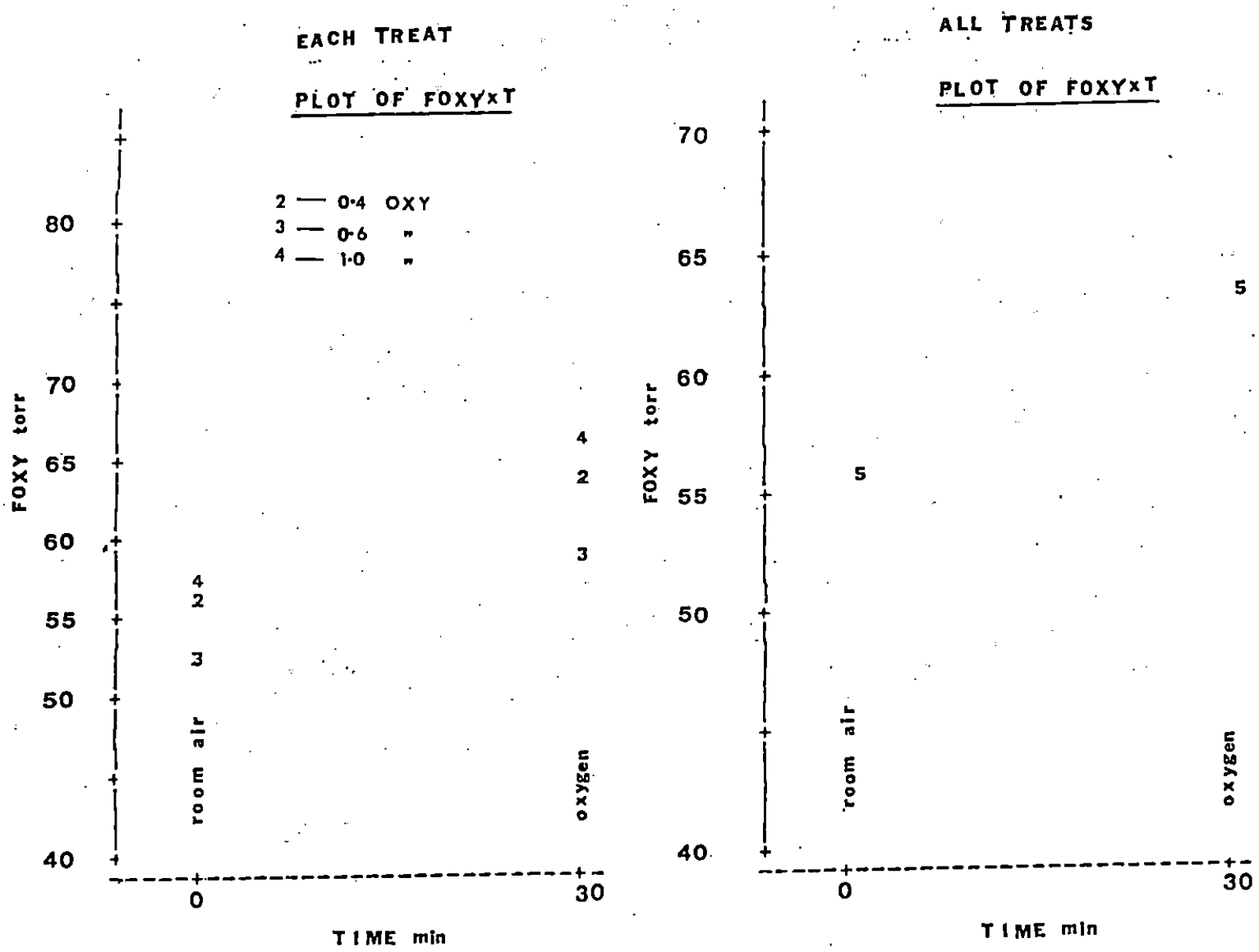


Figure 18 a & b. Mean values of femoral vein blood oxygen tension for each and all treatments

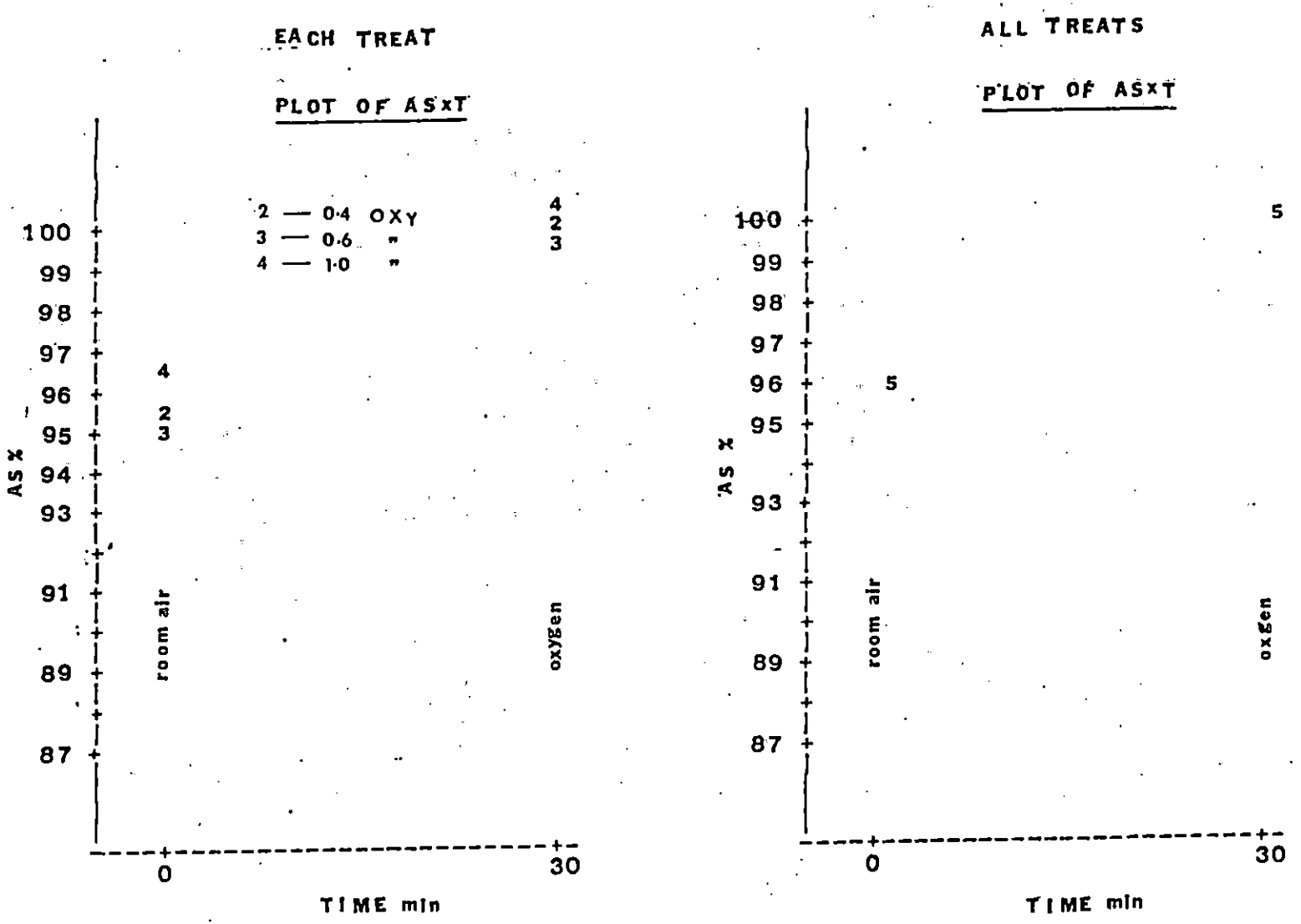


Figure 19 a & b. Mean values of arterial blood hemoglobin oxygen saturation for each and all treatments

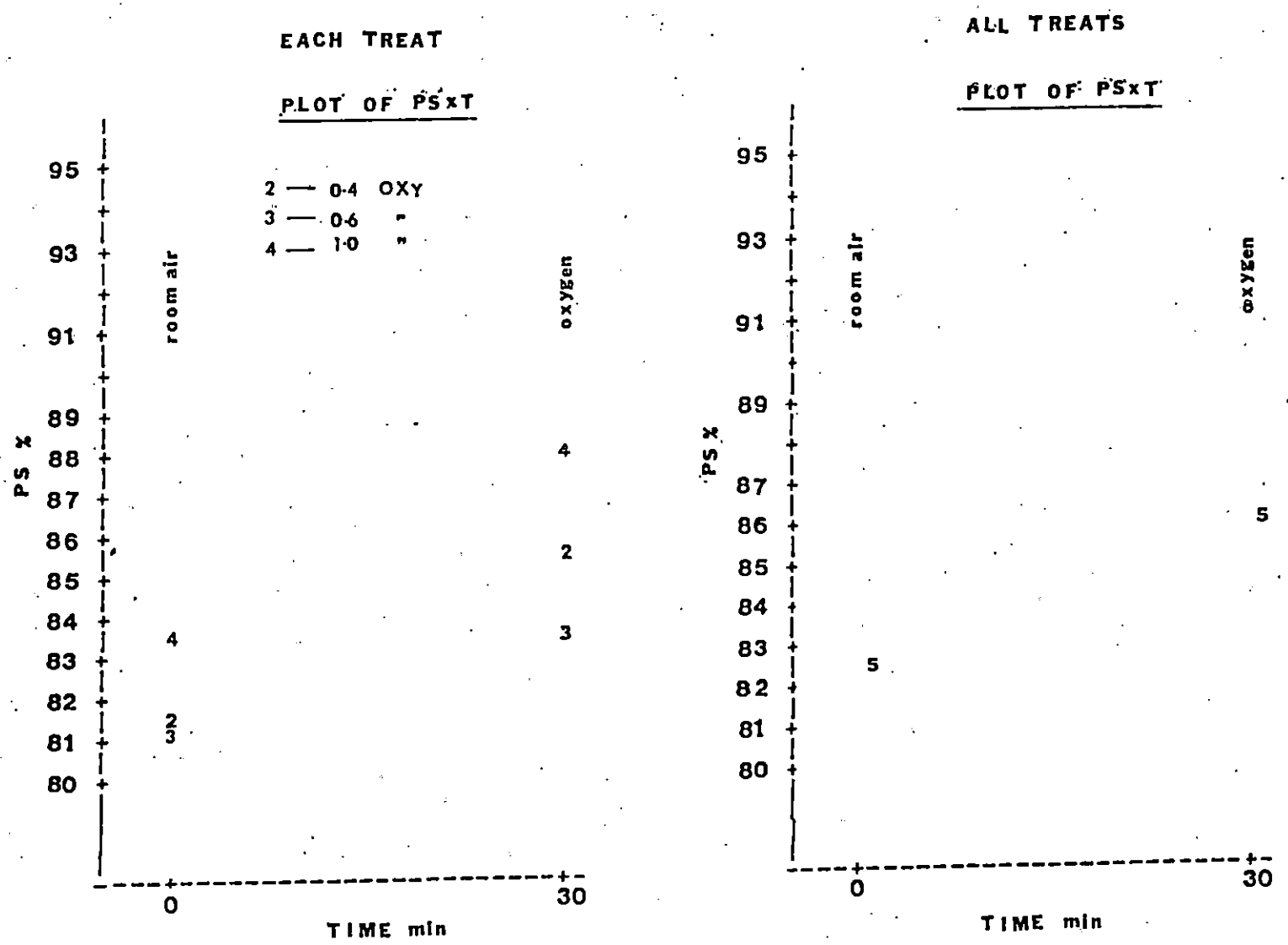


Figure 20 a & b. Mean values of pulmonary artery blood hemoglobin oxygen saturation for each and all treatments

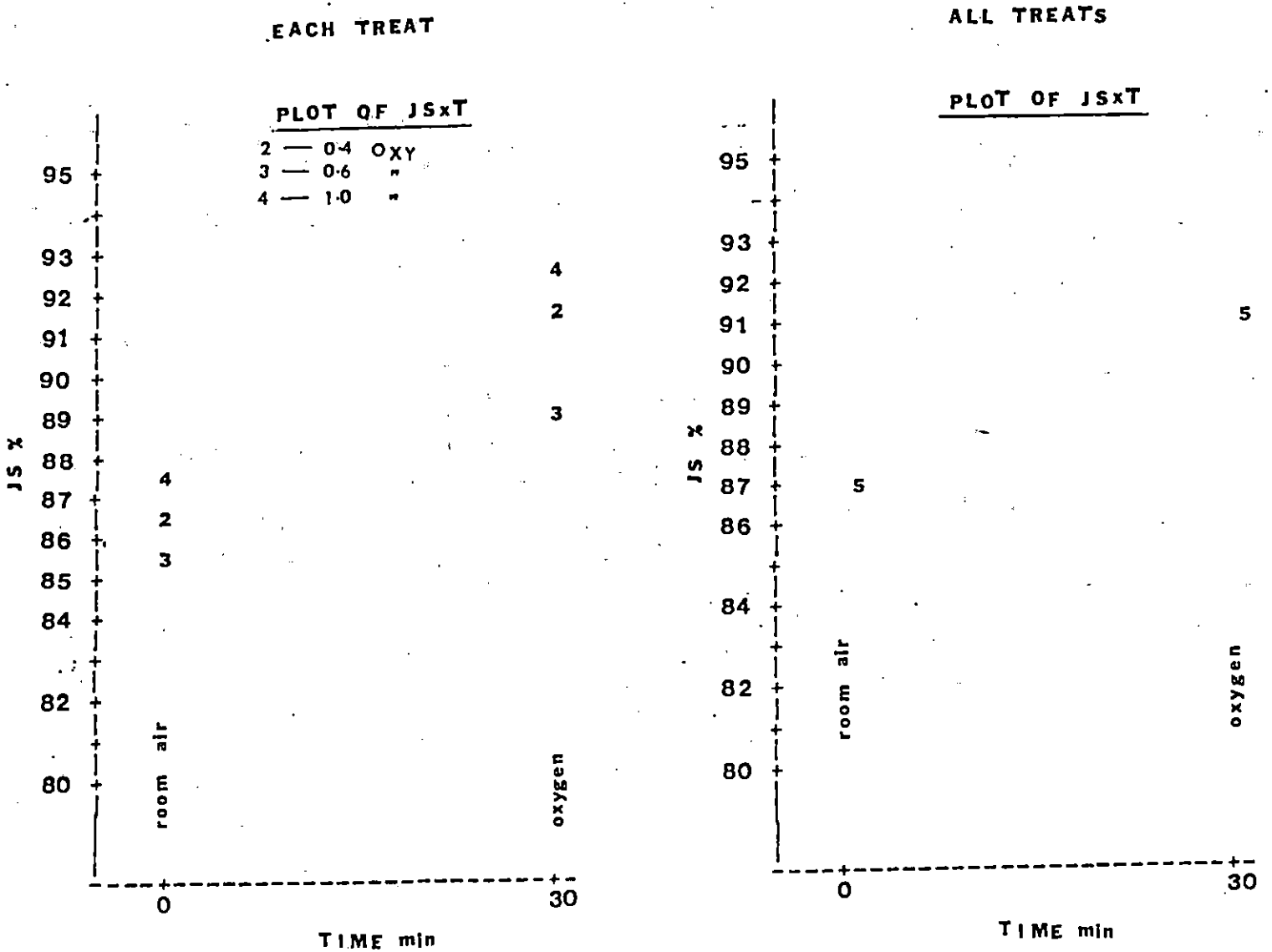


Figure 21 a & b. Mean values of jugular vein blood hemoglobin oxygen saturation for each and all treatments

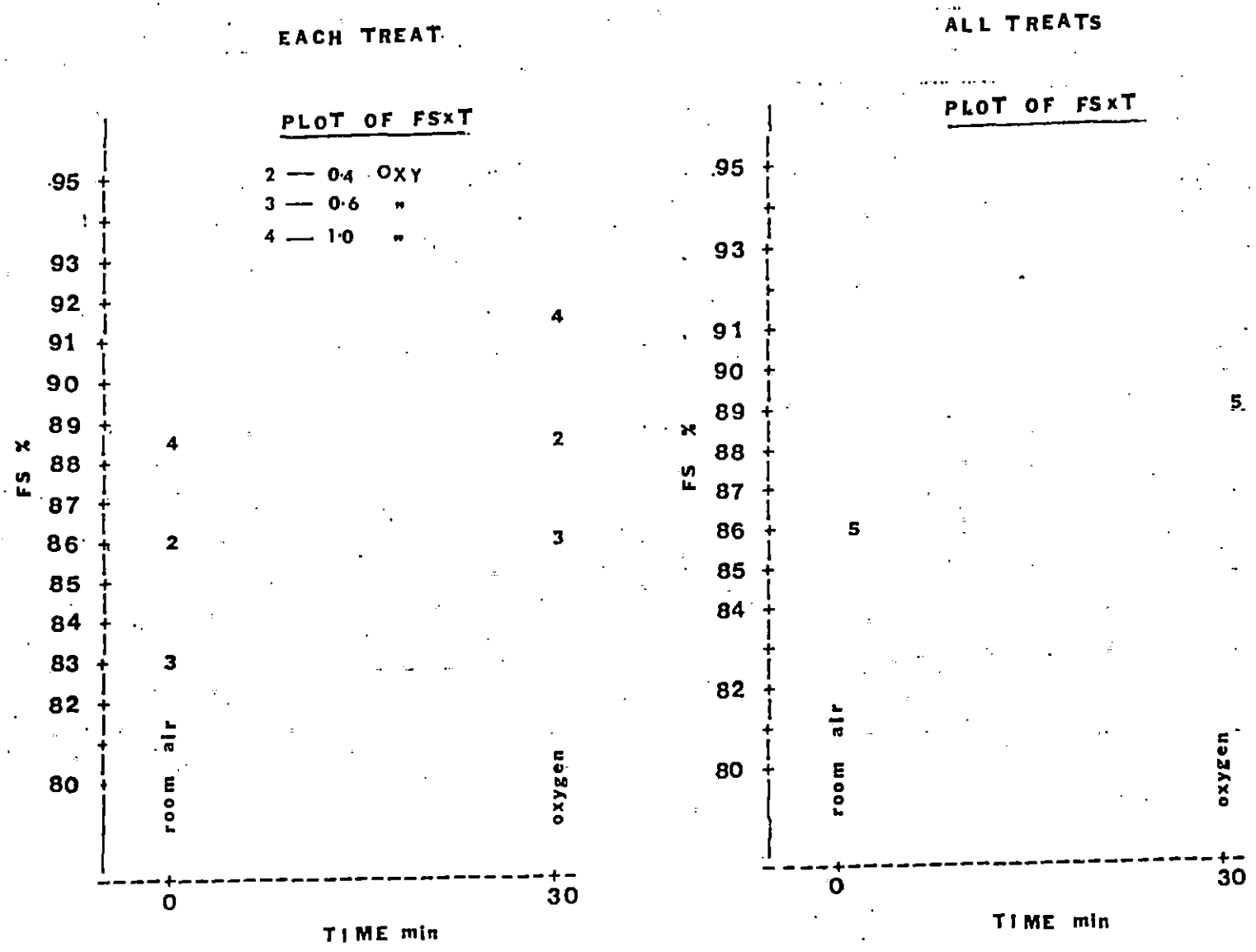


Figure 22 a & b. Mean values of femoral vein blood hemoglobin oxygen saturation for each and all treatments

Blood Oxygen Content and Oxygen Extraction

Oxygen content is defined as the product of hemoglobin's oxygen carrying capacity (1.34 ml oxygen/g), and percent hemoglobin oxygen saturation, plus oxygen dissolved in the plasma (Ø.ØØ3 Vol%/Torr).

Table A7, and Figures 23 through 3Ø represents the mean values of oxygen content for arterial, pulmonary artery, jugular and femoral veins for all groups during normoxic and hyperoxic breathing.

Arterial, pulmonary, jugular and femoral veins blood oxygen content in all four groups increased during hyperoxia when compared with their respective groups normoxia values. Increase in arterial, pulmonary, jugular and femoral veins blood oxygen content in all four groups were less than 1Ø%. Increase of 6.6% and 9.5% in arterial blood oxygen content in groups 2 and 4, respectively, show a significant trend, whereas, an increase of 7.95% in group 5 was statistically significant. Changes in pulmonary artery, jugular and femoral veins blood oxygen content in all four groups were not statistically significant.

Kety and Schmidt (1948) reported that inhalation of high oxygen mixture (85 to 1ØØ%) produced a slight but significant increase in arterial blood oxygen content (a 1.4 Vol% increase).

Oxygen extraction or arterio-venous oxygen content gradient difference is defined as the difference between arterial and venous blood oxygen content. Table A8, and Figures 31 through 36 represents the mean values of oxygen extraction for arterial, pulmonary artery, jugular and femoral veins for all four groups during normoxia and hyperoxia.

Arterial to pulmonary artery, jugular and femoral veins blood oxygen extraction in all four groups increased. There was an increase of 15.2%, 34.8%, 38.9%, and 31.6% in arterial to pulmonary artery blood oxygen extraction in groups 2, 3, 4, and 5, respectively, during oxygen breathing. Changes in group 2 were not significant, in group 4 and 5 changes were highly statistically significant, and group 3 showed a significant trend.

Arterial to jugular vein blood oxygen content difference increased by 13.5%, 37.2%, 46.3%, and 34.3% in groups 2, 3, 4, and 5 respectively. Except for group 5, these changes were not statistically significant. An increase of 34.3% in group 5 was highly statistically significant.

For the arterial to femoral vein blood oxygen content difference, all four groups showed an increase in oxygen extraction during hyperoxia. Groups 2, 3, 4, and 5 demonstrated an increase of 38.2%, 31%, 70.2%, and 46.6% respectively. These changes in groups 2 and 3 were not statistically significant, whereas, in groups 4 and 5 these changes were statistically significant.

Mean values of arterial to pulmonary artery, jugular and femoral veins blood oxygen extraction in all four groups indicate that hyperoxia increases oxygen extraction by general body and regional systems.

Oxygen extraction is a function of cardiac output, and tissue metabolism. We noticed an increase in oxygen extraction during hyperoxia. Reduction in blood flows due to an increase in peripheral vasoconstriction during oxygen exposure increased the oxygen extraction by the tissues, in order to maintain normal tissue oxygen supply.

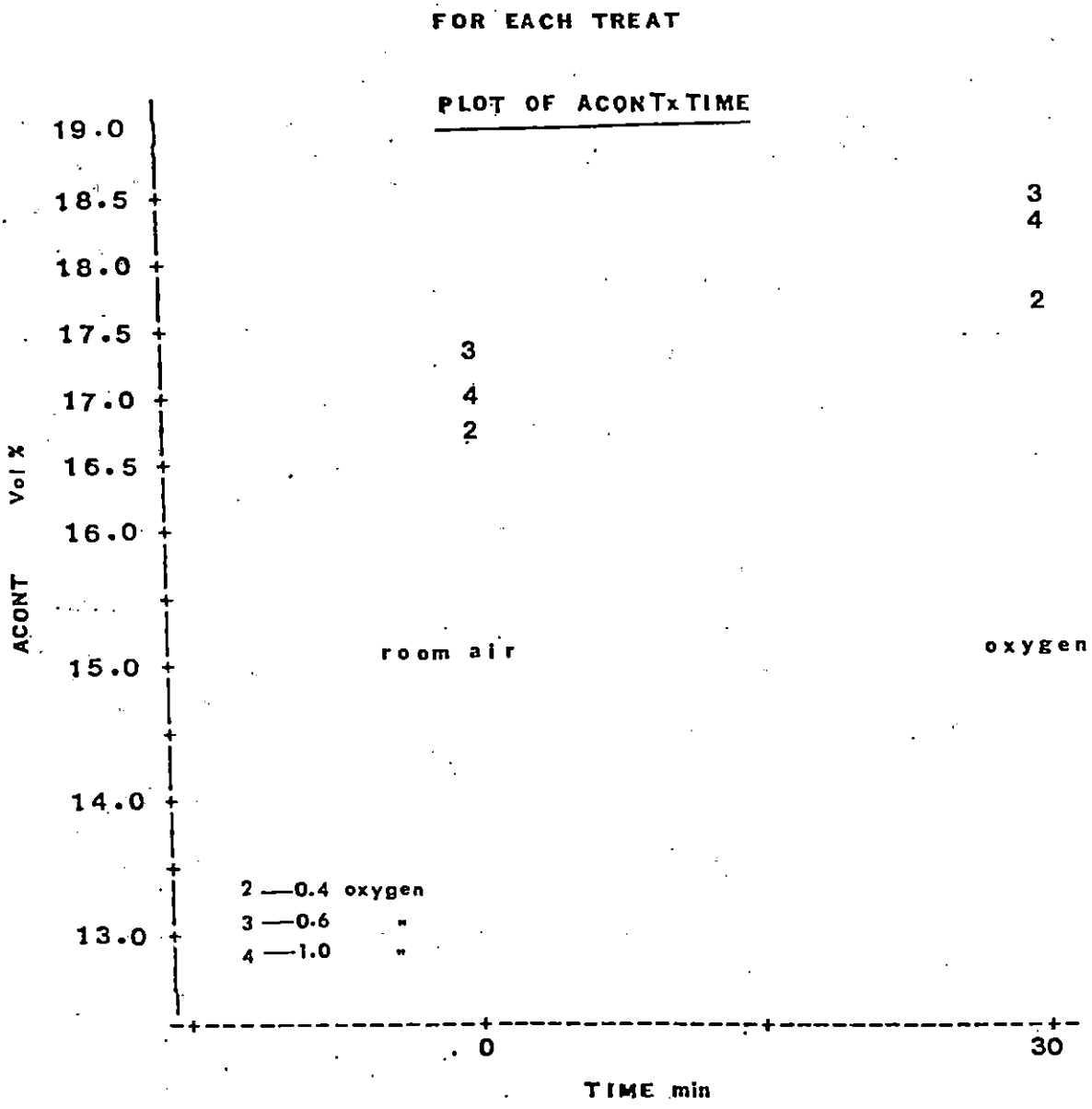


Figure 23. Mean values of arterial blood oxygen content for each treatment

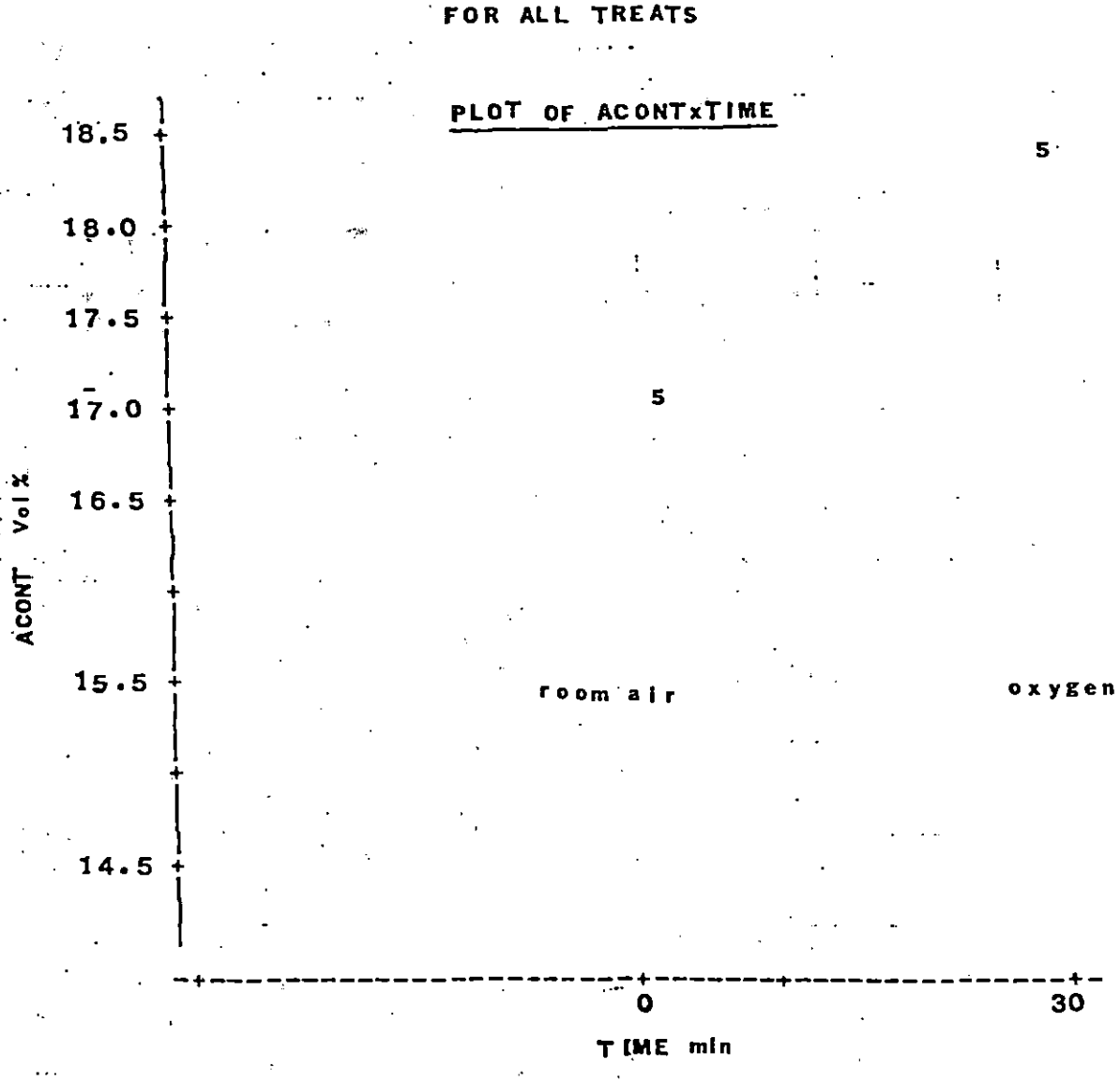


Figure 24. Mean values of arterial blood oxygen content for all treatments

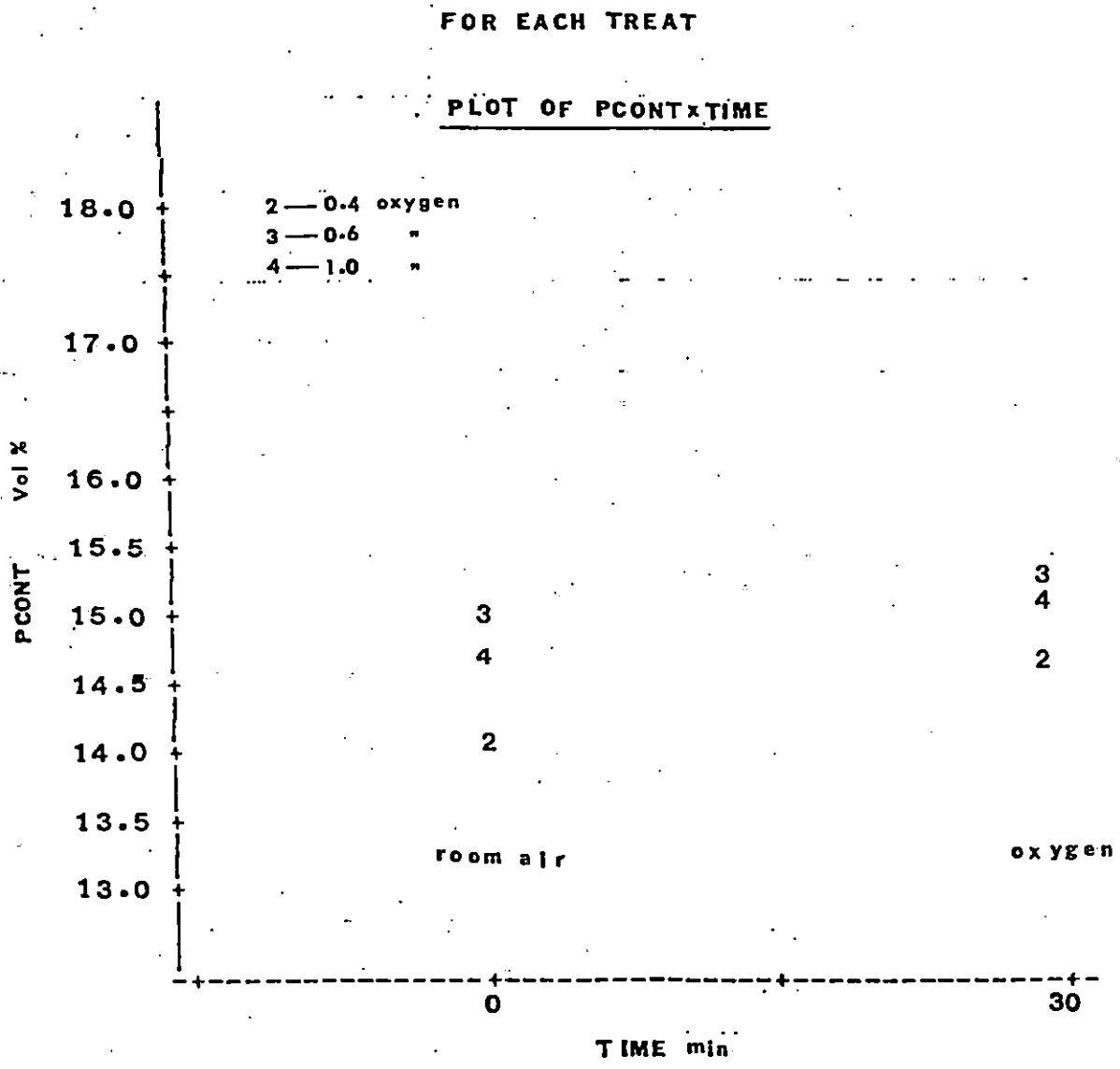


Figure 25. Mean values of pulmonary artery blood oxygen content for each treatment

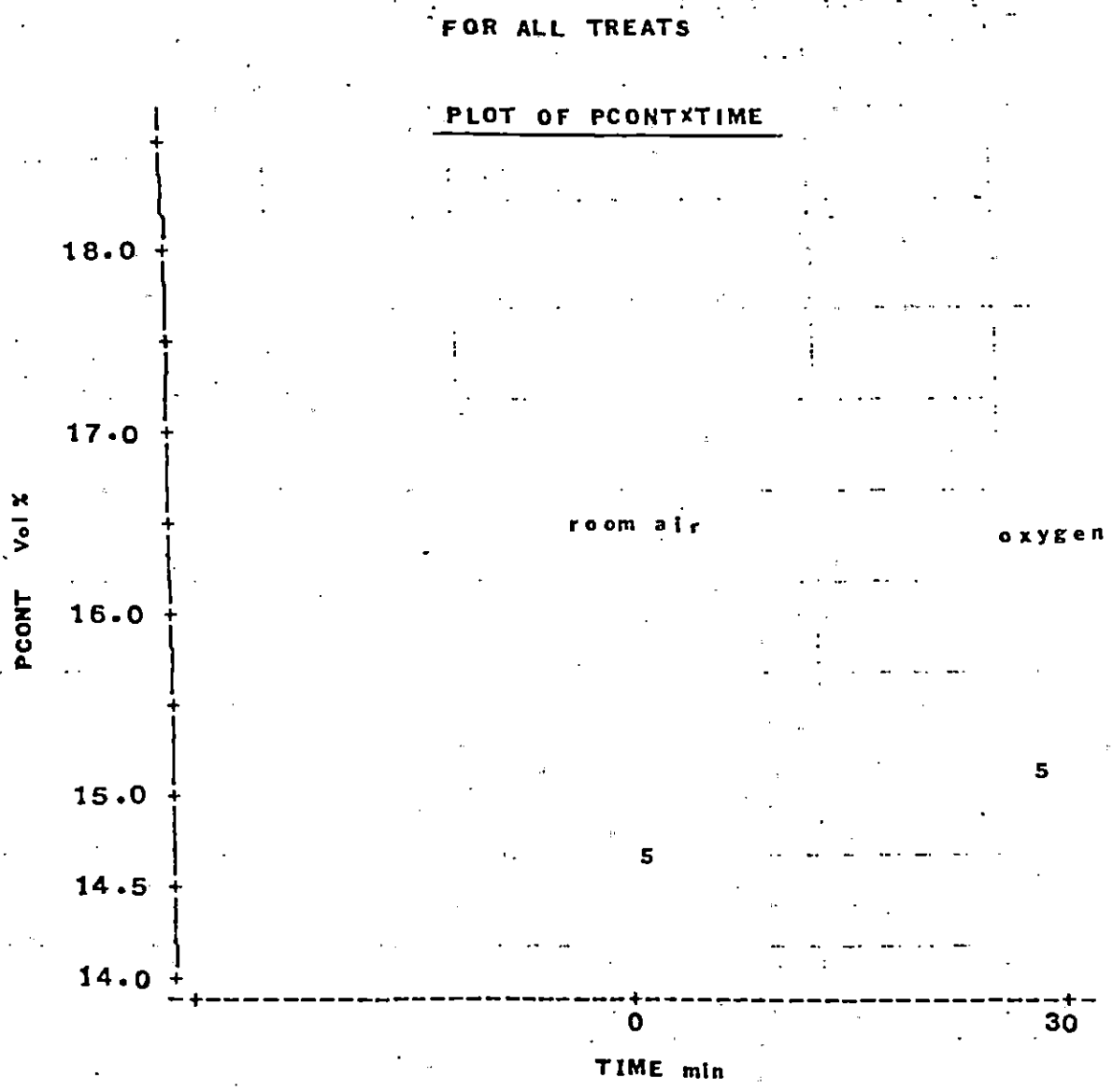


Figure 26. Mean values of pulmonary artery blood oxygen content for all treatments

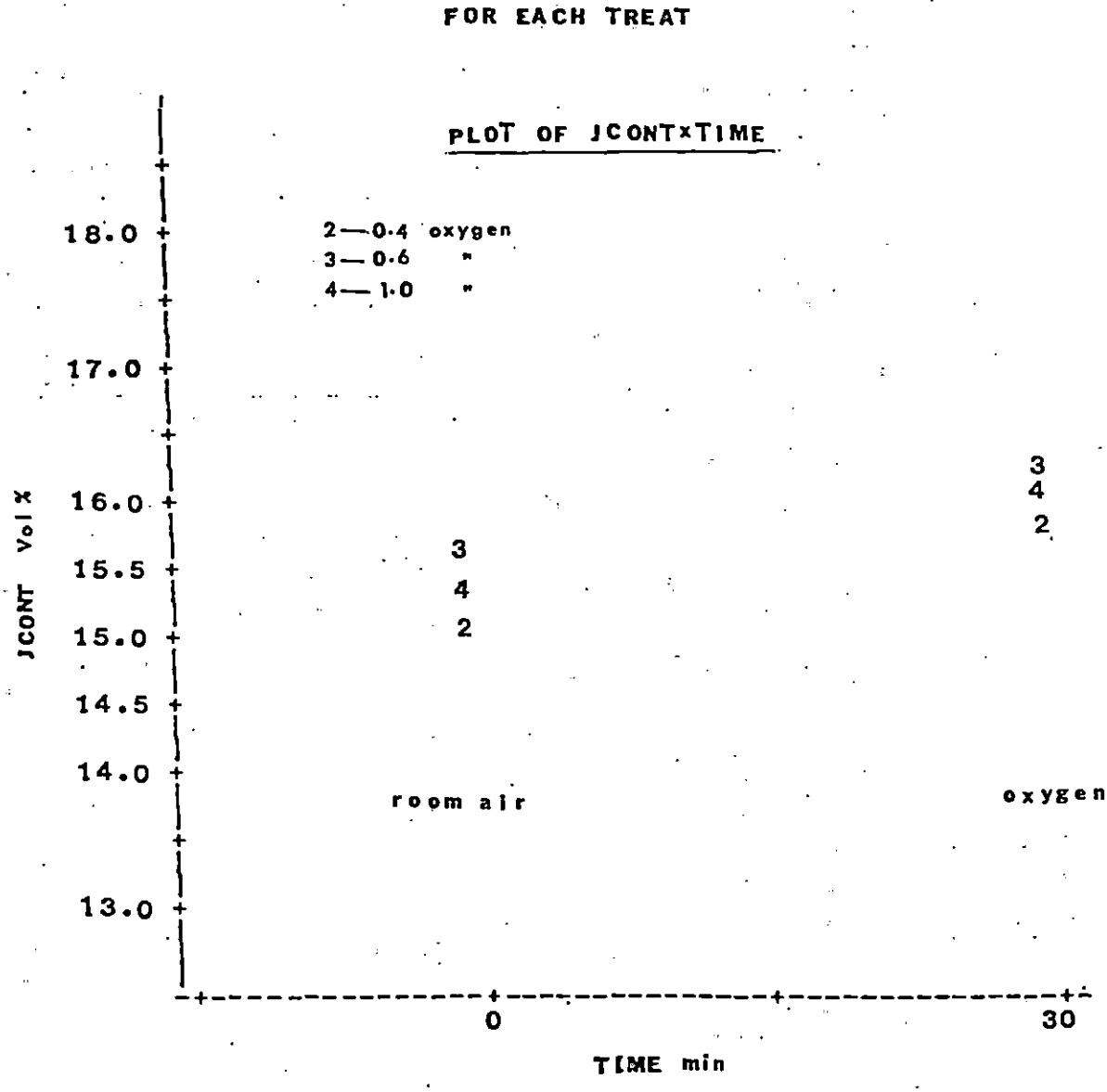


Figure 27. Mean values of jugular vein blood oxygen content for each treatment

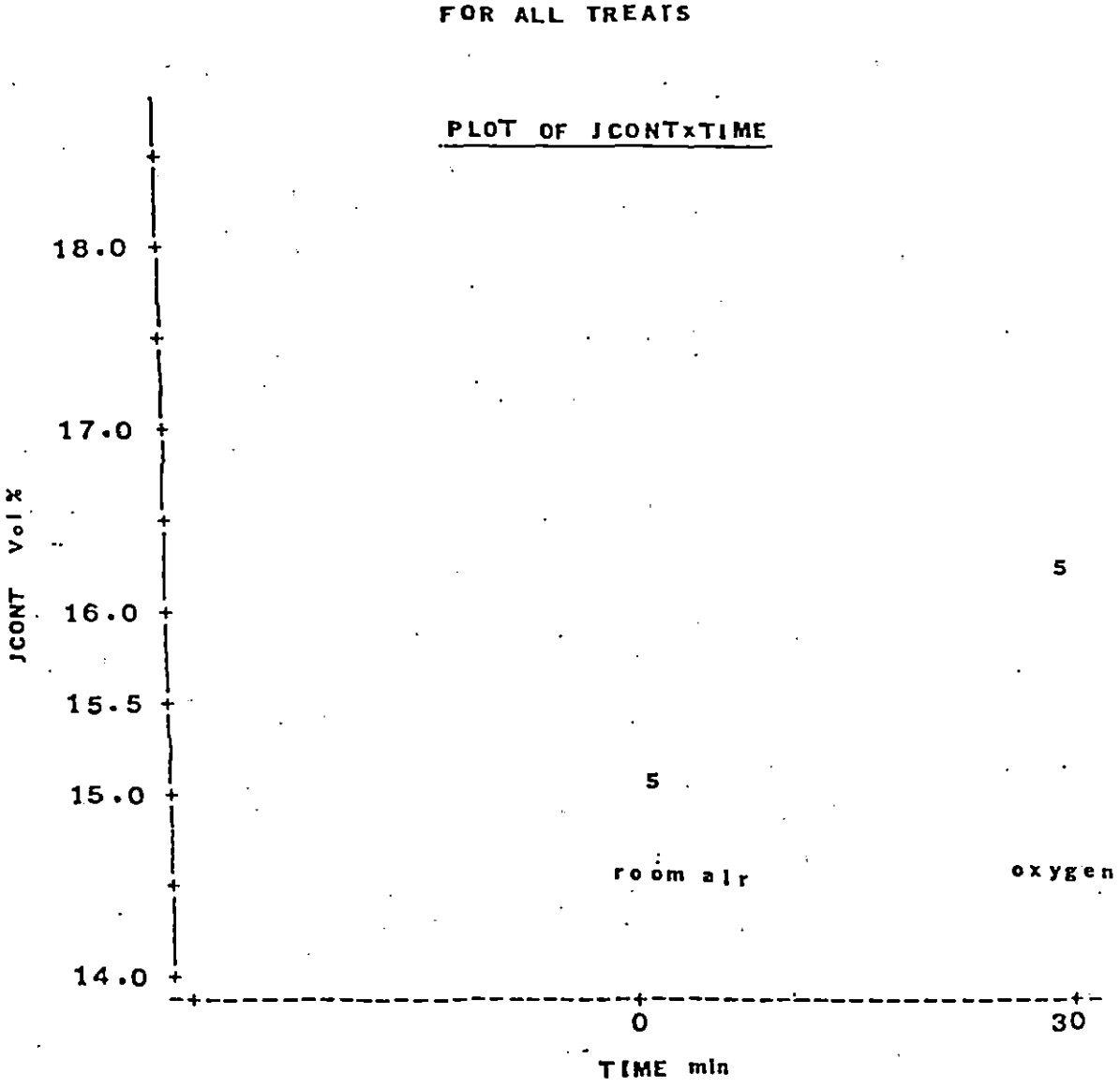


Figure 28. Mean values of jugular vein blood oxygen content for all treatments

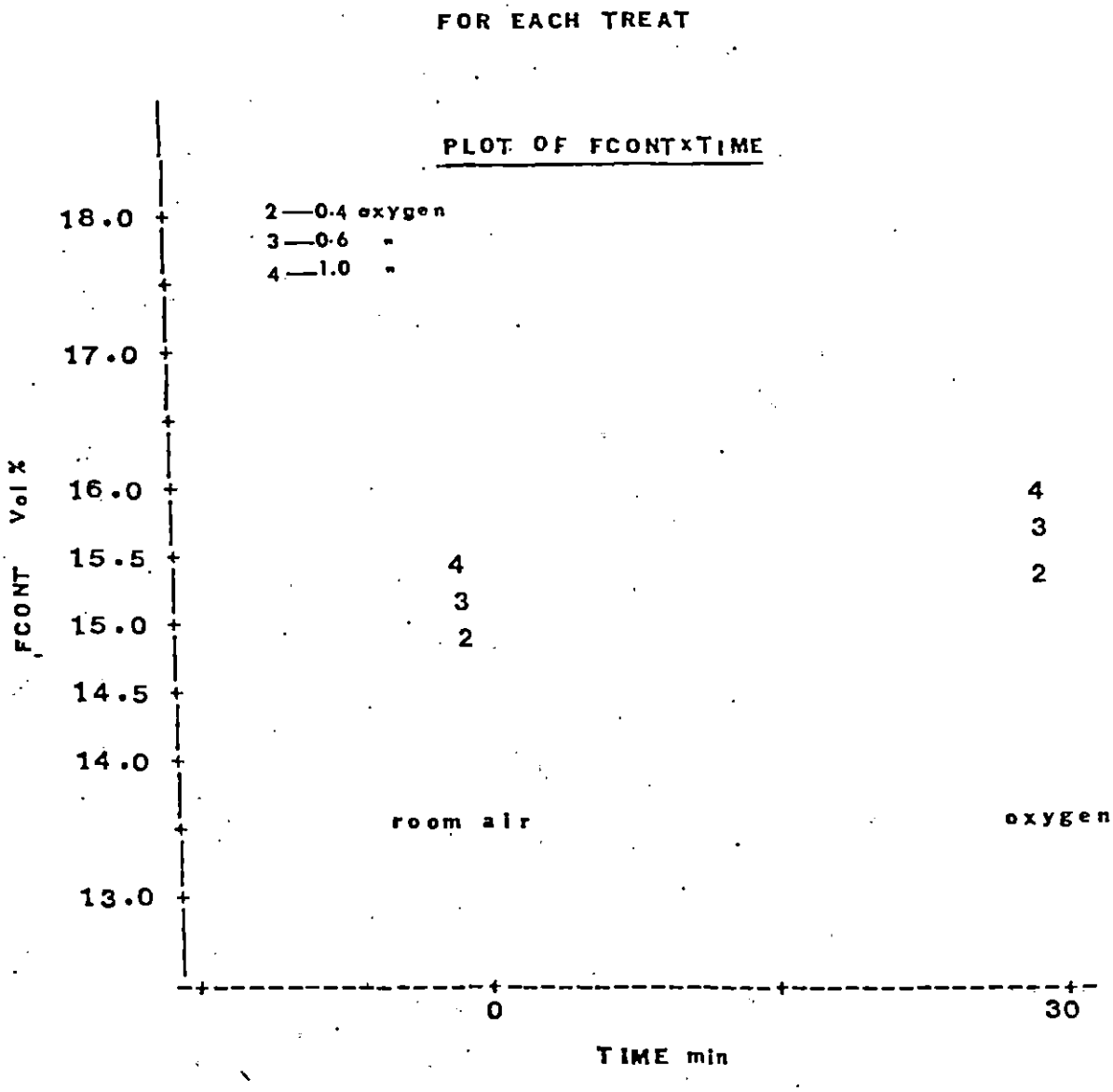


Figure 29. Mean values of femoral vein blood oxygen content for each treatment

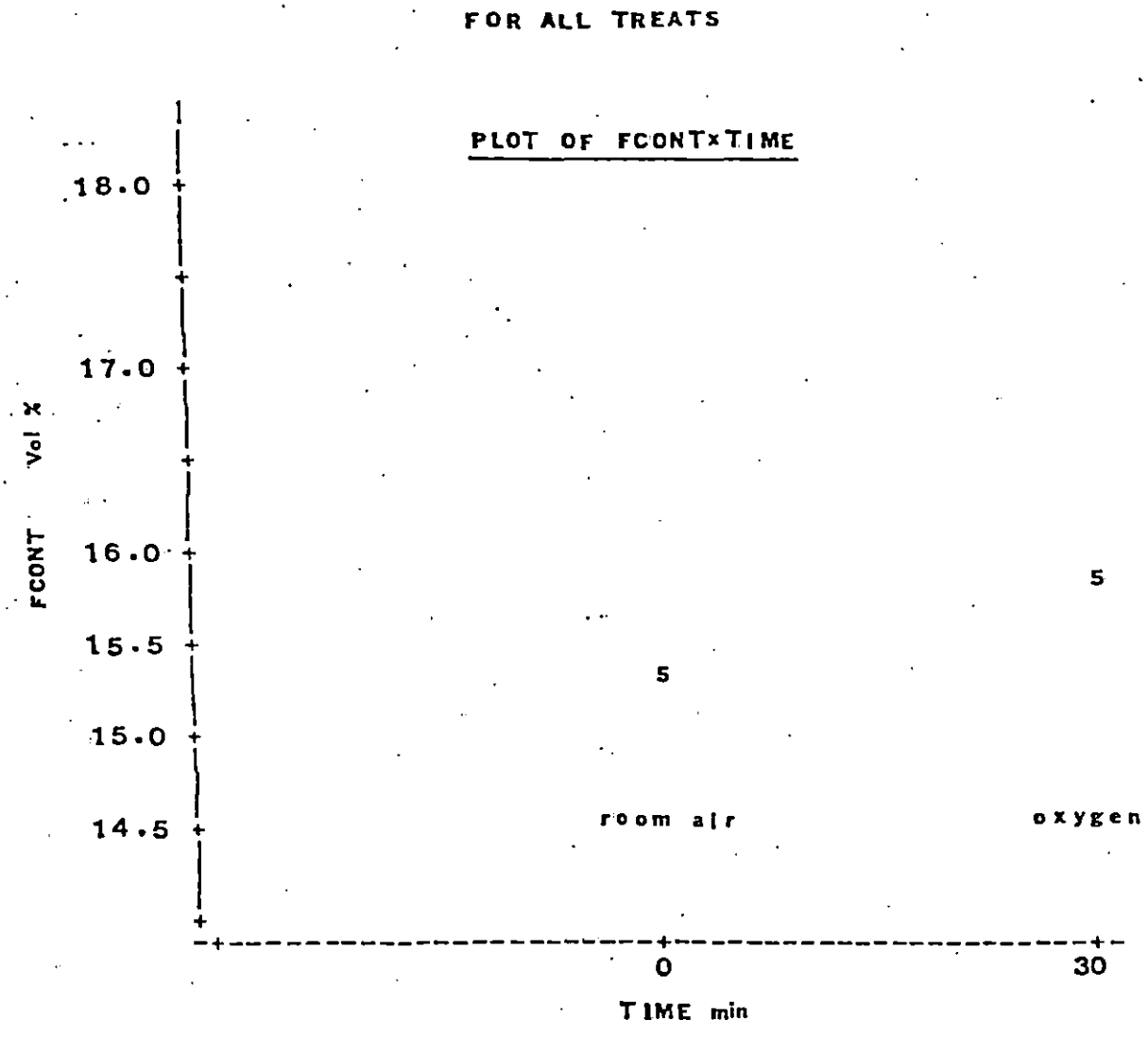


Figure 30. Mean values of femoral vein blood oxygen content for all treatments

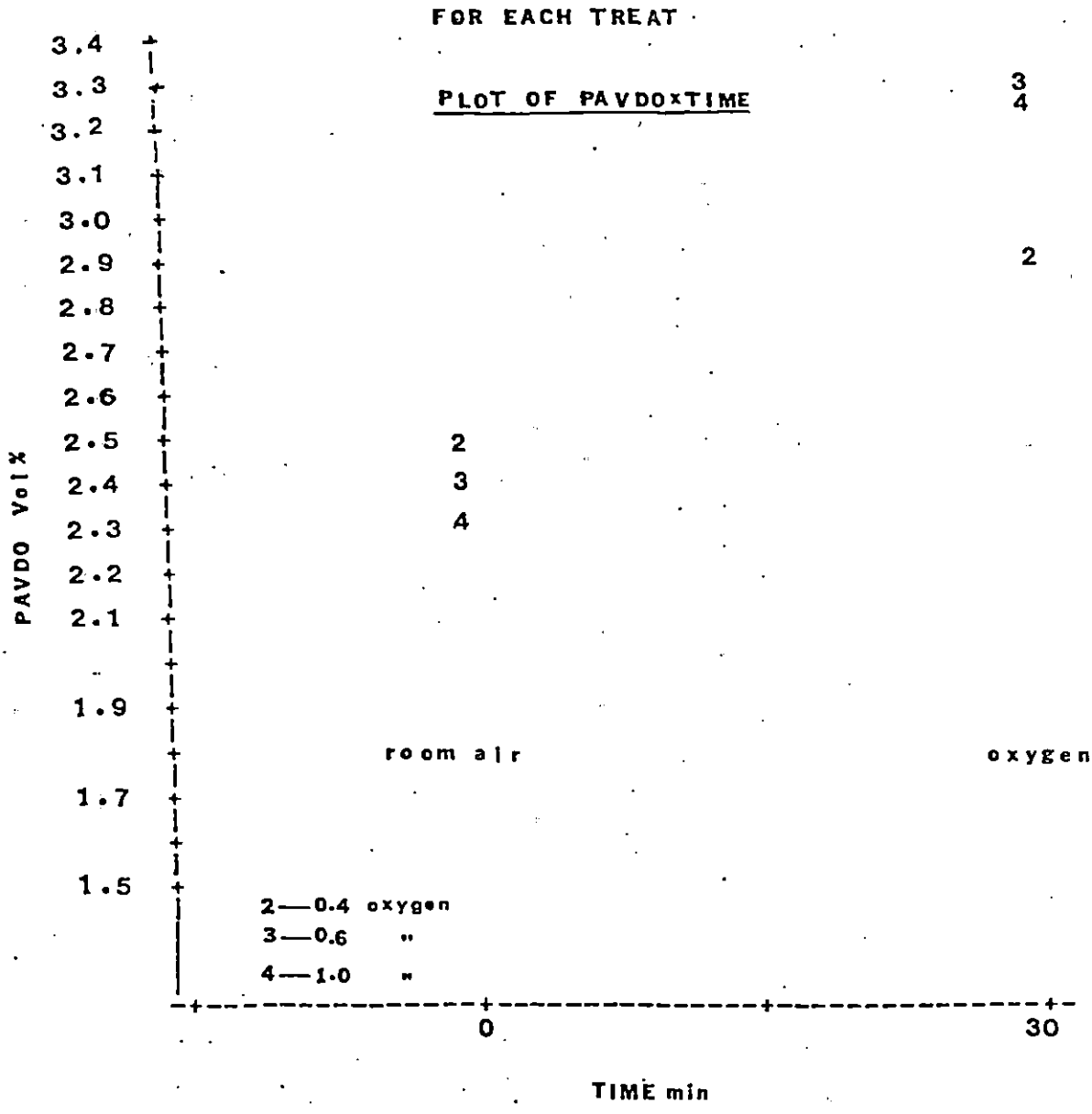


Figure 31. Mean values of arterial-pulmonary artery blood oxygen content for each treatment

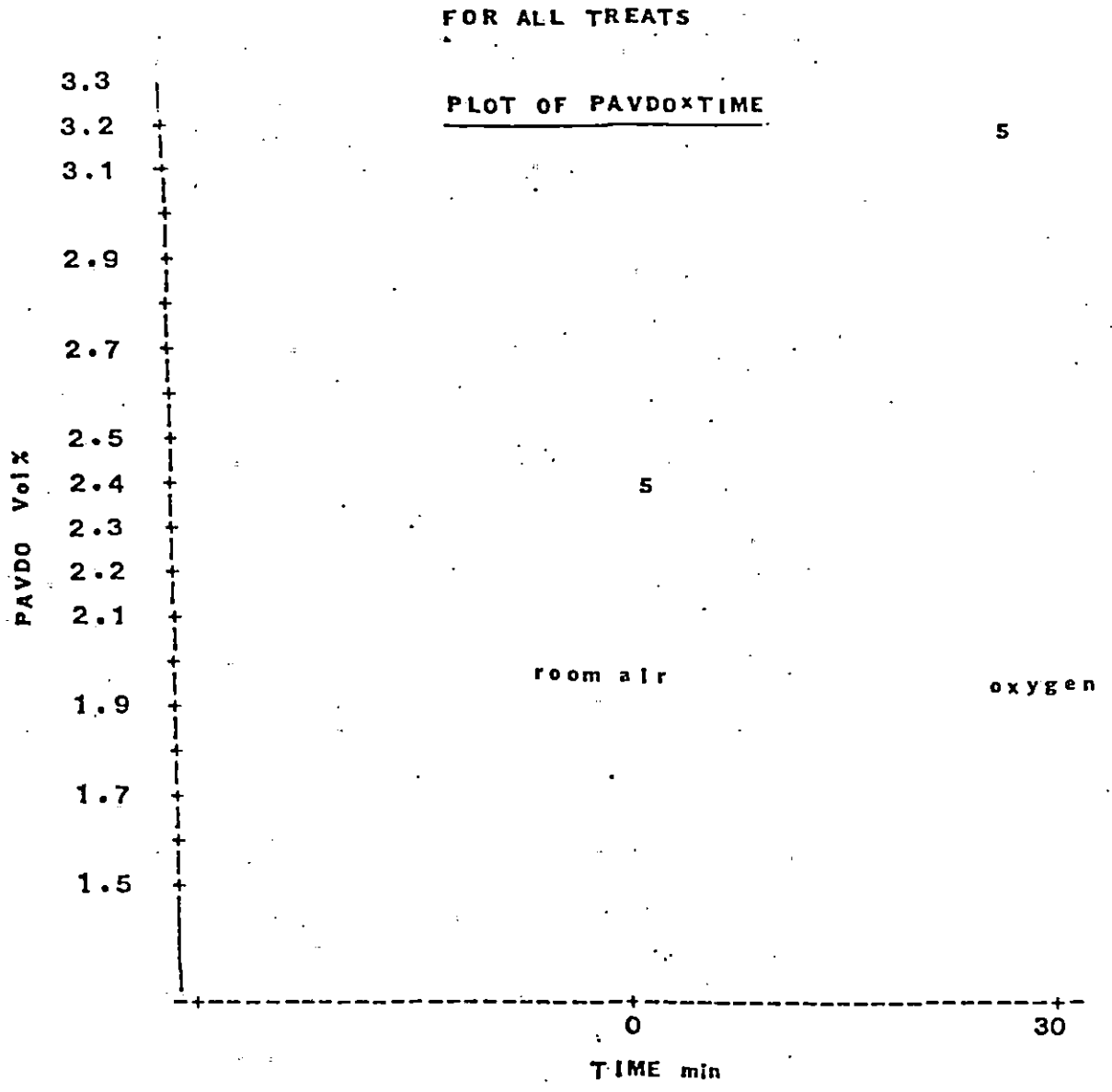


Figure 32. Mean values of arterial-pulmonary artery blood oxygen content for all treatments

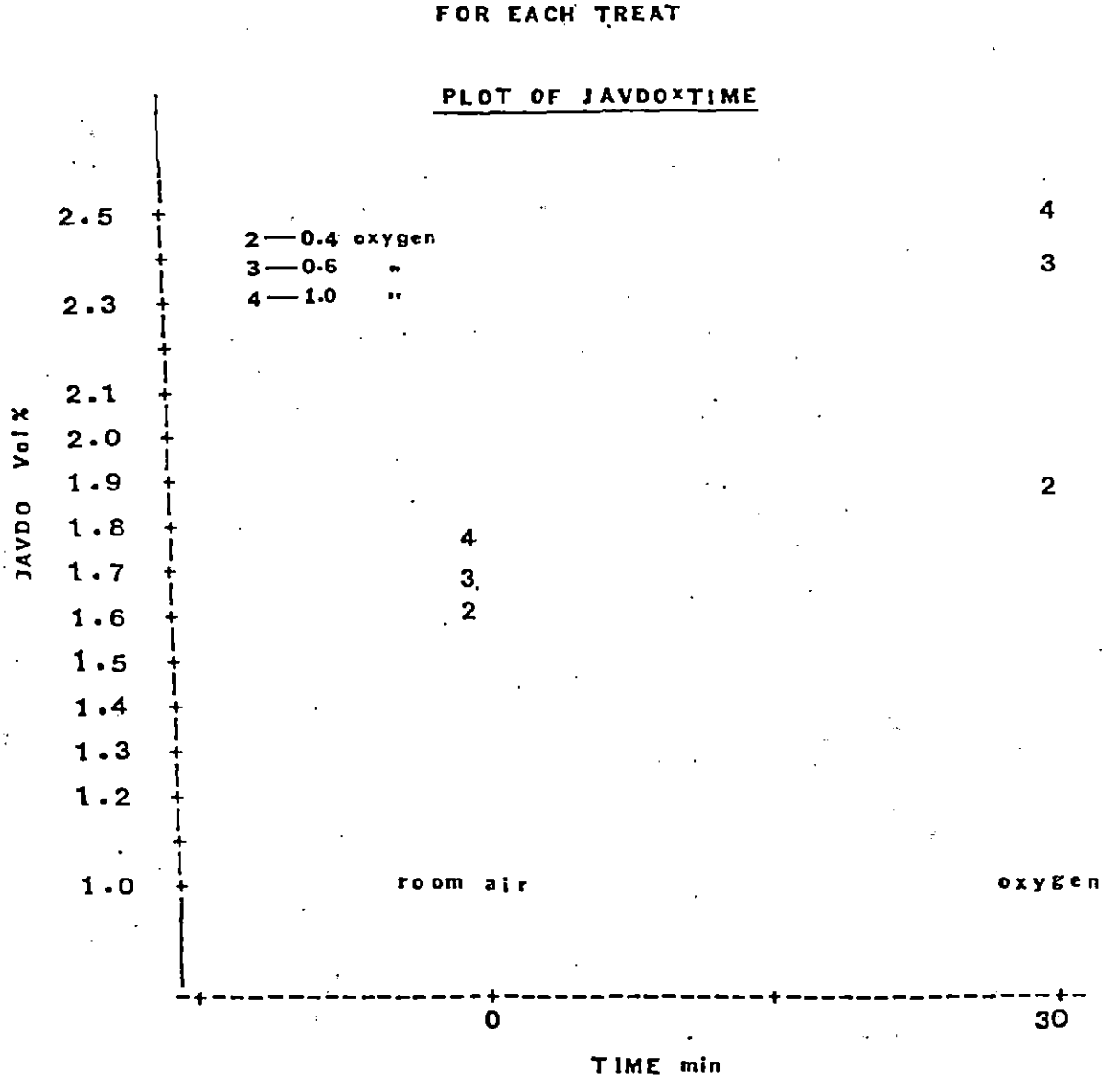


Figure 33. Mean values of arterial-jugular vein blood oxygen content gradient difference for each treatment

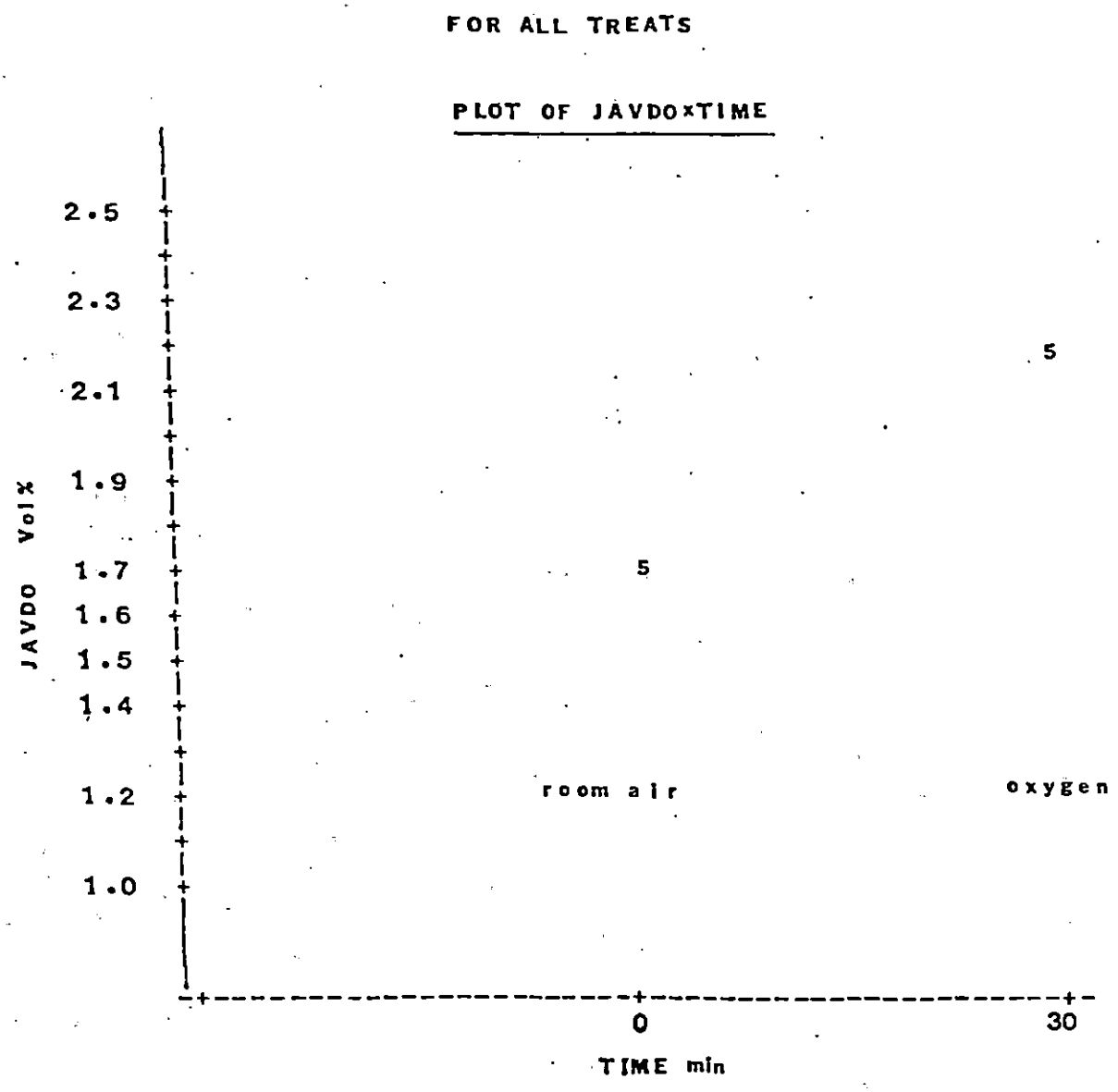


Figure 34. Mean values of arterial-jugular vein blood oxygen content gradient difference for all treatments

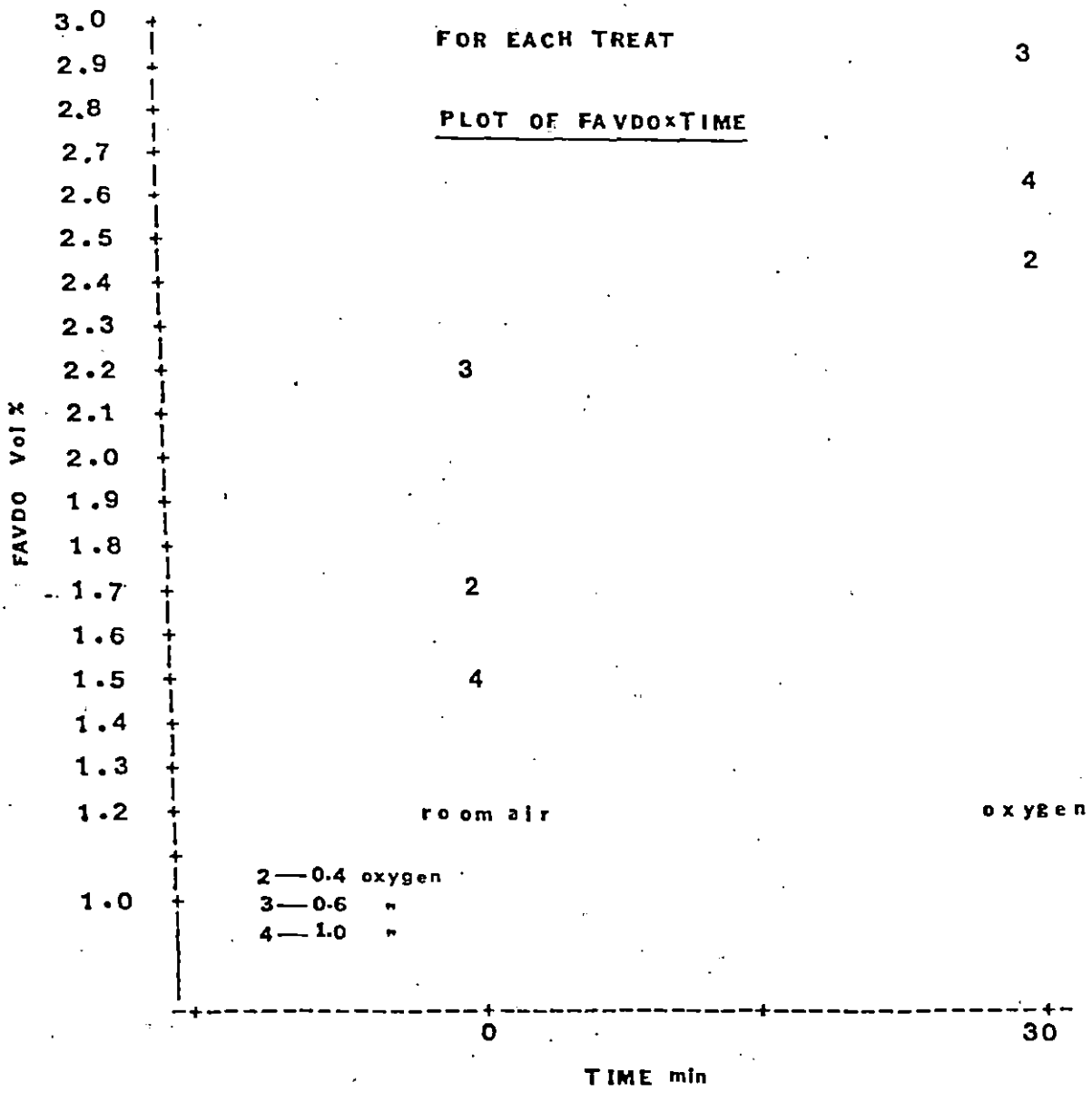


Figure 35. Mean values of arterial-femoral vein blood oxygen content gradient difference for each treatment

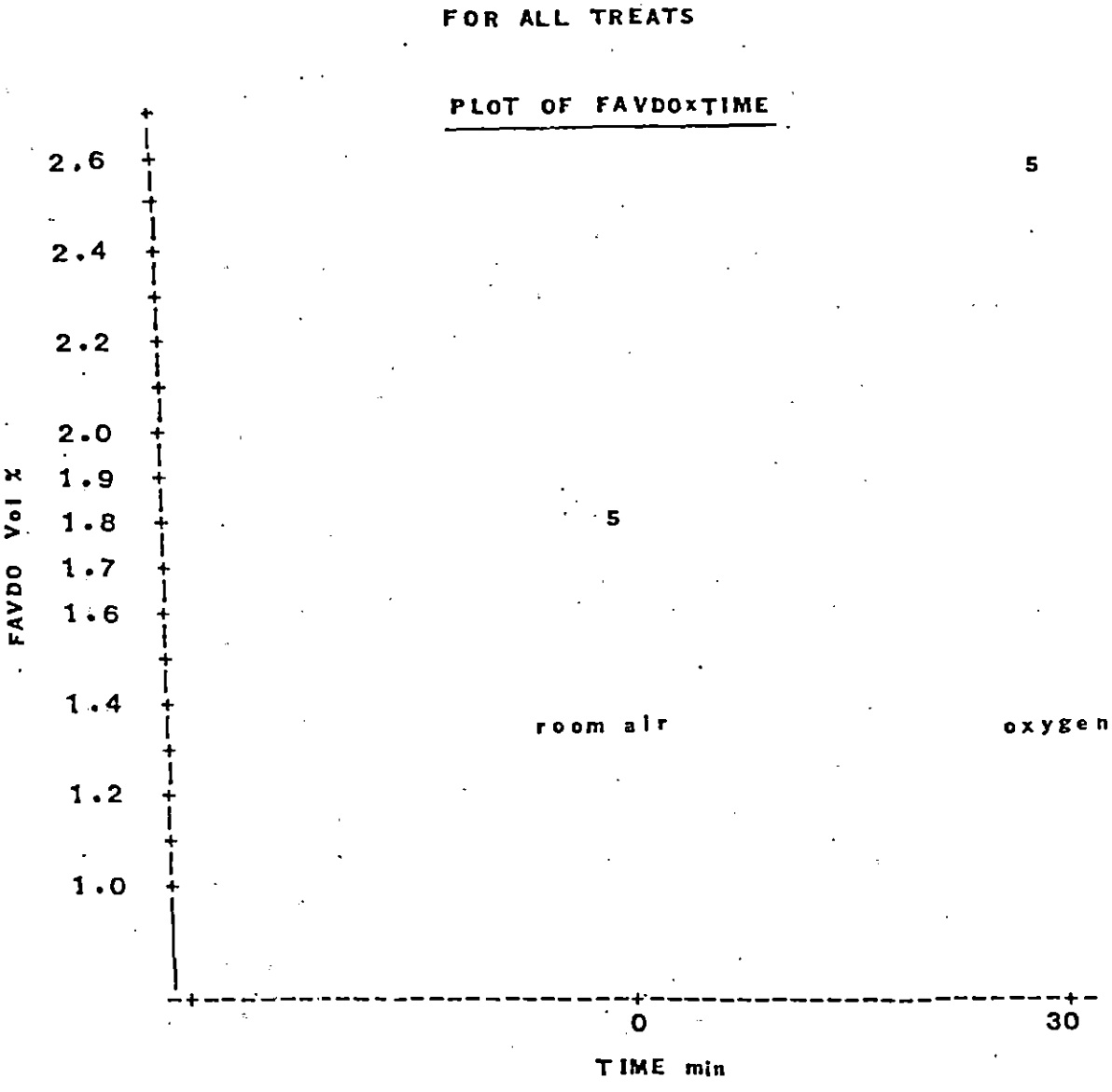


Figure 36. Mean values of arterial-femoral vein blood oxygen content gradient difference for all treatments

Vascular Pressures

Tables A9 and A10, and Figures 37 and 38 show the mean values of pulmonary artery pressure during normoxia and hyperoxia in all groups.

Each group responded differently to hyperoxia. Group 2 showed a moderate increase in mean pulmonary arterial pressure (MPAP) by 14.3% after 15 minutes, at 30 minutes on hyperoxia the MPAP was 8.5% higher when compared with normoxia. At the end of 60 minutes on hyperoxia, the MPAP had dropped 8.5% below room air.

Group 3 showed a decrease in MPAP of 14.6% at 15 minutes, drop by 10.6% at 30 minutes, and decrease by 1.1% at 60 minutes. Group 4 showed a slight increase of 4% in MPAP after 15 minutes, it increased to 5.8% after 45 minutes and did not change after 60 minutes on hyperoxia. Group 5 showed a decrease by 3% in MPAP during 30 minutes, but increased by 3% above normoxic values during the last 30 minutes of oxygen breathing.

Tables A9 and A10, and Figures 39 and 40 show the mean values of systemic arterial pressure (MSAP) for all groups. All the four groups showed a slight increase in MSAP after 15 minutes of oxygen breathing, it continued to rise after 30, 45, and 60 minutes on hyperoxia. After 15 minutes, groups 2 and 3 showed a 3% and 2.5% rise in MSAP, respectively. At the end of 60 minutes on oxygen breathing, MSAP increased by 15.6% and 10%, respectively.

In group 4, MSAP increased only by 5% during 60 minutes of oxygen breathing. For group 5, MSAP increased by 2% initially and continued to increase during hyperoxia, it was up by 9% at 60 minutes of hyperoxia.

Changes with respect to treatment and time, the mean values of pulmonary and systemic arterial pressures in all four groups during hyperoxia were not statistically significant.

Fletcher and Levin (1984) reported that long term (8 weeks) oxygen therapy lowered mean pulmonary arterial pressure during sleep in patients with COPD. Wright et al. (1983) reported a drop in pulmonary arterial and pulmonary wedge pressures during exercise in COPD while breathing oxygen. Pulmonary hypertension occurred in rats exposed to long term (7 days) oxygen breathing (Jones et al. 1983, and Moran and Wolfe 1978).

In our experiment, the changes in pulmonary arterial pressure during hyperoxia were different in each group, but in all four groups studied, hyperoxia increased MPAP very slightly in group 5, with essentially no changes in groups 2, 3, and 4.

Andersen and Hillestad (1970) reported a significant increase in systolic, diastolic, and in mean arterial presure during hyperoxic breathing. Statistically significant increase in mean arterial pressure occurred during 30 minutes on hyperoxia and persisted for 40 minutes after normoxia (Eggers et al. 1962).

Welch et al. (1977) reported that systemic vascular pressure did not change during maximal aerobic exercise in the presence of oxygen breathing. Whereas, Smith and Ledingham (1972) reported that 100% oxygen ventilation caused a rise in left ventricular end diastolic pressure.

We showed essentially the same patterns as described by the above mentioned authors in reporting the increase in systemic arterial pressure during hyperoxic breathing.

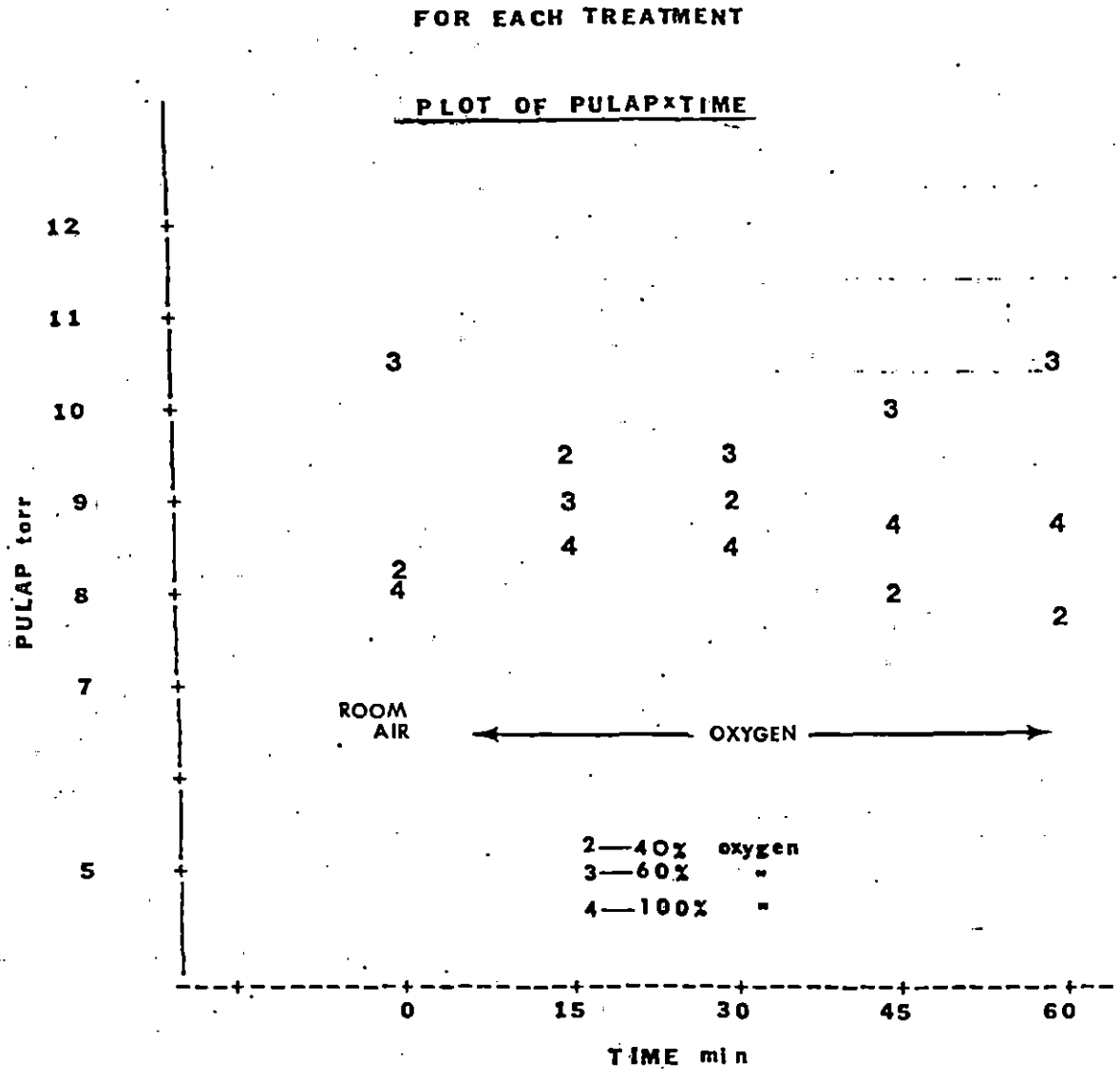


Figure 37. Mean values of pulmonary artery pressure for each treatment

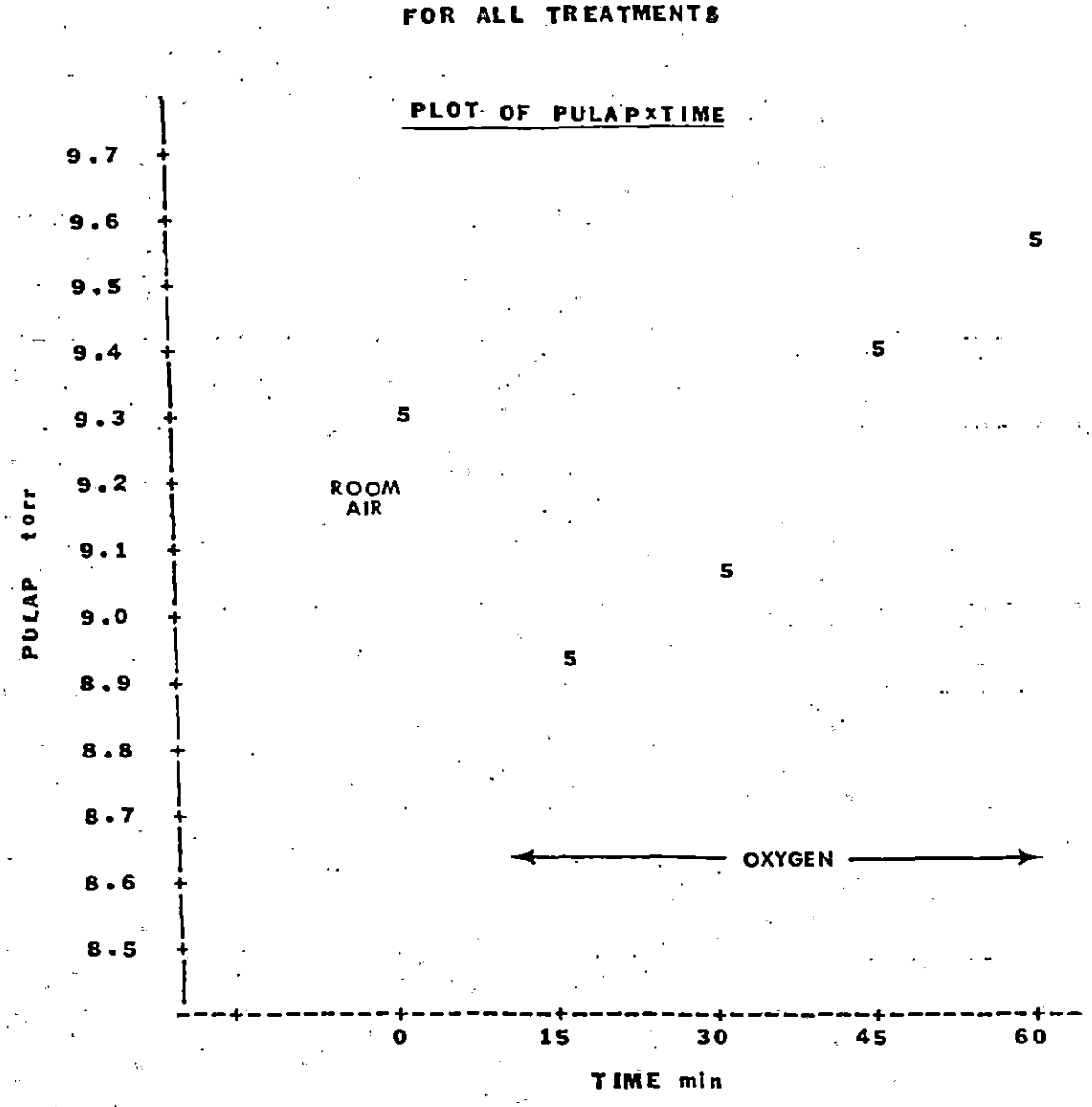


Figure 38. Mean values of pulmonary artery pressure for all treatments

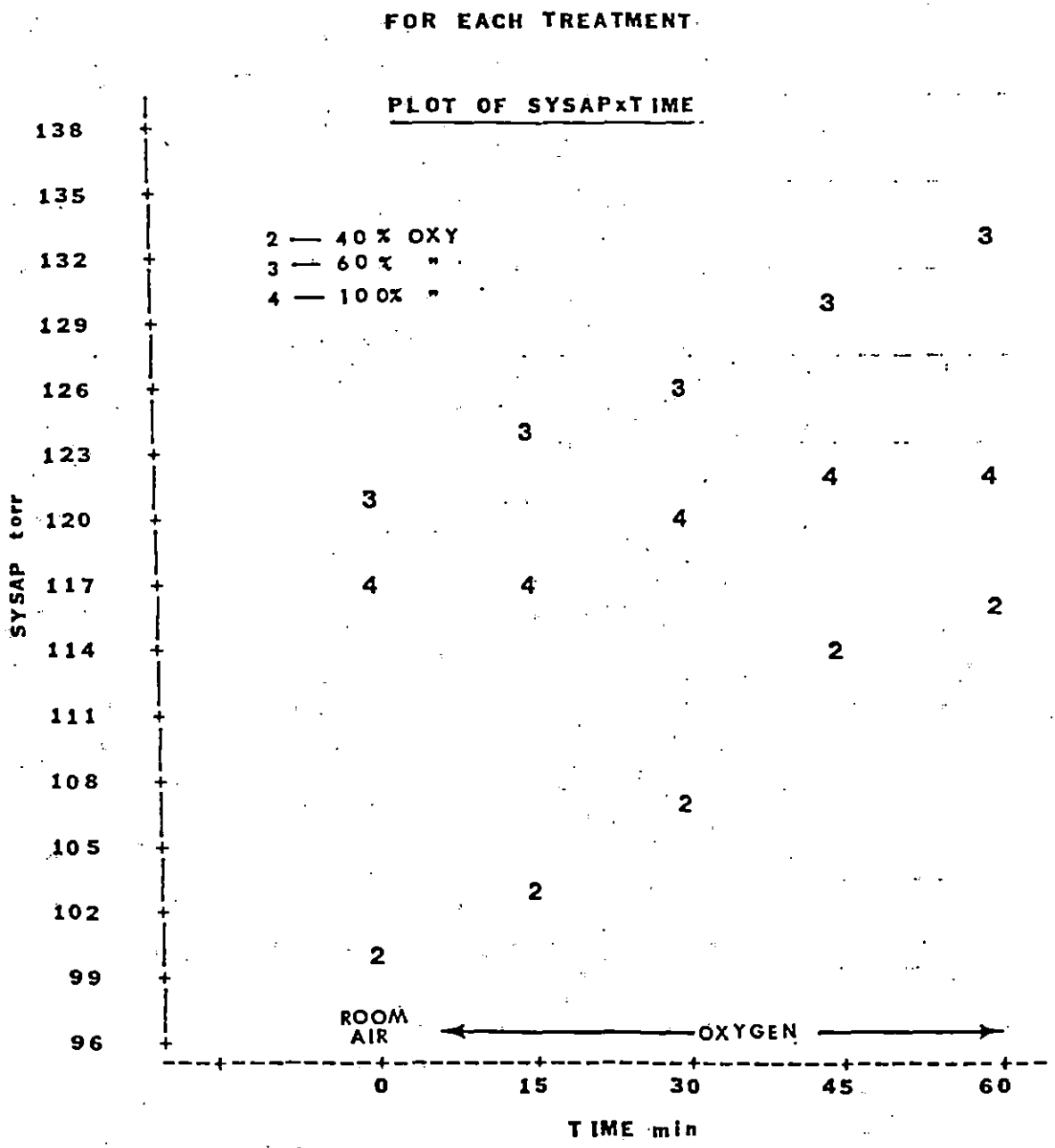


Figure 39. Mean values of systemic arterial pressure for each treatment

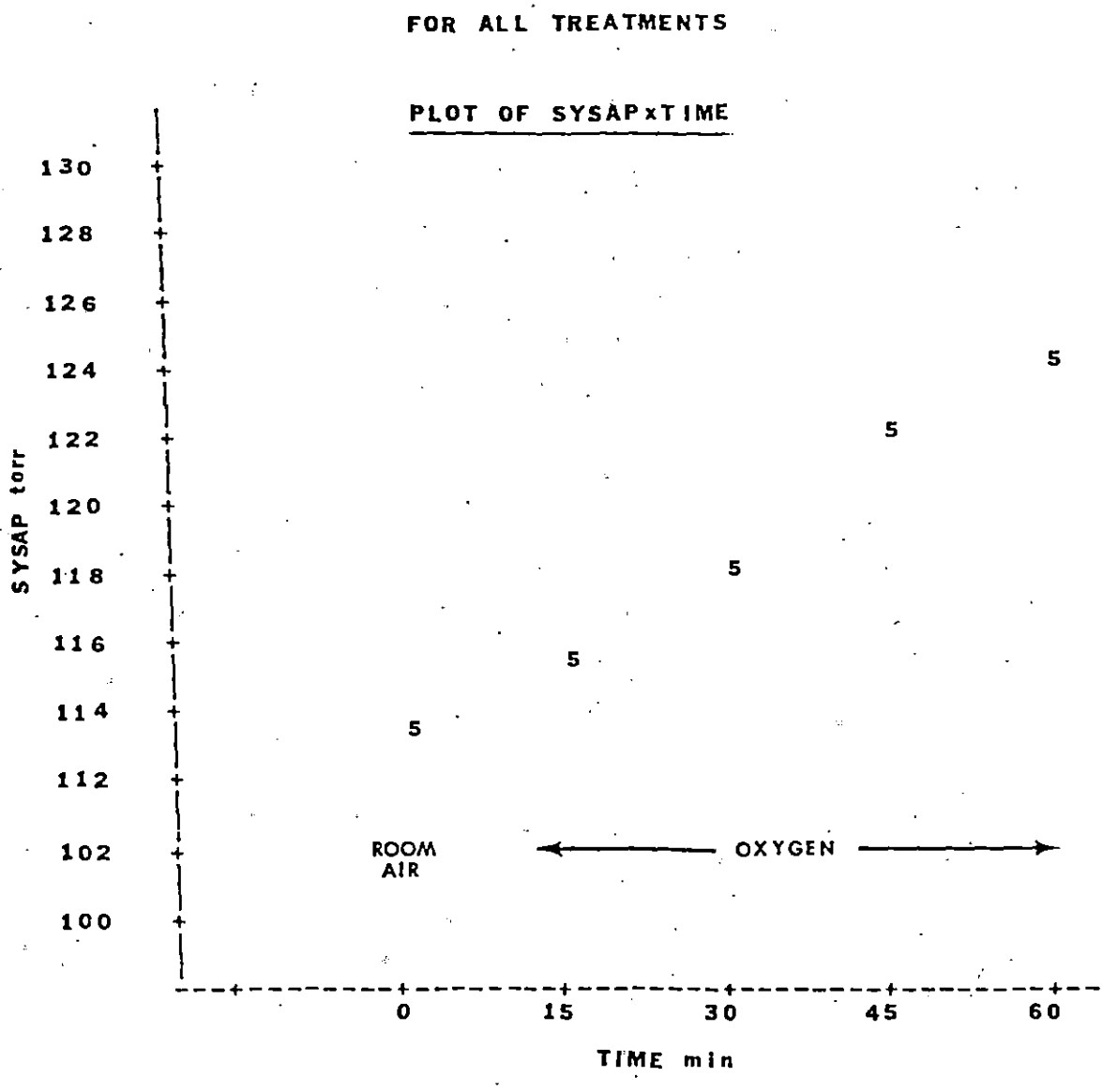


Figure 40. Mean values of systemic arterial pressure for all treatments

Cardiac Output and Organ Blood Flows

Table All, and Figures 41 and 42 represent the mean values of cardiac output during normoxia and hyperoxia for all groups.

Fall in cardiac output was seen in all four groups during hyperoxic breathing when compared with their respective normoxic values. Fall in cardiac output was less in group 2, moderate in group 3, and severe in group 4. Initial drops (30 minutes) in cardiac output were 1.4%, 12.33%, 21%, and 12.5%, and final drops (60 minutes) were 6.2%, 24.25%, 29.4%, and 21% in groups 2, 3, 4, and 5, respectively. With respect to treatment and time, changes in groups 2, 3, and 4 were not statistically significant, whereas, changes in group 5 were statistically significant.

Eggers et al. (1962) reported no changes in central blood volume in patients exposed to oxygen breathing for 30 minutes. Long term (8 weeks) oxygen therapy increased cardiac output in patients with COPD (Fletcher and Levin 1984). Andersen and Hillestad (1970) concluded that breathing of 100% oxygen for 20 minutes in healthy subjects produced consistent cardiac output depression.

In patients with acute decompensation of COPD, hyperoxia caused a decrease in cardiac output. Patients with severe hypoxemia showed no changes in cardiac output, but patients with moderate hypoxemia did show significant decrease in cardiac output during hyperoxia (Degaute et al. 1981). Slight but statistically significant decrease in cardiac output was observed during 100% oxygen breathing for 30 and 60 minutes (Eggers et al. 1962, and Whitehorn et al. 1946).

Irnell and Nordgren (1966) reported a fall of 17% in cardiac output in patients with bronchial asthma during hyperoxia breathing. Whitehorn et al. (1946) reported a 13% fall in cardiac output after 5 minutes on oxygen, and a fall of 19.4% from normoxic values after 60 minutes of oxygen, these changes were statistically significant. Our findings in group 3, and 5 are in total agreement with the findings of Whitehorn et al. (1946).

Tables A12 and A13, and Figures 43, 44, 45, and 46 represent the mean values of carotid artery and femoral artery blood flow during normoxic and hyperoxic breathing in all groups.

After 10 minutes of oxygen breathing, blood flow in the carotid artery and femoral artery was reduced by 1.5 and 14.3% in group 2, by 12.5 and 10.6% in group 3, by 13.2 and 18% in group 4, and by 13.2 and 14.4% in group 5, respectively. Carotid artery and femoral artery blood flow continued to fall during hyperoxia and at 30 minutes, flow was reduced by 10.7 and 24.8% in group 2, by 17.4 and 12% in group 3, by 20.8 and 31.1% in group 4, and by 16.5 and 24.4% in group 5, respectively.

At the end of 60 minutes on hyperoxic breathing, all four groups showed a severe depression in carotid artery and femoral artery blood flow, flow was reduced by 14.5 and 28.6% in group 2, by 20.1 and 16% in group 3, by 24.5 and 40% in group 4, and by 21 and 30% in group 5, respectively. The greatest flow depression was seen in group 4, moderate in groups in 2 and 3, and moderate to severe in group 5. Changes in carotid artery blood flow in all four groups were not statistically significant. For femoral artery blood flow, the changes in group 2 and 3

were not significant, changes in groups 4 and 5 with respect to treatment were not significant, but with respect to time; i.e., changes in blood flow from T=Ø to 1Ø, 2Ø,...,6Ø minutes on hyperoxia, showed a significant trend.

Allison et al. (1979) reported a statistically significant drop in pulmonary lobar blood flow during hyperoxic breathing when compared with the normoxic values. Eggers et al. (1962) reported a moderate increase in pulmonary blood volume in patients exposed to hyperoxia for 3Ø minutes.

Hyperoxia decreased regional blood flow, this effect was most seen in the brain, and least in hindlimb (Bergofsky and Bertun 1966). Grave et al. (197Ø) demonstrated that exposure of neonates and two-week-old puppies to 9Ø% oxygen caused a reduction of 2Ø% in mean cerebral and retinal blood flow. Kety and Schmidt (1948) reported a 13% statistically significant reduction in mean cerebral blood flow during hyperoxia.

Hyperoxia at arterial blood oxygen tension above 2ØØ Torr produced no significant effects upon liver blood flow (Hughes et al. 1979). During hyperoxia, mean regional myocardial blood flow was significantly diminished in nonischemic, intermediate, and ischemic regions (Rivas et al. 198Ø). Whereas, Moran and Wolfe (1978) demonstrated a significantly increased myocardial perfusion to all three layers of ventricular walls.

Total renal blood flow was reduced by 25% during hyperoxia (Shearer et al. 197Ø). Leg blood flow was reduced by 11% during exercise on 1ØØ% oxygen breathing, indicating an increase in resistance to blood flow in the exercising limb during hyperoxia (Welch et al. 1977).

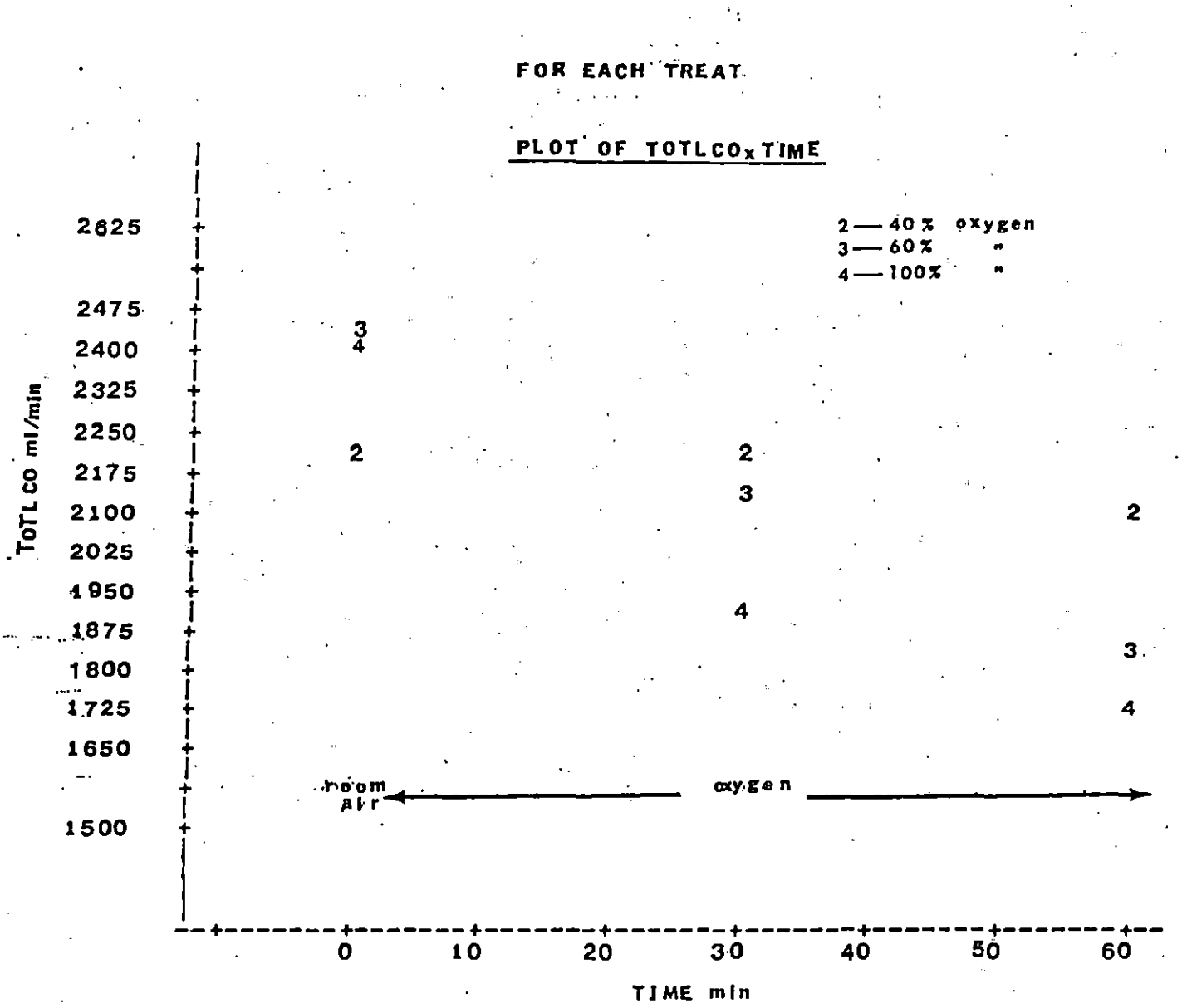


Figure 41. Mean values of cardiac output by treatment

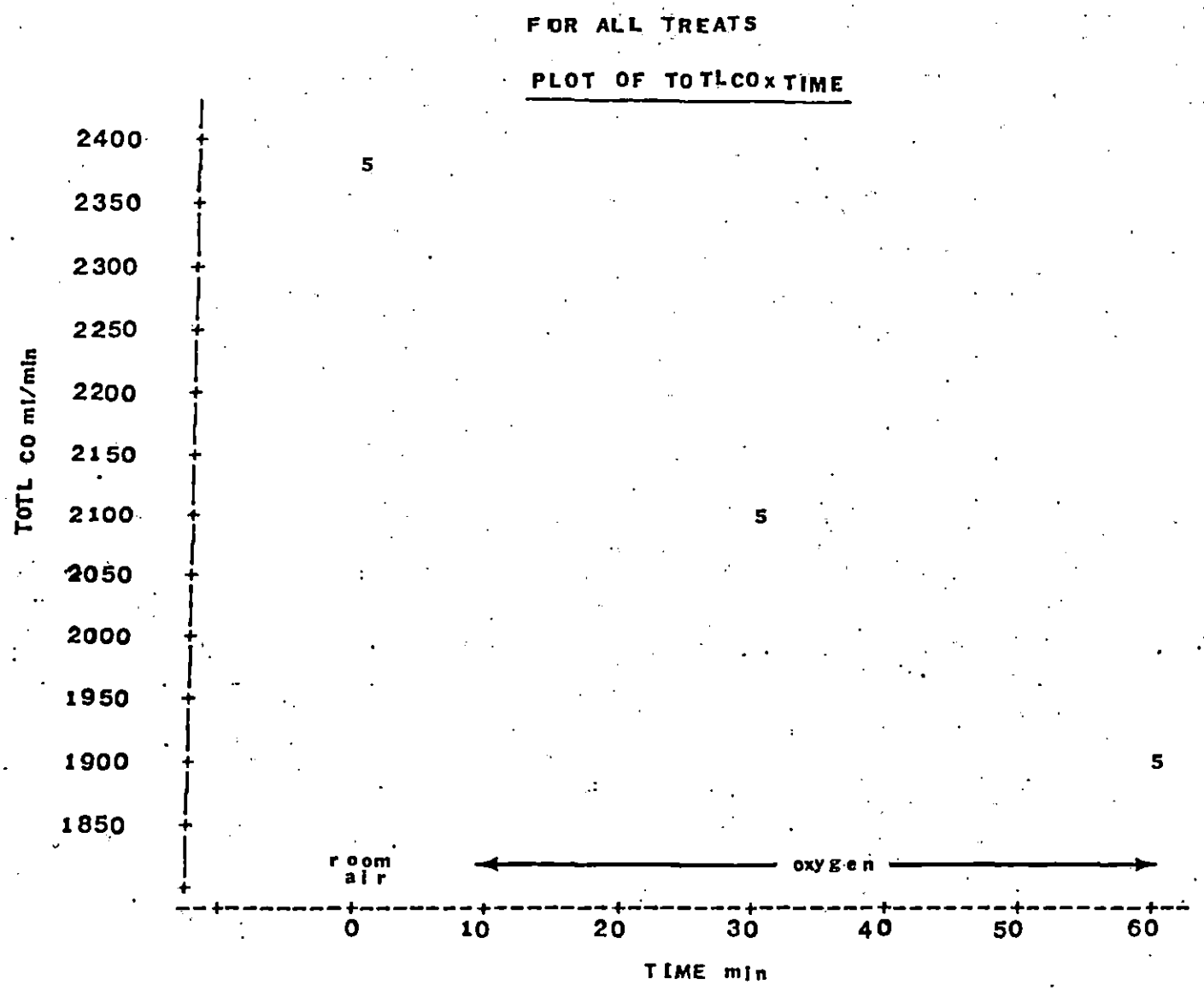


Figure 42. Mean values of cardiac output for all treatments

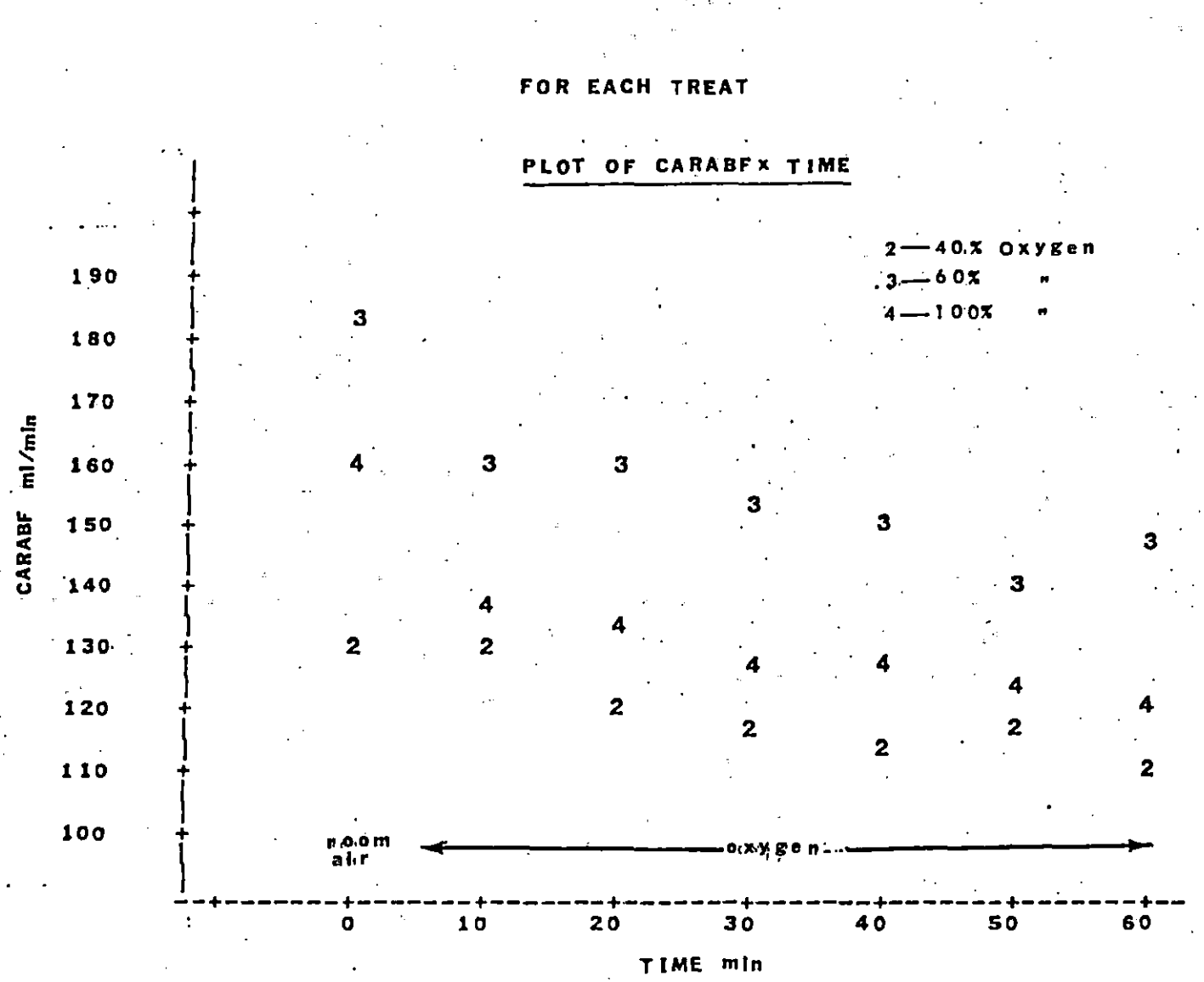


Figure 43. Mean values of caratid artery blood flow by treatment

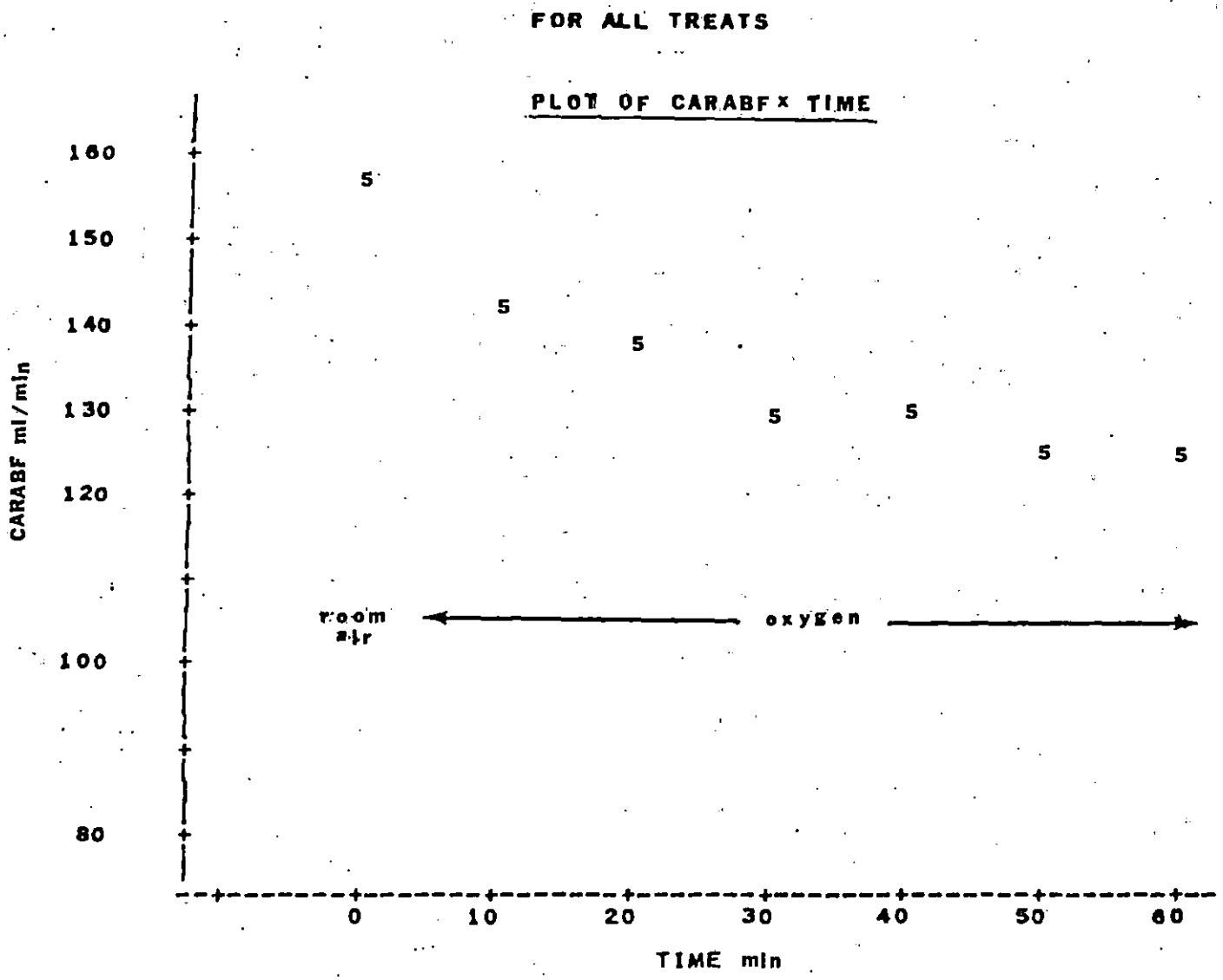


Figure 44. Mean values of carotid artery blood flow for all treatments

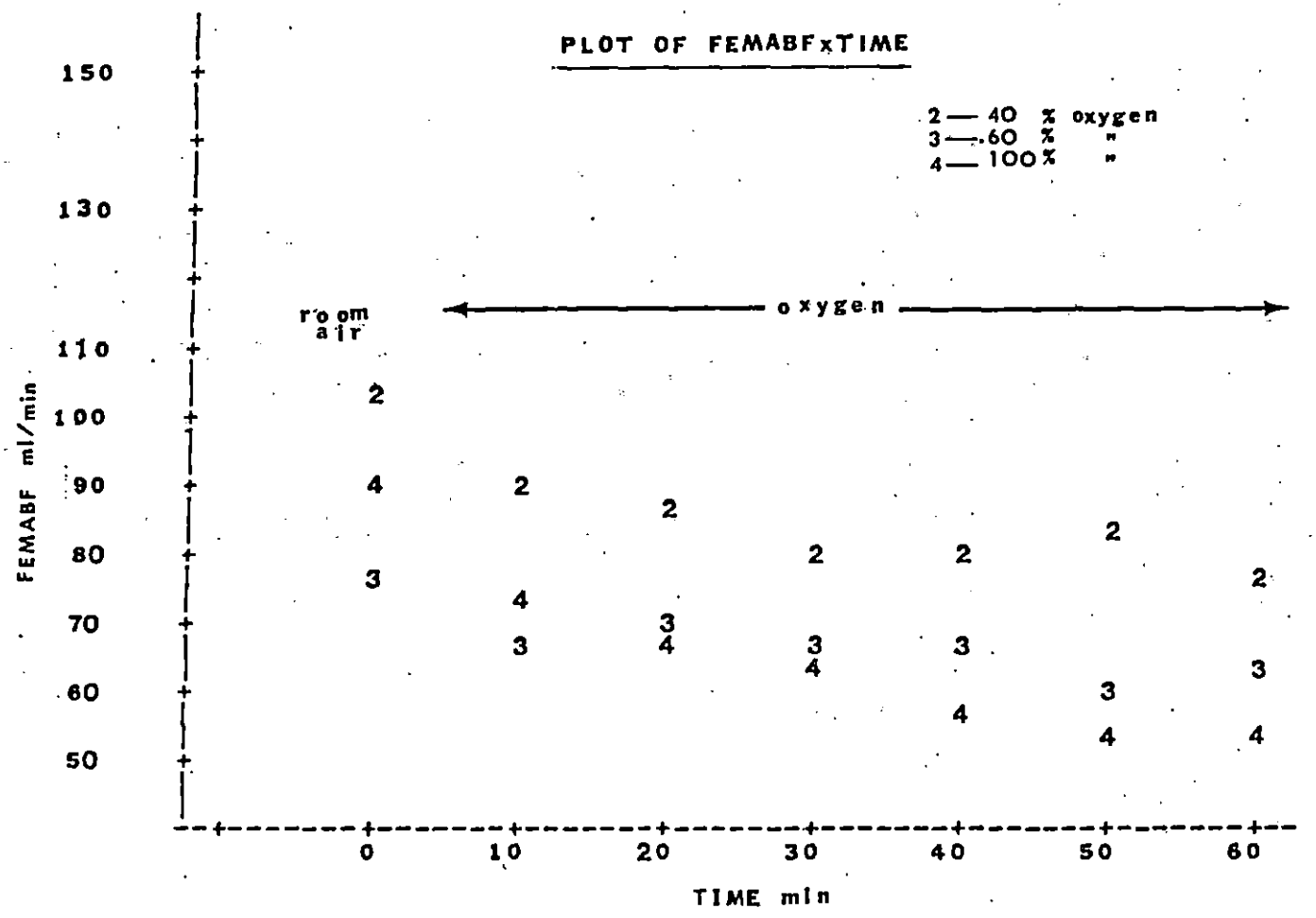


Figure 45. Mean values of femoral artery blood flow for each treatment

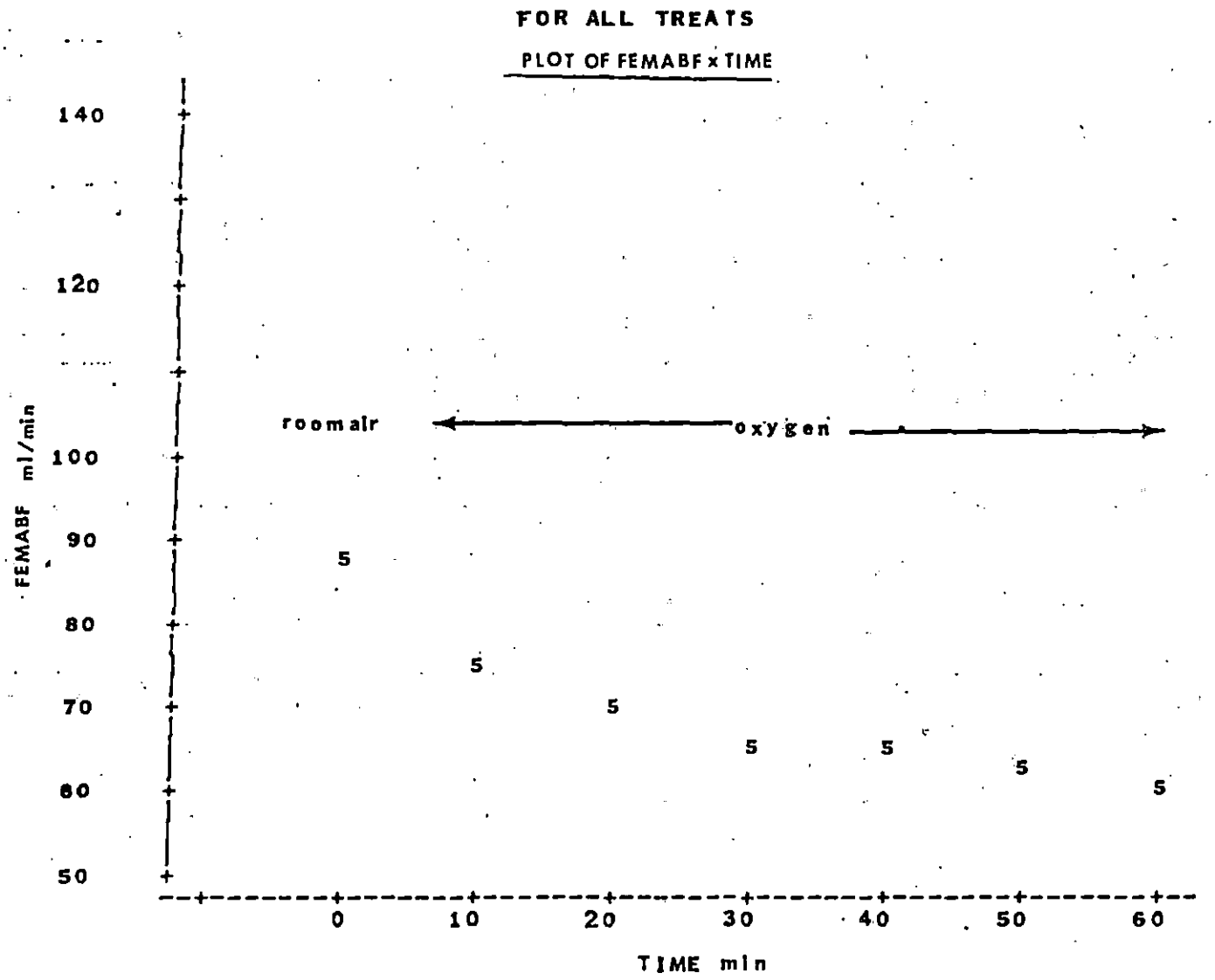


Figure 46. Mean values of femoral artery blood flow for all treatments

Oxygen Delivery and Vascular Resistances

Oxygen delivery or oxygen transport is defined as the product of cardiac output and arterial blood oxygen content.

Table A14, and Figures 47 and 48 give the mean values of oxygen delivery during normoxia and hyperoxia in all four groups.

Except for group 2, all other groups showed a decrease in oxygen delivery to the tissues during hyperoxia when compared with their respective groups normoxic values. Group 2 demonstrated a slight but statistically nonsignificant increase in oxygen delivery. Group 2 showed an increase of 5.7%, whereas, groups 3, and 5 showed a decrease of 5.3%, and 5.4%, respectively in oxygen delivery. Group 4 showed a severe decrease of 13.43% in oxygen delivery during hyperoxia. None of the changes in oxygen delivery to the tissues were statistically significant.

Degaute et al. (1981) demonstrated an increase in oxygen delivery in patients with acute decompensation of COPD during hyperoxia, they reasoned that such an increase in oxygen delivery was due to a sharp increase in arterial blood oxygen content. Welch et al. (1977) reported that oxygen transport to the leg during exercise was not significantly different when comparing hyperoxia with normoxia. Degaute et al. (1981) concluded that hyperoxic breathing in patients with moderate hypoxemia does not effect oxygen delivery, but in patients with severe hypoxemia it does increase the oxygen delivery significantly. Andersen and Hillestad (1970) concluded that 100% oxygen breathing for 20 minutes caused cardiac depression and vasoconstriction, and such hemodynamic effects abolished the expected rise in general and regional oxygen transport.

In our study, we demonstrated that oxygen delivery was depressed moderately during 60%, and severely during 100% oxygen breathing. Whereas, during 40% oxygen breathing, we noticed an increase in oxygen delivery to the tissues.

Vascular resistance is defined as the mean vascular pressure divided by cardiac output.

Tables A16 and A17, and Figures 49, 50, 51, and 52 give the mean values of pulmonary and systemic vascular resistances during normoxic and hyperoxic breathing for all four groups.

All four groups showed an increase in pulmonary vascular resistance (PVR). Group 2 showed an initial increase of 14% in PVR after 30 minutes on hyperoxic breathing, it then dropped by 4.5% below the control values at the end of 60 minutes on oxygen breathing. Group 3 had a 5.3% increase initially in PVR, it further increase by 32% at the end of 60 minutes on hyperoxia. Groups 4, and 5 showed a pattern similar to group 3. None of the changes in PVR were statistically significant.

Haneda et al. (1983) reported that 10 minutes of high oxygen breathing decreased the pulmonary arterial resistance in patients with pulmonary hypertension. Jones et al. (1983) and Moran and Wolfe (1978) reported that long term (7 days) 90% oxygen breathing caused an increase in pulmonary vascular resistance. Whereas, Fletcher and Levin (1984) reported that long term (8 weeks) oxygen therapy in patients with COPD demonstrated a lower pulmonary resistance.

In our experiment, hyperoxia caused an increase in both pulmonary and systemic vascular resistances during 30 and 60 minutes.

Peripheral or systemic vascular resistance (SVR) in all four groups showed an increase when compared with their respective groups normoxic values. In groups 3, 4, and 5, the SVR increased, and after 60 minutes its had doubled in value. The percent change in resistance values at 30 and 60 minutes on hyperoxia were 5.7% and 21.2%, 21.2% and 44%, 30.6% and 50.1%, and 20.4% and 40.1% for groups 2, 3, 4, and 5, respectively. Changes in SVR values in groups 2, 3, and 4 were not statistically significant, whereas, changes in group 5 with respect to treatment and time were statistically significant.

Fletcher and Levin (1984) showed that the long term oxygen exposure caused an increase in total vascular resistance. Welch et al. (1977) concluded that an increase in resistance to the blood flow in the exercising limb reduced the blood flow to that limb during hyperoxia. Kety and Schmidt (1948) expressed a moderate increase in cerebrovascular resistance during hyperoxia, which indicates vasoconstriction in the brain as the probable cause for reduction in cerebral blood flow.

A statistically significant increase in peripheral vascular resistance was documented during 30 minutes on hyperoxia (Eggers et al. 1962). Andersen and Hillestad (1970) reported vasoconstriction and blood pressure rise on hyperoxia for 20 minutes. A 70% rise in systemic vascular resistance was observed during 100% oxygen ventilation (Smith and Ledingham 1972).

We also observed a statistically significant rise in systemic vascular resistance in group 5, and our data follows literature values.

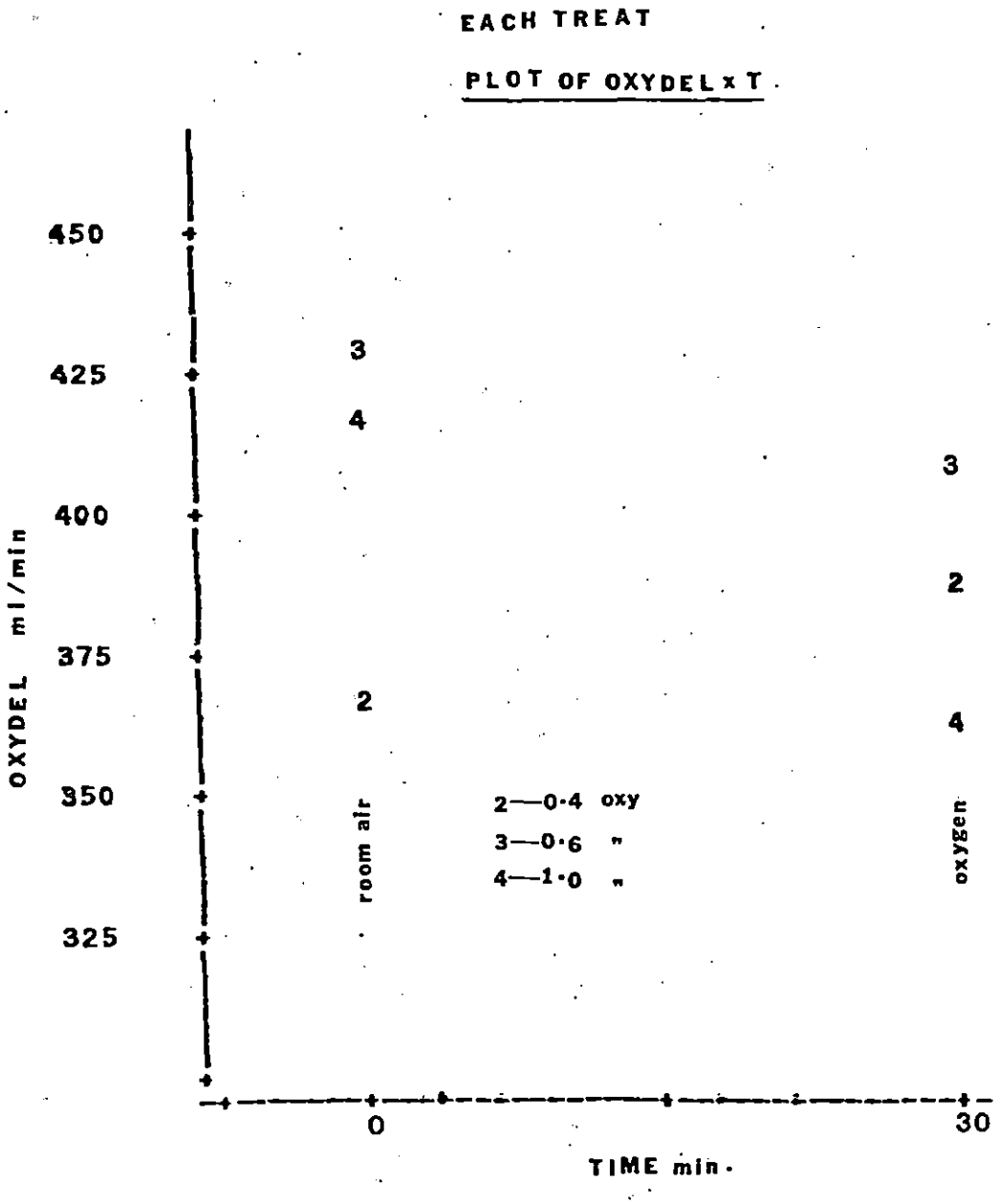


Figure 47. Mean values of oxygen delivery for each treatment.

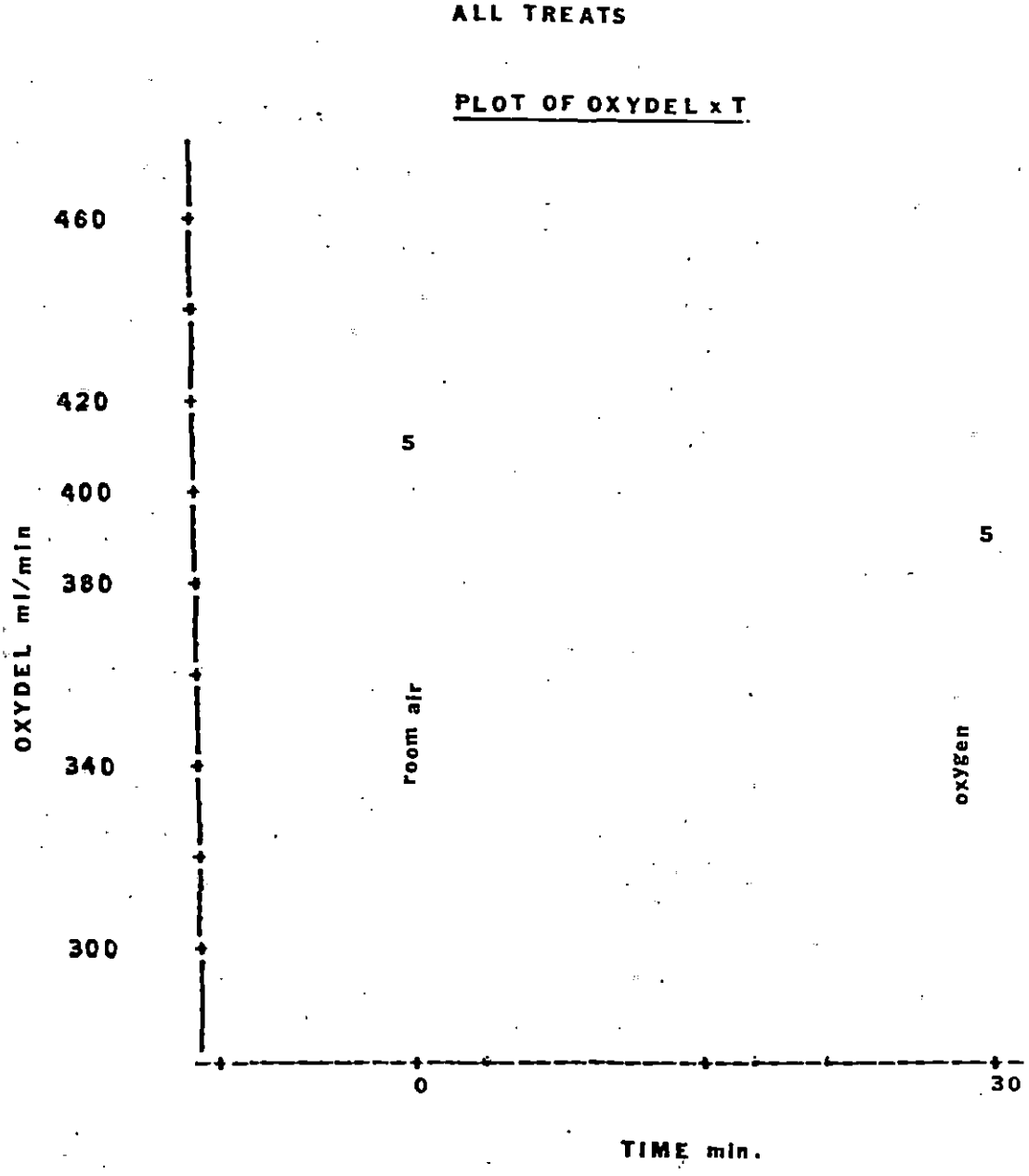


Figure 48. Mean values of oxygen delivery for all treatments

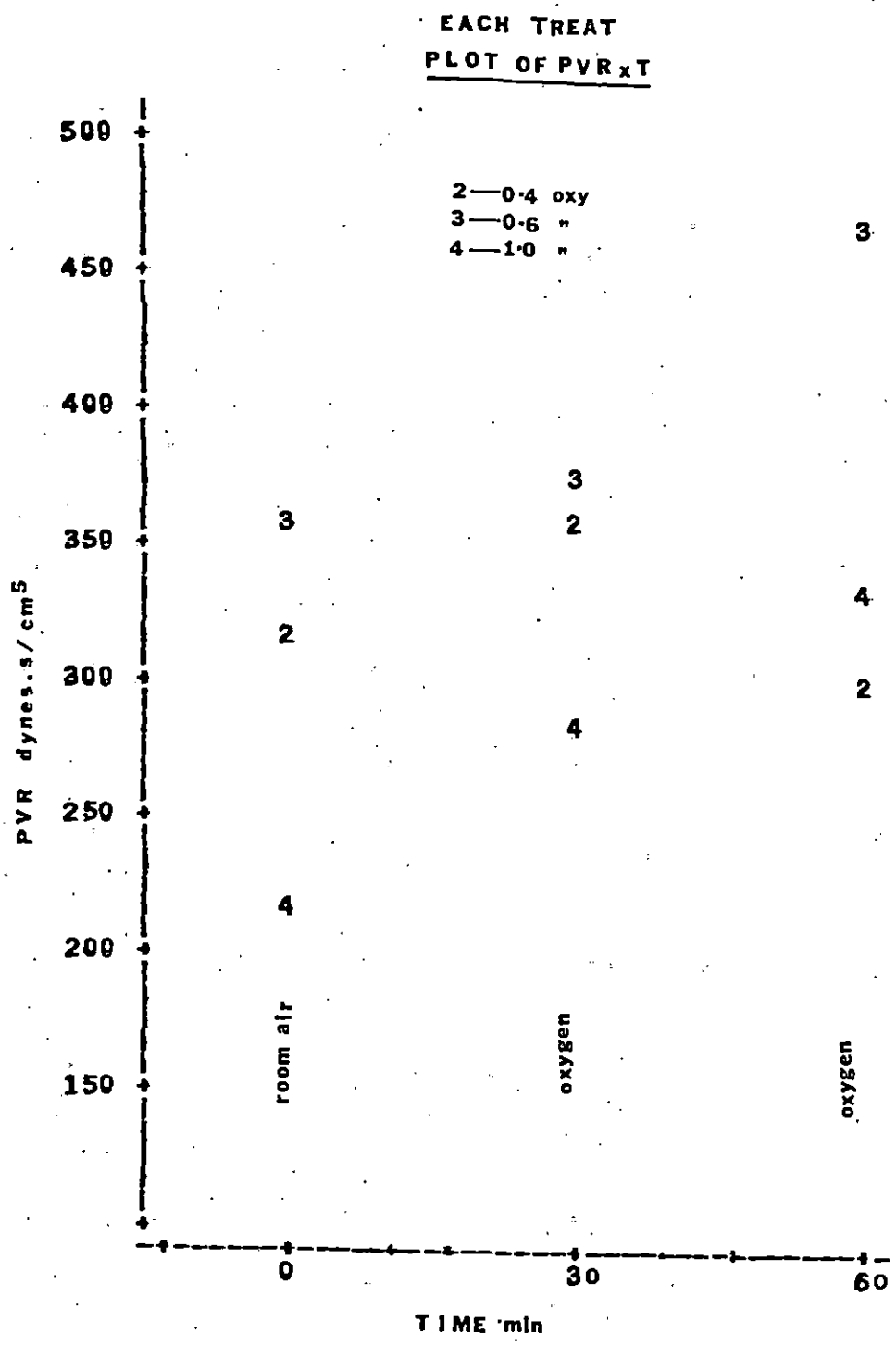


Figure 49. Mean values of pulmonary vascular resistance for each treatment.

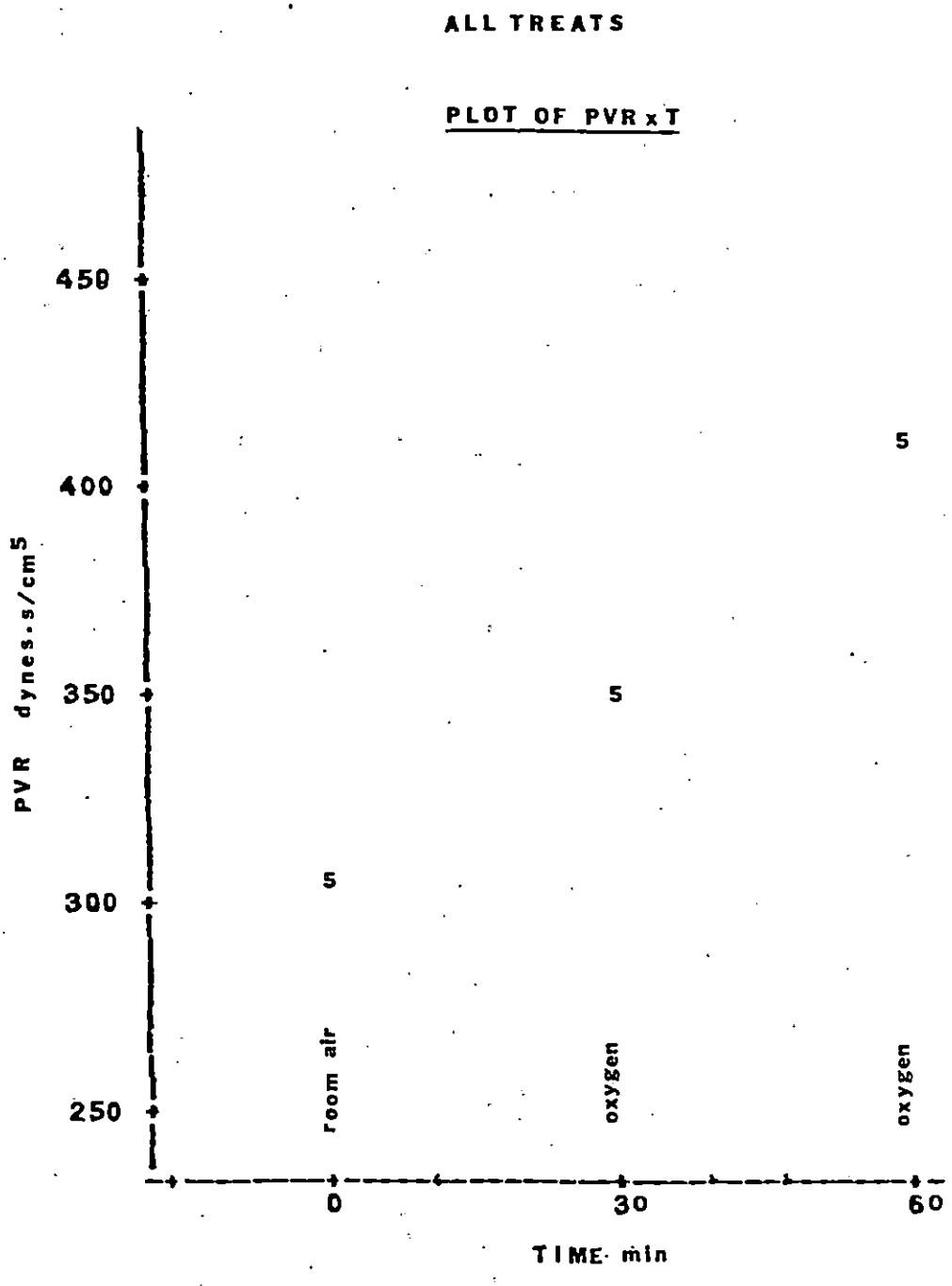


Figure 50. Mean values of pulmonary vascular resistance for all treatments

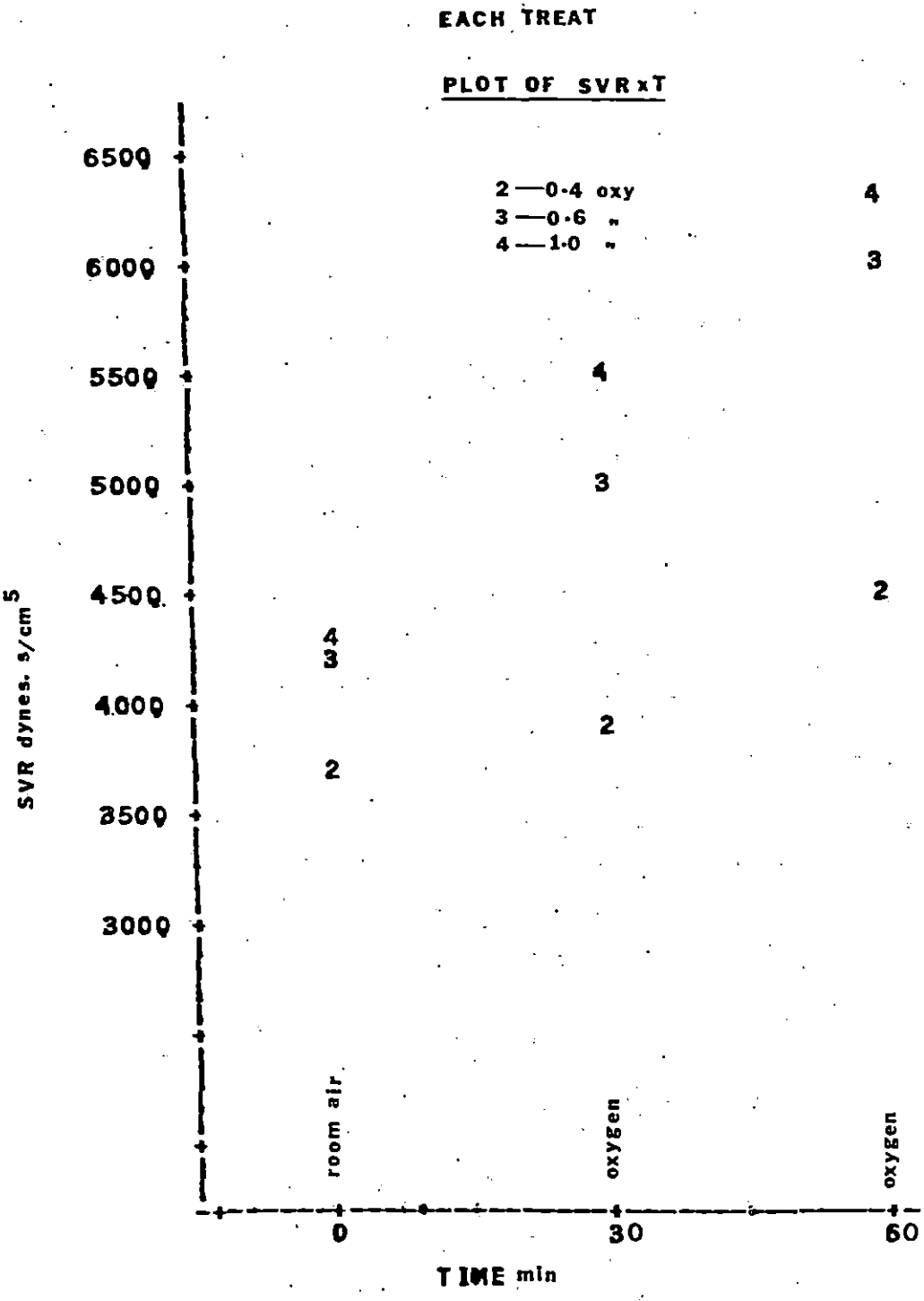


Figure 51. Mean values of systemic vascular resistance for each treatment

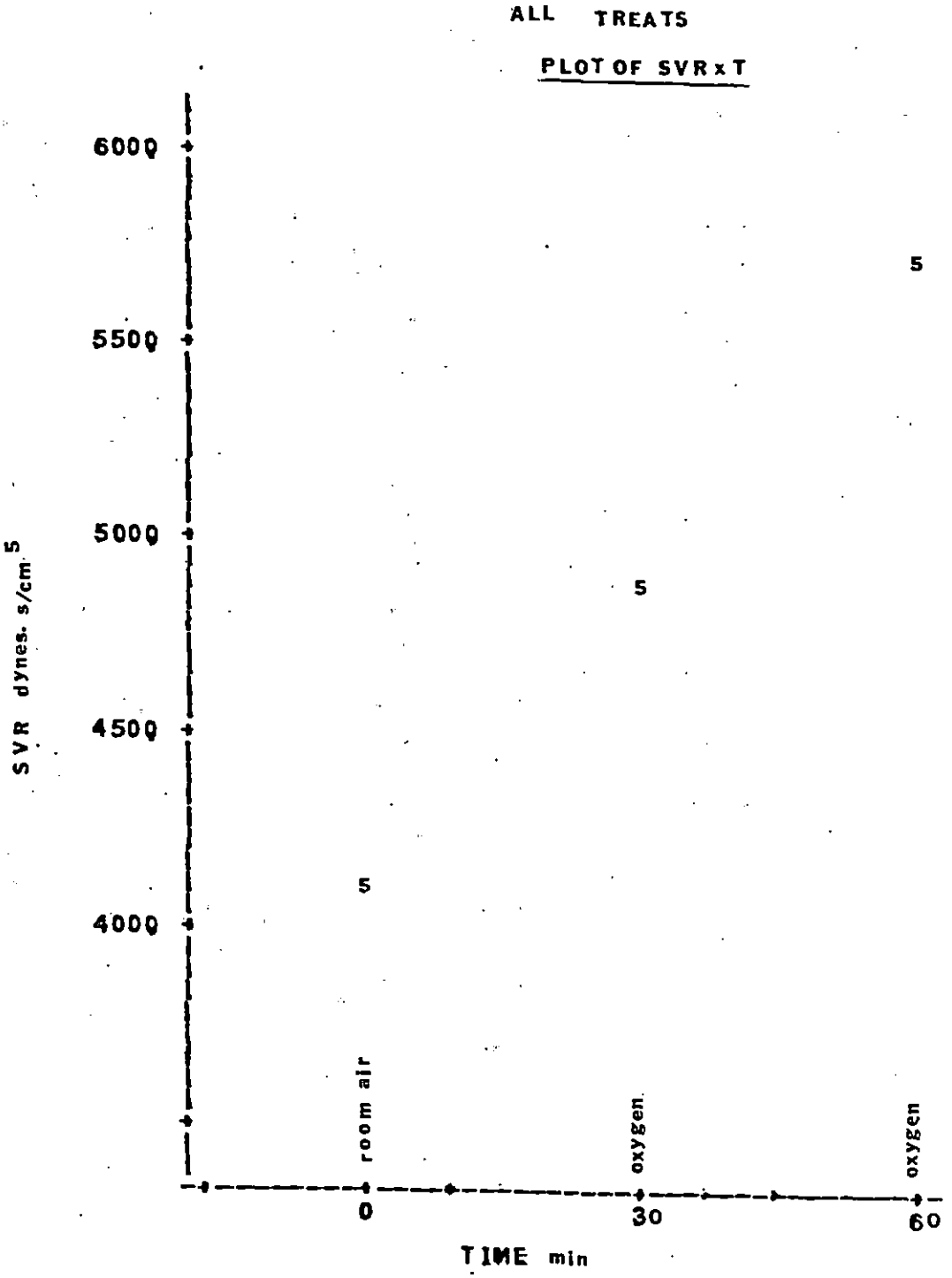


Figure 52. Mean values of systemic vascular resistance for all treatments.

Oxygen Consumption or Oxygen Uptake

The Fick equation defines oxygen consumption as the product of cardiac output and oxygen extraction or arterio-venous blood oxygen content gradient difference.

Table A17, and Figures 53 through 58 represent the mean values of oxygen consumption during normoxia and hyperoxia for total (general) body, cerebral, and hindlimb systems in all four groups.

All groups manifested an increase in oxygen consumption during oxygen breathing. Total (general) oxygen consumption increased the most in group 3 by 17.13%, whereas, in groups 2, 4, and 5 it increased by 13.9%, 10.5%, and 13.6%, respectively. It seems that total oxygen uptake in group 4 did not increase with an increase in oxygen concentration.

Cerebral oxygen uptake increased by 2.4% in group 2, 14.78% in group 3, 18.15% in group 4, and 12.74% in group 5, respectively. It appears that cerebral oxygen consumption increased with an increase in inspired oxygen gas concentration. After 30 minutes on oxygen breathing, we noticed a 46.3% increase in oxygen extraction (page 55, herein) with a 20.8% reduction in cerebral blood flow (page 77, herein). Even though oxygen extraction increased sharply (46.3%) and cerebral blood flow decreased markedly (20.8%) during 100% oxygen breathing, the over all cerebral oxygen uptake in group 4 increased by 18.15%.

Hindlimb oxygen uptake showed a similar pattern as observed with cerebral oxygen consumption. Groups 2, 3, 4, and 5 showed an increase by 1.11%, 15.72%, 19.38%, and 11.76%, respectively in hindlimb oxygen uptake during hyperoxia. The most oxygen uptake was during 100% oxygen

breathing in proup 4.

Hughes et al. (1979) reported a small increase in hepatic oxygen consumption without any changes in liver blood flow. During hyperoxia, patients with bronchial asthma demonstrated a 23% increase in oxygen uptake when compared with resting normoxic values (Irnell and Nordgren 1966).

Welch and Pedersen (1981) reported that oxygen consumption during maximal exercise condition was significantly higher in oxygen breathing subjects. Whereas, Welch et al. (1977) demonstrated that oxygen consumption of exercising limb was not different during oxygen breathing, even though leg blood flow was reduced by 11%. Cassuto and Farhi (1979) reported that the oxygen uptake during 100% oxygen breathing was the same as in the control normoxia.

We also observed an increase in oxygen consumption specially in the cephalic region during hyperoxia breathing, and this was primarily due to an increase in oxygen extraction in that region. Our data follow literature statements. We demonstrated that oxygen consumption increased in normal, healthy, resting, and spontaneously breathing dogs during hyperoxia, and the oxygen uptake by the cephalic and hindlimb regions increased with an increase in inspired oxygen gas concentration.

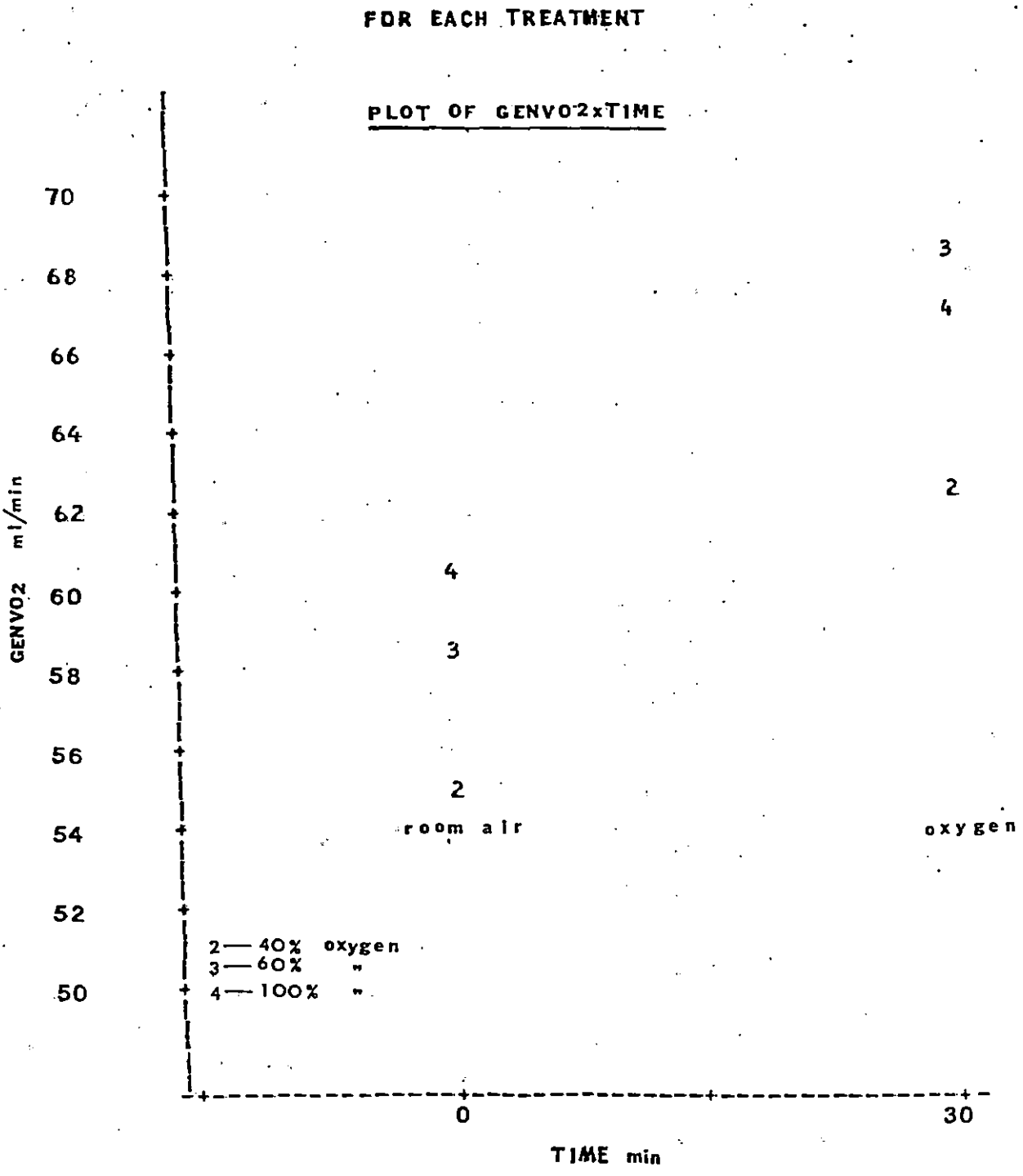


Figure 53. Mean values of total general oxygen consumption for each treatment

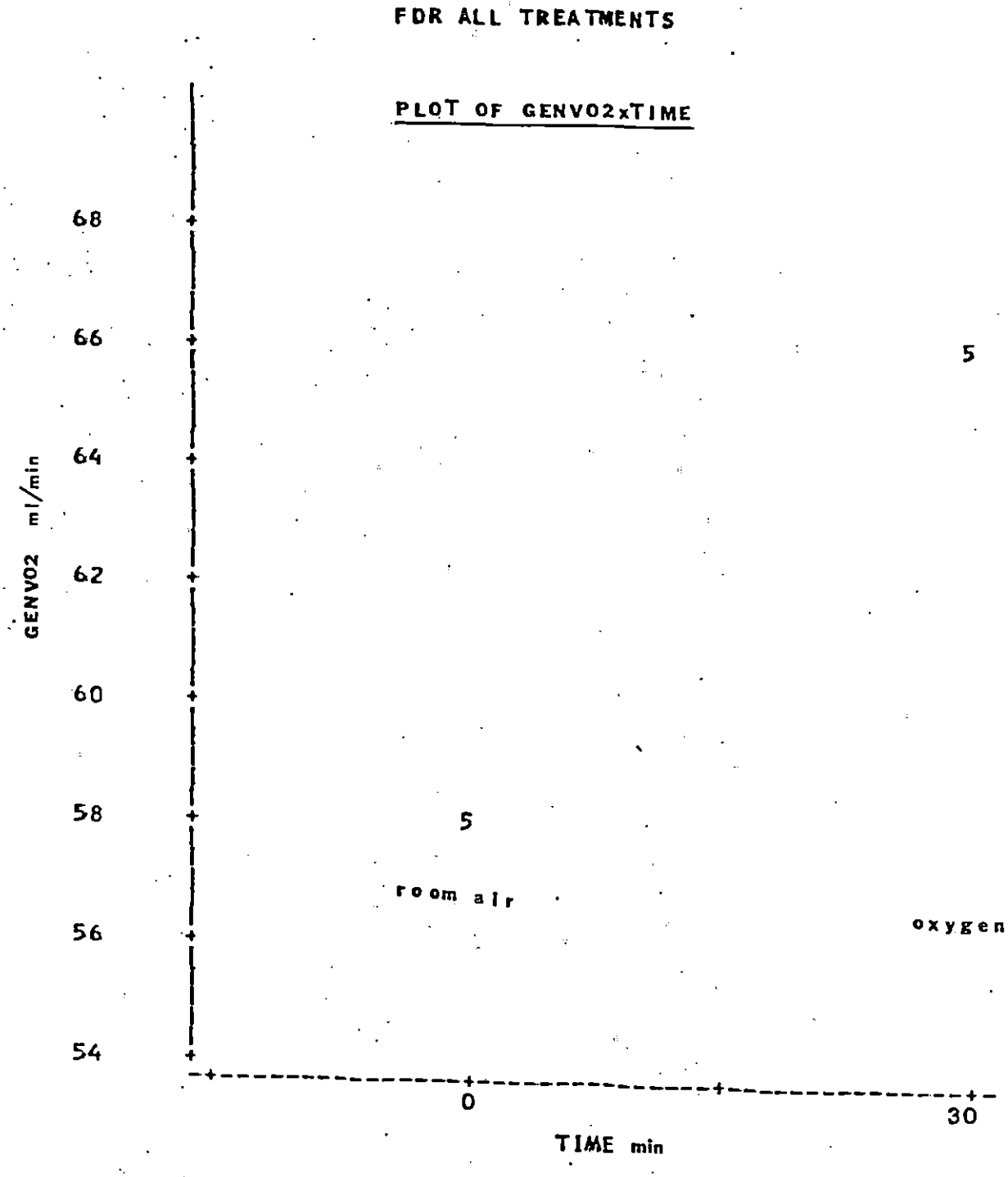


Figure 54. Mean values of total general oxygen consumption for all treatments

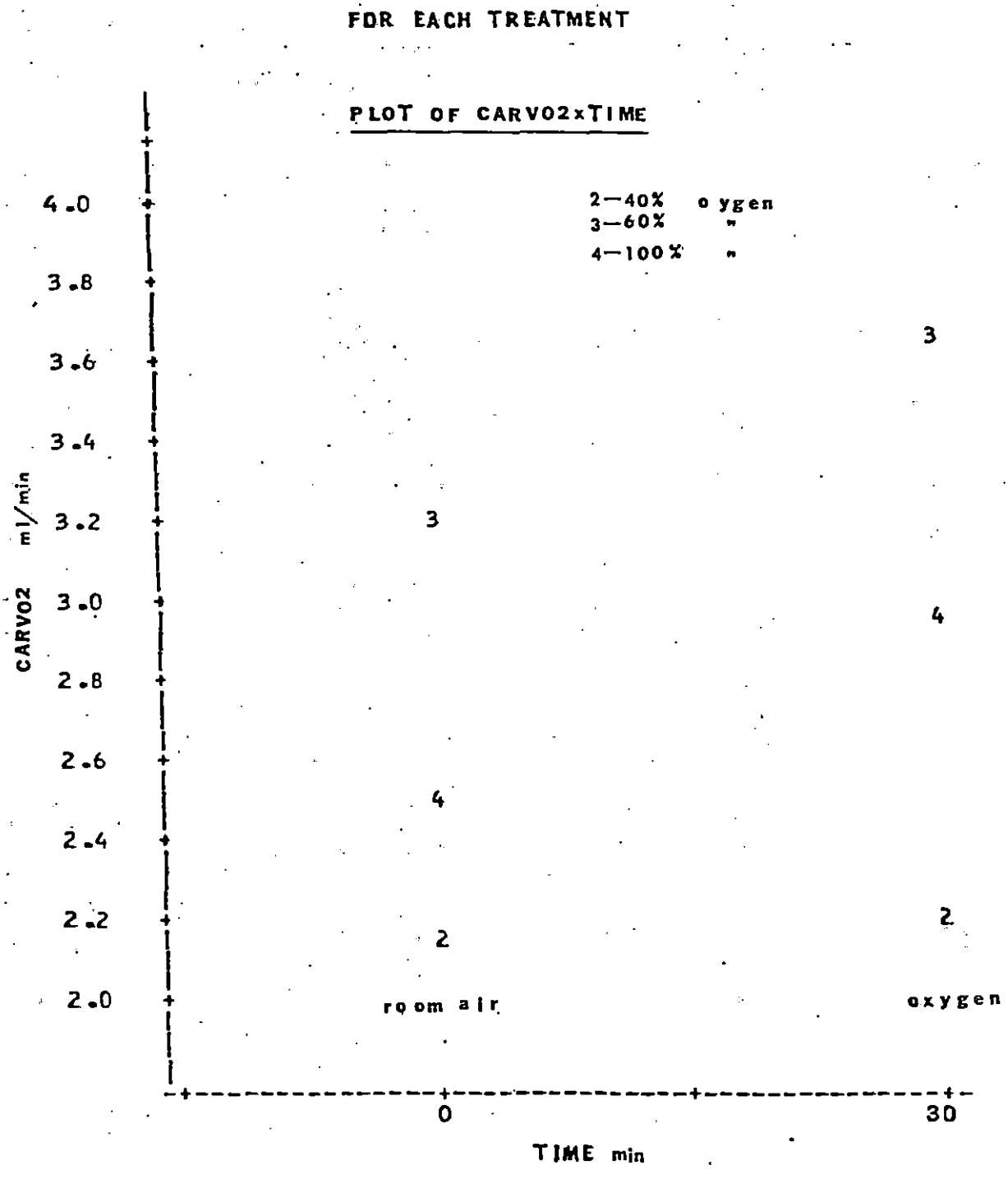


Figure 55. Mean values of regional cerebral oxygen consumption for each treatment

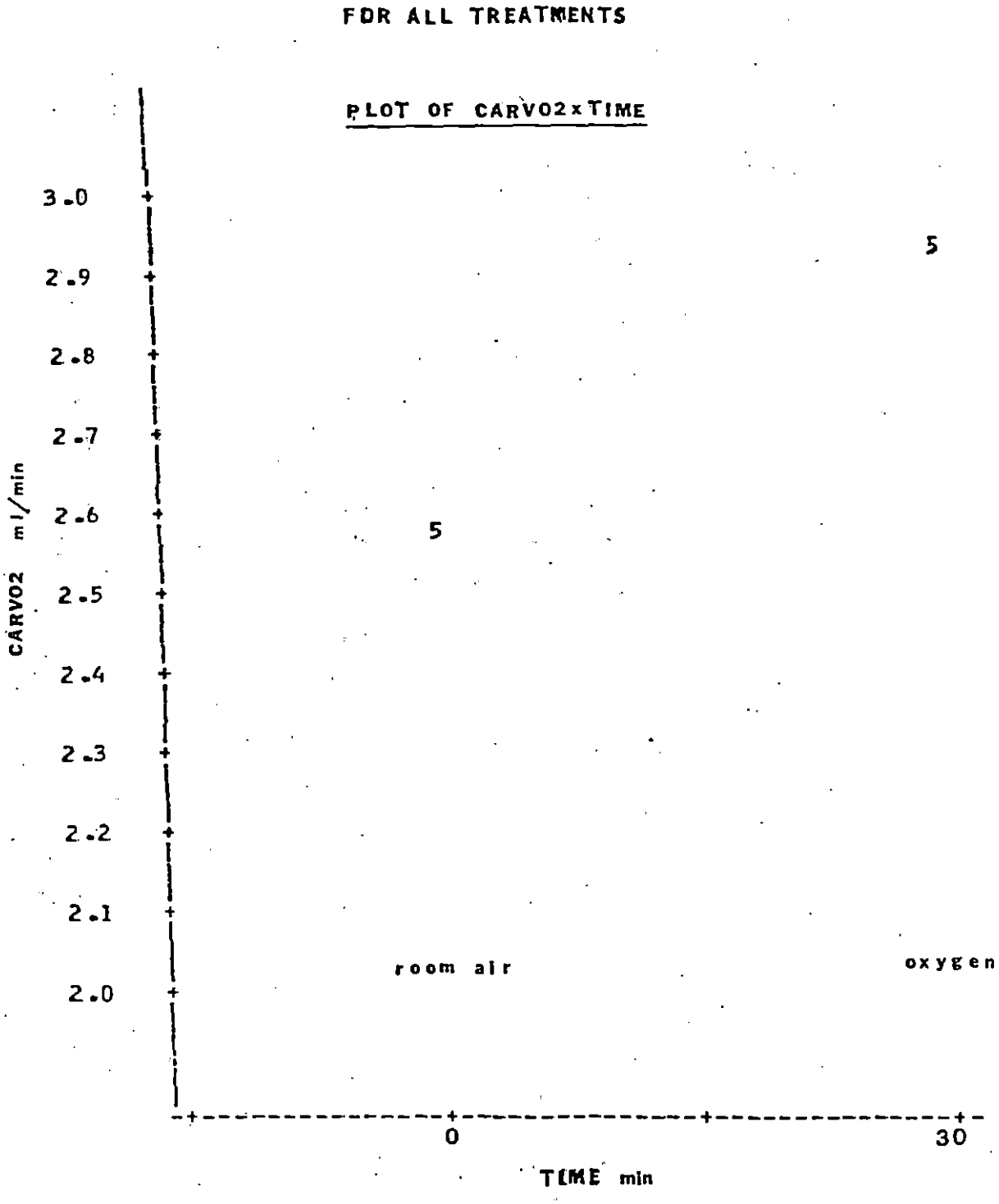


Figure 56. Mean values of regional cerebral oxygen consumption for all treatments

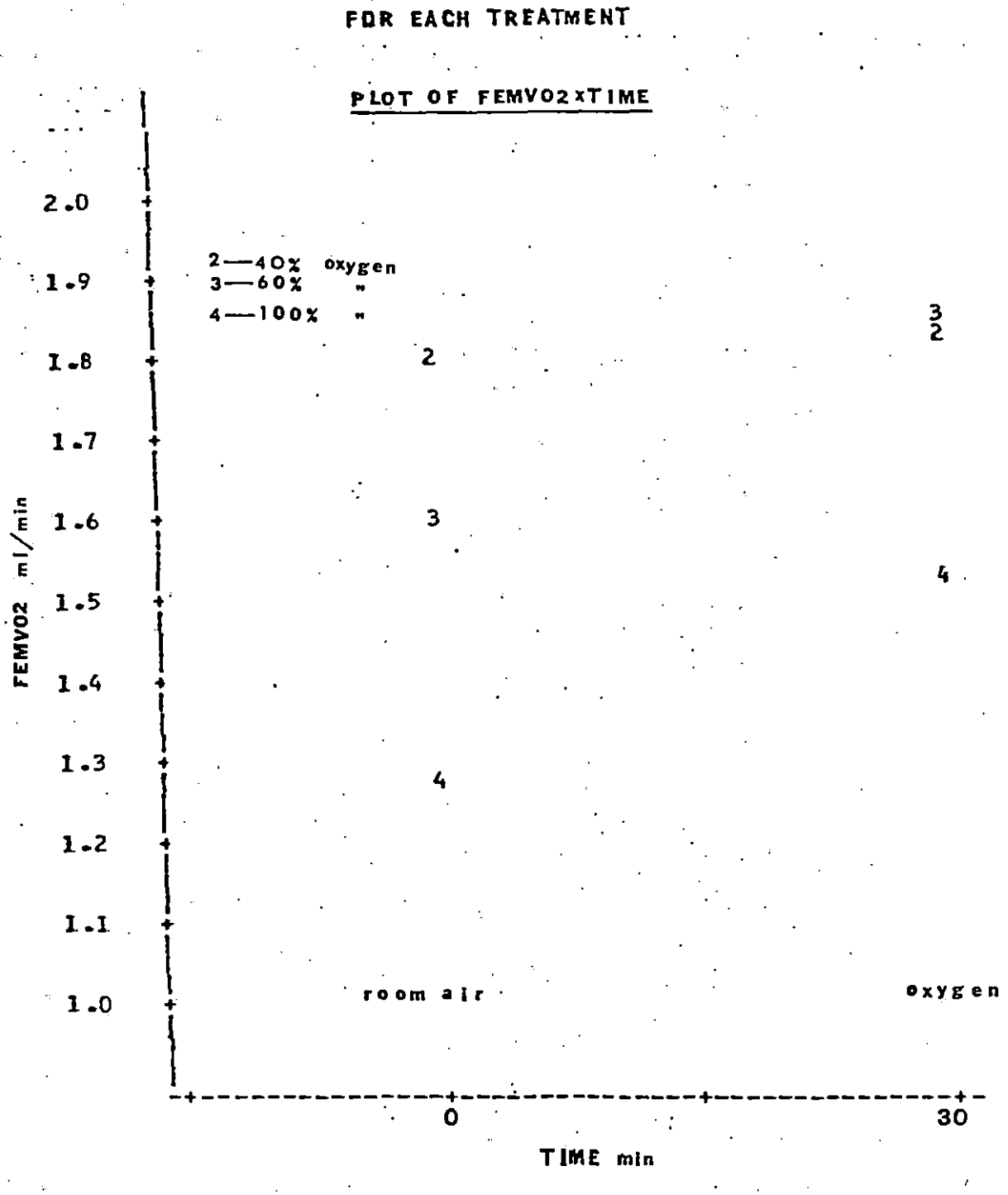


Figure 57. Mean values of regional hindlimb oxygen consumption for each treatment

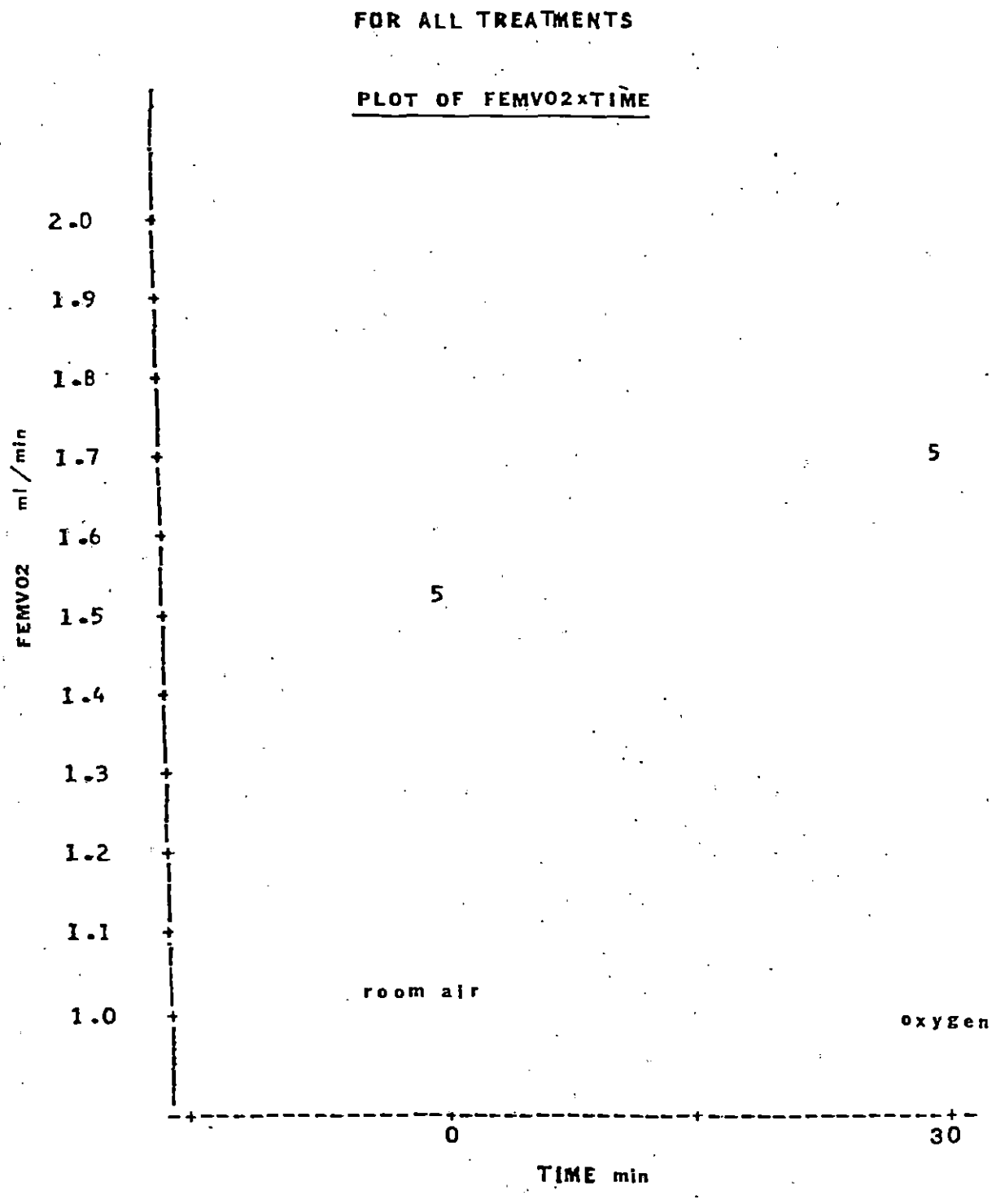


Figure 58. Mean values of regional hindlimb oxygen consumption for all treatments

SUMMARY AND CONCLUSIONS

The purpose of this study was to examine the effects of different concentrations of inspired oxygen on circulatory, and vascular systems, and to demonstrate its effects at the cellular level in terms of oxygen uptake by the tissues. Our major findings in this research were.

1) Oxygen breathing caused an increase in resting minute ventilation, this was due to an increase in both the respiratory frequency and tidal volume.

2) Blood pH dropped slightly, and blood carbon-dioxide increased slightly during oxygen breathing. Thus, indicating a presence of slight respiratory acidosis during hyperoxia. There was an expected rise in blood oxygen tension and hemoglobin oxygen saturation during oxygen breathing.

3) Blood oxygen content increased during hyperoxia, which resulted from an increase in blood oxygen tension, in hemoglobin oxygen saturation, and in dissolved oxygen content in the plasma.

4) Oxygen extraction by the total (general) body system increased the most during 60%, moderate during 40%, and less during 100% oxygen breathing. Cerebral oxygen extraction increased as the concentration of the inspired oxygen increased. Cerebral oxygen extraction was greater during 100% oxygen breathing, which resulted from a severely depressed cerebral blood flow at that oxygen concentration. Oxygen extraction in the hindlimb was enhanced the most during 100%, and least during 40% oxygen breathing.

5) Pulmonary vascular pressure did not change during 60% hyperoxia, decreased slightly at 40%, and increased slightly at 100% oxygen breathing. Systemic vascular pressure was higher during hyperoxia; the greatest increase was during 40%, moderate during 60% and least during 100% oxygen breathing.

6) Cardiac output was also affected while inhaling oxygen, depressed severely at 100%, moderately at 60%, and slightly at 40% oxygen breathing. Similarly, blood flows in the carotid and femoral arteries were severely depressed at the end of 60 minutes on oxygen breathing, particularly at the 60 minutes of 100% hyperoxic exposure.

7) Oxygen delivery or oxygen transport to the tissues was reduced during 60% and 100% oxygen breathing, but during 40% oxygen breathing, oxygen delivery to the tissues was enhanced. Despite an increase in arterial blood oxygen content during hyperoxia, decrease in cardiac output was the most probable cause of reduced oxygen delivery to the tissues.

8) Pulmonary and systemic vascular resistances were higher during oxygen breathing. This increase in resistance was due to the vasoconstrictive effects of oxygen on the vasculature system. It was due to an increase in resistance that caused an increase in pulmonary and systemic vascular pressures, reduced total cardiac output, and blood flows in the carotid and femoral arteries.

9) Oxygen uptake by the general body system was enhanced during 40% and 60% oxygen breathing, whereas, it was enhanced, but not so much during 100% oxygen. Cerebral oxygen consumption increased during all

concentrations of oxygen breathing, 100% oxygen breathing increased the cerebral oxygen uptake the most, and this was primarily due to a sharp increase in oxygen consumption. Hindlimb oxygen uptake was also influenced during hyperoxia in a similar fashion as stated above for cerebral oxygen consupmtion.

Increase in cerebral oxygen consumption was due to a sharp increase in oxygen extraction, despite a marked decrease in cerebral blood flow during oxygen exposure. Decrease in cerebral blood flow was due to an increase in peripheral vascular resistance. Decrease in oxygen transport was mainly due to a decrease in cerebral blood flow, despite an increase in arterial blood oxygen content that had occurred during hyperoxic exposure. Increase in peripheral vascular resistance was due to the vasoconstrictive effects of oxygen on peripheral vasculature. Similarly, the same phenomenon may have occurred in the hindlimb during hyperoxia.

Increase in oxygen consumption in the presence of hyperoxia was due to the compensatory response by the central nervous system to a reduce blood flow that was witnessed during oxygen breathing. Reduce blood flow means reduce oxygen delivery, and that means reduced oxygen availability to the tissues. Thus natural compensatory mechanism to extract more oxygen from the hemoblobin occurred.

Our findings in terms of changes in blood gases, blood oxygen content and transport, systemic vascular pressure and resistance, total cardiac output, cerebral and hindlimb blood flows, total and regional oxygen uptake, during short term oxygen breathing were all in agreements with the literature values.

On the contrary, we observed a slight increase in minute ventilation and essentially no changes in the pulmonary vascular pressure during hyperoxia. Also, we noticed an increase in pulmonary vascular resistance, which was primarily due to depressed cardiac output during short term oxygen exposure. We observed that an increase in oxygen consumption, which was primarily due to an increase in oxygen extraction. It is seldom mentioned in the literature that hyperoxia enhances tissue oxygen extraction. We were able to demonstrate that cephalic and hindlimb oxygen uptakes were directly related to the inspired oxygen gas concentration and or to the partial pressure of oxygen in the arterial blood, even though oxygen exposure caused a reduction in blood flow and oxygen transport to the tissues.

Arterioles accounts for approximately 75% of the total resistance to flow. Smooth muscle surrounds the arterioles. Oxygen plays a central role in metabolic autoregulation of peripheral blood flow, a rise in blood oxygen tension above normal induces vasoconstriction, whereas, a fall in blood oxygen tension causes a vasodilation. Oxygen may act directly on vascular smooth muscle or indirectly by causing the release of vasoconstrictive substances from the parenchymal or other cells. Changes in blood oxygen tension produce different reactions in smooth muscle cells of different precapillary resistance vessels.

In any event, oxygen is important to the intrinsic regulation of all tissues in situation resembling reactive hyperemia and in normal circumstances in some tissus with a high metabolic rate, e.g., the heart, brain, and exercising muscle.

BIBLIOGRAPHY

Abraham, E., R. D. Bland, J. C. Cobo, and W. C. Shoemaker. 1984. Sequential cardiorespiratory patterns associated with outcome in septic shock. Chest 85:75-79.

Allison, D. J., T. P. Clay, and H. S. Stanbrook. 1979. Pulmonary vasoconstrictor response to hyperoxia. J. Physiol. (Lond.) 289:73-74P.

Andersen, A., and L. Hillestad. 1970. Hemodynamic responses to oxygen breathing and the effect of pharmacological blockade. Acta Medica Scand. 188:419-24.

Aubier, M., D. Murciano, J. Milic-Emili, E. Touaty, J. Daghfous, R. Pariente, and J. P. Derenne. 1980. Effects of the administration of oxygen on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. Am. Rev. Respir. Dis. 122:747-54.

Barclay, J. K., C. M. Boulianne, B. A. Wilson, and S. J. Tiffin. 1979. Interaction of hyperoxia and blood flow during fatigue of canine skeletal muscle in situ. J. Appl. Physiol.: Respir. Environ. Exercise Physiol. 47(5):1018-24.

Bergofsky, E. H., and P. Bertun. 1966. Response of regional circulations to hyperoxia. J. Appl. Physiol. 21(2):567-72.

Cassuto, Y., and L. E. Farhi. 1979. Circulatory response to arterial hyperoxia. J. Appl. Physiol. 46(5):973-77.

Degaute, J. P., G. Domenighetti, R. Naeije, J. L. Vincent, D. Treyvaud, and Cl. Perret. 1981. Oxygen delivery in acute exacerbation of chronic obstructive pulmonary disease. Effects of controlled oxygen therapy. Am. Rev. Respir. Dis. 124:26-30

Dewar, K. M. S., G. Smith, A. A. Spence, and I. McA. Ledingham. 1972. Effect of hyperoxia on airways resistance in man. J. Appl. Physiol. 32(4):486-90.

Divertie, M. B., and J. C. McMichan. 1984. Continuous monitoring of mixed venous oxygen saturation. Chest 85:423-28.

Dressendorfer, R. H., C. E. Wade, and E. M. Bernauer. 1977. Combined effects of breathing resistance and hyperoxia on aerobic work tolerance. J. Appl. Physiol. 42(3):444-48.

Eggers, G. W. N., H. W. Paley, J. J. Leonard, and J. V. Warren. 1962. Hemodynamic responses to oxygen breathing in man. J. Appl. Physiol. 17(1):75-79.

Finch, C. A., and C. Lenfant. 1972. Oxygen transport in man. N. Engl. J. Med. 286:407-15.

Fleetham, J. A., C. A. Bradley, M. H. Kryger, and N. R. Anthonisen. 1980. The effect of low flow oxygen therapy on the chemical control of ventilation in patients with hyperoxic COPD. Am. Rev. Respir. Dis. 122:833-40.

Fleetham, J., P. West, B. Mezon, W. Conway, T. Roth, and M. Kryger. 1982. Sleep, arousals, and oxygen desaturation in chronic obstructive pulmonary disease. The effect of oxygen therapy. Am. Rev. Respir. Dis. 126:429-33.

Fletcher, E. C., and D. C. Levin. 1984. Cardiopulmonary hemodynamics during sleep in subjects with chronic obstructive pulmonary disease. The effect of short- and long-term oxygen. Chest 85:6-14.

Freedman, A. R., B. T. Mangura, and M. H. Lavietes. 1983. Minute ventilation in asthma. Enhancement by mouthpiece and depression by oxygen administration. Am. Rev. Respir. Dis. 128:800-05.

Grave, G. D., C. Kennedy, J. Jehle, and L. Sokoloff. 1970. The effects of hyperoxia on cerebral blood flow in newborn dogs. Neurology 20:397-98.

Guenard, H., M. Verhas, A. Todd-Prokopek, F. Solvignon, C. Crouzel, P. Manigne, and F. Soussaline. 1982. Effects of oxygen breathing on regional distriburion of ventilation and perfusion in hypoxemic patients with chronic lung disease. Am. Rev. Respir. Dis. 125:12-17.

Haneda, T., T. Nakajima, K. Shirato, S. Onodera, and T. Takishima. 1983. Effects of oxygen breathing on pulmonary vascular input impedence in patients with pulmonary hypertension. Chest 83:520-27.

Harkema, J. R., J. L. Mauderly, and F. F. Hahn. 1982. The effects of emphysema on oxygen toxicity in rats. Am. Rev. Respir. Dis. 126:1058-65.

Harrison, R. A. 1983. The Fick equation and pulmonary artery blood gases. A key to differentiating cardiopulmonary disease. Respiratory Therapy 1983:95-101.

Hughes, R. L., R. T. Mathie, D. Campbell, and W. Fitch. 1979. Systemic hypoxia and hyperoxia, and liver blood flow and oxygen consumption in the greyhound. Pflugers Arch. 381:151-57.

Irnell, L., and L. Nordgren. 1966. Effects of hypercapnoea and hyperoxia on pulmonary cirulation in patients with bronchial asthma. Acta Medica Scand. 180:355-62.

Ivanov L. A., and N. D. Chebotarev. 1980. Effect of hyperoxia on oxygen transport properties of blood. Moscow Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina in Russian 1:54-59.

Jones, R., W. M. Zapol, and L. Reid. 1983. Pulmonary arterial wall injury and remodelling by hyperoxia. Chest 85:40-43S.

Kety, S. S., and C. F. Schmidt. 1948. The effects of altered arterial tension of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men. J. Clinical Invest. 27:484-92.

Libby, D. M., W. A. Briscoe, and T. K. C. King. 1981. Relief of hypoxia related bronchoconstriction by breathing 30 per cent oxygen. Am. Rev. Respir. Dis. 123:171-75.

Linnarsson D., J. Karlsson, L. Fagraeus, and B. Saltin. 1974. Muscle metabolites and oxygen deficit with exercise in hypoxia and hyperoxia. J. Appl. Physiol. 36(4):399-02.

Minami, T., M. Ogawa, T. Sugimoto, and K. Katsurada. 1973. Hyperoxia of internal jugular venous blood in brain death. J. Neurosurg. 39:442-47.

Miyamura, M., H. Th. Folgering, R. A. Binkhorst, F. D. J. Smolders, and F. Kreuzer. 1976. Ventilatory responses to CO2 at rest and during positive and negative work in normoxia and hyperoxia. Pflugers Arch. 364:7-15.

Moran, J. F., and W. G. Wolfe. 1978. Hemodynamic effects of prolonged hyperoxia. Ann. Surg. 187(1):73-78.

Reinstorff, D., and A. Fenner. 1972. Ventilatory response to hyperoxia in premature and newborn infants during the first three days of life. Respiration Physiol. 15:159-65.

Rivas, F., J. C. Rembert, R. J. Bache, F. R. Cobb, and J. C. Greenfield, Jr. 1980. Effect of hyperoxia on regional blood flow after coronary occlusion in awake dogs. Am. J. Physiol. (Heart Circ. Physiol. 7) 238:244-48H.

Shearer, J. R., J. N. Norman, J. MacIntyre, and G. Smith. 1970. The effects of hypoxia and hyperoxia on renal blood flow. Br. J. Surg. 57(11):851.

Smith, C. W., P. H. Lehan, and J. J. Monks. 1963. Cardiopulmonary manifestations with high oxygen tensions at atmospheric pressure. J. Appl. Physiol. 18(5):849-53.

Smith, G., and I. McA. Ledingham. 1972. The effect of prolonged hyperoxia on the cardiovascular system of anaesthetized dogs. Brit. J. Anaesth. 44:469-72.

Spier, S., J. Rivlin, D. Hughes, and H. Levison. 1984. The effect of oxygen on sleep, blood gases, and ventilation in cyctic fibrosis. Am. Rev. Respir. Dis. 129:712-18.

Tammivaara-Hilty, R. 1973. Central haemodynamics during hypoxia, hyperoxia and hypercapnoea in severe chronic obstructive lung disease. Upsala J. Med. Sci. 78:116-32.

Welch, H. G. 1982. Hyperoxia and human performance: A brief review. Med. Sci. Sports Exercise 14(4):253-62.

Welch, H. G., and P. K. Pedersen. 1981. Measurement of metabolic rate in hyperoxia. J. Appl. Physiol. 51(3):725-31.

Welch, H. G., F. Bonde-Petersen, T. Graham, K. Klausen, and N. Secher. 1977. Effects of hyperoxia on leg blood flow and metabolism during exercise. J. Appl. Physiol.: Respir. Environ. Exercise Physiol. 42(3):385-90.

Whitehorn, W. V., A. Edelmann, and F. A. Hitchcock. 1946. The cardiovascular responses to the breathing of 100 per cent oxygen at normal barometric pressure. Am. J. Physiol. 146:61-65.

Wright J. L., L. Lawson, P. D. Pare, R. O. Hooper, D. I. Peretz, J. M. (Bill) Nelems, M. Schulzer, and J. C. Hogg. 1983. The structure and function of the pulmonary vasculature in mild chronic obstructive pulmonary disease. The effect of oxygen and exercise. Am. Rev. Respir. Dis. 128:702-07.

ACKNOWLEDGEMENTS

ALHUMDU-LILLAH-HI-RUBBIL-A-LAMEEN: All praise be to Allah; the lord of the universe.

I would like to thank my major professor, Dr. Richard L. Engen for his support, guidance, criticism, encouragement, and advice in completion of this thesis. These few words do not fully express the gratitude and admiration I feel.

My thanks to Dr. David L. Carlson, and Dr. Frederick B. Hembrough for serving in my committee.

Many thanks to Dr. Donald F. Young for his advice and extended financial support in order to continue this research.

One of the crucial parts of this research would have not been accomplished with out the kind, sincere, and friendly help from my fellow graduate student Mike Brune, my special thanks to him. Not to forget, my thanks to Dr. Ayaad Asaad for his invaluable help in running blood tests on dogs to check for heart worms. I appreciate the great help from Dr. Micheal Engwall on SAS computer for data analysis; thanks to him.

Deepest appreciation is extended to Pam Mc Allister for her surgical and technical assistance in setting up the experiment. Her expertise was of great help and benefit to me in this project.

My thanks to K. C. Hummel, and D. Johnson for their friendly technical assistance throughout this research. Dr. Joan G. Hopper and her staff at Laboratory Animal Resources were always helpful in searching the best dog that I could use, thanks to them also.

And finally, I express my deepest and sincere appreciation to my wife. Without her tremendous amount of love, patience, support, understanding, and dedication this research would have been very difficult to complete. Much love to my little five month old son Taysir, and many thanks to my parents to whom I dedicate this research for their prayers and indispensable love for me.

ASSALA MU ALAIKUM WA RAHIMA TUL LAHI WA BARA KATA HOO.

APPENDIX

Table A1. Mean values of respiratory parameters by treatment and time for groups 2, 3, & 4

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 2	Treatment 21	Time 0				
RESPR[a] b/min	5	9.92	7.92	4.19	23.60	3.54
TIDVOL[b] liter	1	0.474	.	.474	0.474	.
MINVOL[c] l/min	1	3.557	.	3.557	3.557	.
Group 2	Treatment 22	Time 60				
RESPR	5	10.67	8.29	4.34	24.80	3.71
TIDVOL	5	0.420	0.101	0.260	0.522	45.15
MINVOL	5	3.834	1.675	2.089	6.443	749.23
GROUP 3	Treatment 31	Time 0				
RESPR	5	11.36	5.32	5.14	18.10	2.38
TIDVOL	5	0.397	0.101	0.272	0.529	44.9
MINVOL	5	4.259	1.727	2.389	6.590	772.15
GROUP 3	Treatment 32	Time 60				
RESPR	5	13.48	8.77	4.60	25.70	3.92
TIDVOL	5	0.389	0.119	0.250	0.546	53.42
MINVOL	5	4.800	2.769	2.234	8.758	1238.45
GROUP 4	Treatment 41	Time 0				
RESPR	7	14.45	6.37	5.96	24.90	2.41
TIDVOL	7	0.340	0.094	0.220	0.492	35.50
MINVOL	7	4.575	1.683	2.564	7.713	636.14
Group 4	Treatment 42	Time 60				
RESPR	7	14.65	5.08	5.30	21.90	1.93
TIDVOL	7	0.351	0.105	0.247	0.566	39.66
MINVOL	7	4.785	1.230	3.000	6.442	465.06

[a] Respiratory rate.
[b] Tidal volume.
[c] Minute volume.

Table A2. Mean values of respiratory parameters for all treatment by time in group 5

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 5	Treatments AIR	Time 0 Minute				
RESPR[a] b/min	17	12.21	6.49	4.19	24.90	1.57
TIDVOL[b] liter	13	0.372	0.098	0.220	0.529	0.027
MINVOL[c] l/min	13	4.375	1.580	2.388	7.713	0.438
GROUP 5	Treatments OXY	Time 60				
RESPR	17	13.14	7.01	4.34	25.70	1.70
TIDVOL	17	0.383	0.105	0.247	0.566	0.026
MINVOL	17	4.510	1.841	2.089	8.758	0.446

[a] Respiratory rate.
[b] Tidal volume.
[c] Minute volume.

Table A3. Mean values of arterial blood gases by treatment in group 2

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 2	Treatment 21/22					
APH[a]	5	7.35/7.34	0.044/0.068	7.28/7.23	7.39/7.41	0.020/0.031
PPH[a]	5	7.35/7.35	0.077/0.086	7.24/7.21	7.45/7.44	0.035/0.038
JPH[a]	5	7.33/7.32	0.054/0.068	7.25/7.21	7.39/7.39	0.024/0.031
FPH[a]	5	7.34/7.32	0.055/0.066	7.25/7.21	7.39/7.38	0.024/0.029
ACO2[b] Torr	5	40.12/40.64	3.241/6.834	36.00/35.90	42.90/52.30	1.449/3.056
PCO2[b] Torr	5	43.28/42.72	10.288/10.657	26.20/26.40	52.30/55.60	4.600/4.766
JCO2[b] Torr	5	45.20/45.44	4.620/6.504	38.30/41.60	51.20/56.90	2.066/2.909
FCO2[b] Torr	5	44.98/46.16	3.782/5.666	37.90/41.80	52.50/55.70	2.478/2.534
AOXY[c] Torr	5	84.20/193.0	7.294/25.15	72.00/167.0	91.00/221.0	3.261/11.25
POXY[c] Torr	5	50.48/56.92	6.585/10.77	42.40/40.10	59.10/69.30	2.945/4.816
JOXY[c] Torr	5	57.74/68.62	6.217/8.493	48.80/55.10	65.10/76.20	2.781/3.800
FOXY[c] Torr	5	56.54/63.24	3.782/10.82	52.50/47.10	61.30/75.20	1.691/4.840
AS[d] PERCENT	5	95.60/100.0	2.074/0.000	92.00/100.0	97.00/100.0	0.927/0.000
PS[d] PERCENT	5	81.60/85.60	4.980/8.764	75.00/70.00	87.00/90.00	2.227/3.920
JS[d] PERCENT	5	86.60/91.40	5.225/2.881	80.00/87.00	91.00/94.00	2.337/1.288
FS[d] PERCENT	5	86.00/88.40	3.674/5.177	80.00/80.00	89.00/93.00	1.643/2.315

[a] Arterial, pulmonary artery, jugular and femoral blood pH.
[b] Arterial, pulmonary artery, jugular and femoral blood carbon-dioxide tensions.
[c] Arterial, pulmonary artery, jugular and femoral blood oxygen tensions.
[d] Arterial, pulmonary artery, jugular and femoral blood hemoglobin oxygen saturations.

Table A4. Mean values of arterial blood gases by treatment in group 3

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 3	Treatment 31/32					
APH[a]	5	7.36/7.35	0.054/0.070	7.32/7.29	7.45/7.46	0.024/0.031
PPH[a]	5	7.34/7.33	0.049/0.075	7.29/7.25	7.42/7.44	0.022/0.034
JPH[a]	5	7.35/7.33	0.039/0.070	7.31/7.26	7.41/7.44	0.017/0.031
FPH[a]	5	7.34/7.32	0.045/0.078	7.30/7.25	7.41/7.44	0.020/0.035
ACO2[b] Torr	5	41.26/42.00	8.09/10.08	29.50/28.00	50.70/54.90	3.62/4.51
PCO2[b] Torr	5	45.82/48.54	9.45/10.71	32.60/33.50	58.60/60.20	4.23/4.79
JCO2[b] Torr	5	46.40/48.18	8.11/10.27	36.70/34.00	59.00/61.00	3.63/4.59
FCO2[b] Torr	5	47.10/49.36	7.40/11.16	37.90/34.40	57.40/61.40	3.31/5.00
AOXY[c] Torr	5	77.60/199.8	8.26/59.73	69.00/97.00	90.00/245.0	3.70/26.7
POXY[c] Torr	5	49.70/54.70	3.33/11.53	45.20/38.40	52.90/70.90	1.49/5.16
JOXY[c] Torr	5	55.46/64.50	7.00/15.31	47.40/43.40	65.40/82.10	3.11/6.85
FOXY[c] Torr	5	52.28/58.26	6.07/11.13	43.40/41.80	60.20/68.90	2.71/5.00
AS[d] PERCENT	5	94.8/99.6	1.30/0.89	93/98	96/100	0.58/0.40
PS[d] PERCENT	5	81.6/83.6	3.51/6.66	76/74	85/91	1.57/2.98
JS[d] PERCENT	5	85.6/88.8	3.58/5.45	82/81	91/95	1.60/2.44
FS[d] PERCENT	5	83.0/85.8	3.94/6.22	79/79	89/91	1.76/2.78

[a] Arterial, pulmonary artery, jugular and femoral blood pH.
[b] Arterial, pulmonary artery, jugular and femoral blood carbon-dioxide tensions.
[c] Arterial, pulmonary artery, jugular and femoral blood oxygen tensions.
[d] Arterial, pulmonary artery, jugular and femoral blood hemoglobin oxygen saturations.

Table A5. Mean values of arterial blood gases by treatment in group 4

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 4	Treatment 41/42					
APH[a]	5	7.40/7.41	0.053/0.078	7.33/7.29	7.48/7.49	0.020/0.029
PPH[a]	5	7.38/7.36	0.048/0.069	7.33/7.26	7.46/7.43	0.018/0.026
JPH[a]	5	7.39/7.37	0.041/0.061	7.34/7.26	7.45/7.43	0.015/0.023
FPH[a]	5	7.38/7.36	0.048/0.061	7.33/7.27	7.45/7.44	0.018/0.023
ACO2[b] Torr	5	35.4/34.3	5.92/8.18	26.5/26.1	42.7/49.2	2.24/3.09
PCO2[b] Torr	5	40.2/41.0	5.74/8.44	30.2/31.2	47.6/54.3	2.17/3.19
JCO2[b] Torr	5	39.7/40.4	5.44/8.16	31.5/31.8	46.3/56.2	2.05/3.08
FCO2[b] Torr	5	39.2/41.3	5.19/7.69	32.0/32.0	45.9/54.6	1.96/2.91
AOXY[c] Torr	5	89.9/438.1	5.55/76.1	82.0/274.0	97.0/511.0	2.10/28.7
POXY[c] Torr	5	51.2/58.0	6.17/6.08	45.2/51.3	61.6/68.5	2.33/2.30
JOXY[c] Torr	5	58.4/70.3	12.3/11.6	45.6/56.1	80.7/88.1	4.63/4.37
FOXY[c] Torr	5	57.5/66.7	8.01/12.3	46.0/49.5	69.8/85.3	3.03/4.65
AS[d] PERCENT	5	96.7/100.0	0.49/0.00	96/100	97/100	0.18/0.00
PS[d] PERCENT	5	83.7/87.9	4.46/2.67	76/84	90/92	1.69/1.01
JS[d] PERCENT	5	87.7/92.6	6.18/2.88	77/89	96/96	2.34/1.09
FS[d] PERCENT	5	88.4/91.6	3.15/3.10	83/87	93/96	1.19/1.17

[a]Arterial, pulmonary, jugular and femoral blood pH.
[b]Arterial, pulmonary, jugular and femoral blood carbon-dioxide tensions.
[c]Arterial, pulmonary, jugular and femoral blood oxygen tensions.
[d]Arterial, pulmonary, jugular and femoral blood hemoglobin oxygen saturations.

Table A6. Mean values of arterial blood gases for all treatments in group 5

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN
GROUP 5	Treatment AIR/OXY					
APH[a]	5	7.38/7.37	0.054/0.076	7.28/7.23	7.48/7.49	0.013/0.018
PPH[a]	5	7.36/7.34	0.057/0.072	7.24/7.21	7.46/7.44	0.014/0.018
JPH[a]	5	7.36/7.34	0.050/0.065	7.25/7.21	7.45/7.44	0.012/0.016
FPH[a]	5	7.36/7.34	0.051/0.067	7.25/7.21	7.45/7.44	0.012/0.016
ACO2[b] Torr	5	38.5/38.4	6.29/8.66	26.5/26.1	50.7/54.9	1.53/2.10
PCO2[b] Torr	5	42.8/43.7	8.19/9.73	26.2/26.4	58.6/60.2	2.00/2.36
JCO2[b] Torr	5	43.3/44.2	6.54/8.59	31.5/31.8	59.0/61.0	1.59/2.08
FCO2[b] Torr	5	43.2/45.1	6.64/8.58	32.0/32.0	57.4/61.4	1.61/2.08
AOXY[c] Torr	5	84.6/296	8.33/135	69.0/97.0	97.0/511	2.02/32.8
POXY[c] Torr	5	50.5/56.7	5.32/8.84	42.4/38.4	61.6/70.9	1.29/2.14
JOXY[c] Torr	5	57.3/68.1	8.93/11.5	45.6/43.4	80.7/88.1	2.17/2.80
FOXY[c] Torr	5	55.8/63.2	6.52/11.4	43.4/41.8	69.8/85.3	1.58/2.76
AS[d] PERCENT	5	95.8/99.9	1.51/0.49	92/98	97/100	0.37/0.12
PS[d] PERCENT	5	82.5/85.9	4.23/6.03	75/70	90/92	1.02/1.46
JS[d] PERCENT	5	86.8/91.1	5.02/3.90	77/81	96/96	1.22/0.95
FS[d] PERCENT	5	86.1/88.9	4.04/5.12	79/79	93/96	0.98/1.24

[a] Arterial, pulmonary artery, jugular and femoral blood pH.
[b] Arterial, pulmonary artery, jugular and femoral blood carbon-dioxide tensions.
[c] Arterial, pulmonary artery, jugular and femoral blood oxygen tensions.
[d] Arterial, pulmonary artery, jugular and femoral blood hemoglobin oxygen saturations.

Table A7. Mean values of blood oxygen contents by treatment in all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREATMENT
GROUP 2						
ACONT[a] Vol%	5	16.59/17.68	0.66/0.69	15.60/16.45	17.17/18.08	21/22
PCONT[a] Vol%	5	14.09/14.79	0.86/1.51	13.19/12.31	15.33/15.86	"
JCONT[a] Vol%	5	14.97/15.83	0.85/0.62	14.08/15.07	16.05/16.60	"
FCONT[a] Vol%	5	14.86/15.29	0.67/0.84	14.10/14.08	15.51/16.08	"
GROUP 3						
ACONT	5	17.38/18.61	1.44/1.58	15.09/16.43	19.03/20.87	31/32
PCONT	5	14.93/15.32	1.68/2.21	12.16/12.81	16.74/18.63	"
JCONT	5	15.66/16.23	1.63/1.82	13.61/14.43	17.78/18.84	"
FCONT	5	15.18/15.73	1.59/2.15	12.80/12.65	16.96/18.42	"
GROUP 4						
ACONT	5	16.98/18.60	1.38/1.49	15.50/17.21	19.56/21.52	41/42
PCONT	5	14.65/15.35	1.77/1.16	13.16/14.15	17.66/17.06	"
JCONT	5	15.34/16.20	1.83/1.25	13.45/15.14	18.28/18.29	"
FCONT	5	15.48/16.03	1.67/1.47	13.98/14.48	18.49/18.30	"
GROUP 5						
ACONT	17	16.98/18.33	1.20/1.33	15.09/16.43	19.56/21.52	AIR/OXY
PCONT	17	14.57/15.18	1.48/1.54	12.16/12.31	17.66/18.63	"
JCONT	17	15.33/16.10	1.48/1.24	13.45/14.43	18.28/18.84	"
FCONT	17	15.21/15.72	1.37/1.50	12.80/12.65	18.49/18.42	"

[a] Arterial, pulmonary artery, jugular and femoral veins blood oxygen contents.

Table A8. Mean values of blood oxygen extractions by treatment in all groups.

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREATMENT
GROUP 2						
PAVDO[a] Vol%	5	2.50/2.88	0.89/1.53	1.64/2.05	3.98/5.61	21/22
JAVDO[a] Vol%	5	1.63/1.85	0.79/0.48	0.93/1.38	2.90/2.60	"
FAVDO[a] Vol%	5	1.73/2.39	0.34/0.91	1.35/1.54	2.15/3.84	"
GROUP 3						
PAVDO	5	2.44/3.29	0.36/0.90	2.03/2.24	2.93/4.65	31/32
JAVDO	5	1.78/2.36	0.68/0.81	0.98/1.37	2.57/3.33	"
FAVDO	5	2.20/2.88	0.61/0.80	1.36/2.14	3.06/3.78	"
GROUP 4						
PAVDO	5	2.33/3.25	0.69/0.61	1.37/2.60	3.58/4.46	41/42
JAVDO	5	1.64/2.40	1.05/0.53	0.23/1.81	3.40/3.22	"
FAVDO	5	1.51/2.57	0.55/0.50	0.81/1.82	2.56/3.22	"
GROUP 5						
PAVDO	17	2.42/3.16	0.64/0.98	1.37/2.05	3.98/5.61	AIR/OXY
JAVDO	17	1.66/2.23	0.83/0.62	0.23/1.37	3.40/3.33	"
FAVDO	17	1.78/2.61	0.57/0.71	0.81/1.55	3.06/3.84	"

[a]Arterial to pulmonary artery, jugular and femoral veins blood oxygen extractions.

Table A9. Mean values of vascular pressures by treatment and time in groups 2 & 3

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUPS 2/3							
PULAP[a] Torr	2/4	8.34/10.60	1.68/2.62	7.15/7.15	9.53/12.85	21/31	00
SYSAP[b] Torr	5/5	100.5/121.0	16.6/9.12	80/108	115/133	21/31	00
PULAP	1/5	9.53/9.05	0.00/2.67	9.53/6.20	9.53/12.38	22/32	15
SYSAP	5/5	100.5/124.0	14.8/13.5	85/113	115/148	"	15
PULAP	1/5	9.05/9.48	0.00/3.54	9.05/6.20	9.05/14.75	"	30
SYSAP	5/5	107.0/126.5	16.1/13.9	88/115	125/150	"	30
PULAP	1/5	8.10/10.05	0.00/2.87	8.10/6.44	8.10/14.28	"	45
SYSAP	5/5	114.0/130.0	11.8/11.6	100/123	130/150	"	45
PULAP	1/5	7.63/10.48	0.00/3.49	7.63/6.20	7.63/6.20	"	60
SYSAP	5/5	116.0/133	14.7/12.5	100/125	130/155	"	60

[a] Pulmonary artery pressure.
[b] Systemic arterial pressure.

Table A10. Mean values of vascular pressures by treatment and time in groups 4 & 5

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUPS 4/5							
PULAP[a] Torr	3/9	8.26/9.32	0.72/2.13	7.63/7.15	9.05/12.85	41/AIR	00
SYSAP[b] Torr	7/17	117/113	10.84 14.50	100/80	128/133	41/AIR	00
PULAP	3/9	8.58/8.95	0.48/1.93	8.10/6.20	9.05/12.38	42/OXY	15
SYSAP	7/17	118/115	14.79/15.86	90/85	140/148	"	15
PULAP	3/9	8.42/9.08	0.72/2.58	7.63/6.20	9.05/14/75	"	30
SYSAP	7/17	120/118	14.68/16.03	95/88	145/150	"	30
PULAP	3/9	8.74/9.40	0.99/2.24	7.63/6.44	9.53/14.28	"	45
SYSAP	7/17	122/122	14.39/13.64	105/100	150/150	"	45
PULAP	3/9	8.74/9.58	0.99/2.75	7.63/6.20	9.53/15.7	"	60
SYSAP	6/16	123/124	15.97/15.30	105/100	150/155	"	60

[a] Pulmonary artery pressure.
[b] Systemic arterial pressure.

Table A11. Mean values of cardiac output by treatment and time in all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUP 2							
TOTLCO[a] l/min	5	2.23	0.349	1.69	2.63	21	00
"	"	2.20	0.208	2.02	2.52	22	30
"	"	2.09	0.292	1.83	2.56	22	60
GROUP 3							
TOTLCO	5	2.45	0.568	1.63	3.08	31	00
"	"	2.15	0.622	1.29	3.04	32	30
"	"	1.86	0.440	1.23	2.49	32	60
GROUP 4							
TOTLCO	6	2.43	0.799	1.58	3.60	41	00
"	"	1.92	0.574	1.31	2.75	42	30
"	"	1.72	0.588	1.05	2.63	42	60
GROUP 5							
TOTLCO	16	2.37	0.584	1.58	3.60	R.AIR	00
"	"	2.08	0.490	1.29	3.04	OXY	30
"	"	1.88	0.464	1.05	2.63	OXY	60

[a] Total cardiac output.

Table A12. Mean values of carotid and femoral arteries blood flows (ml/min) by treatment and time in groups 2&3

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUPS 2/3							
CARABF [a]	5/5	131/184	22.4/35.2	99/144	160/233	21/31	00
"	"	129/160	24.3/35.1	93/118	154/207	22/32	10
"	"	121/160	28.4/41.0	87/106	160/207	"	20
"	"	117/152	37.2/37.2	68/106	170/200	"	30
"	"	115/149	41.4/38.7	68/93	181/195	"	40
"	"	117/139	41.0/39.3	68/80	181/176	"	50
"	"	112/147	39.0/25.8	61/110	170/169	"	60
FEMABF [b]	5/5	105/75	47.9/23.9	49/49	161/105	21/31	00
"	"	90/67	32.2/13.1	60/49	138/83	22/32	10
"	"	86/71	39.3/14.6	49/49	150/85	"	20
"	"	79/66	44.2/14.5	38/49	150/85	"	30
"	"	79/68	43.9/15.7	43/49	150/85	"	40
"	"	82/57	42.1/22.3	43/26	150/85	"	50
"	"	75/63	41.3/15.7	38/49	138/80	"	60

[a] Carotid artery blood flow.
[b] Femoral artery blood flow.

Table A13. Mean values of carotid and femoral arteries blood flows (ml/min) by treatment and time in groups 4 & 5

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUPS 4/5							
CARABF[a]	7/17	159/158	46.9/41.3	110/99	245/245	41/AIR	00
"	"	138/142	46.4/37.8	89/89	220/220	42/OXY	10
"	"	134/138	45.5/40.6	89/87	220/220	"	20
"	"	126/131	45.9/41.1	83/68	220/220	"	30
"	"	128/130	47.4/42.8	83/68	226/226	"	40
"	"	123/126	50.3/42.9	72/68	226/226	"	50
"	7/16	120/125	49.4/41.4	72/61	220/220	"	60
FEMABF[b]	7/17	90/90	26.9/33.6	54/49	116/161	41/AIR	00
"	"	74/77	19.5/23.1	49/49	100/138	42/OXY	10
"	"	66/73	22.9/26.7	35/35	100/150	"	20
"	"	62/68	19.1/27.1	35/35	88/150	"	30
"	"	58/67	21.8/42.8	35/35	89/150	"	40
"	"	55/64	22.2/42.9	25/25	83/150	"	50
"	7/16	54/63	25.5/29.2	20/20	89/138	"	60

[a] Carotid artery blood flow.
[b] Femoral artery blood flow.

Table A14. Mean values of oxygen delivery (ml/min) by treatment in all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREATMENT
GROUP 2						
OXYDEL[a]	5	368.2	48.5	286.5	410.7	21
OXYDEL	5	388.8	46.6	331.7	454.0	22
GROUP 3						
OXYDEL	5	430.0	119.4	246.1	543.9	31
OXYDEL	5	407.3	150.4	211.3	634.6	32
GROUP 4						
OXYDEL	6	416.5	169.0	244.3	703.6	41
OXYDEL	6	360.5	136.9	226.2	591.0	42
GROUP 5						
OXYDEL	16	405.6	121.1	244.3	703.6	AIR
OXYDEL	16	384.0	115.2	211.3	634.6	OXY

[a] Oxygen delivery or oxygen transport.

Table A15. Mean values of pulmonary vascular resistance (dynes.s/cm^5) by treatment and time in all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUP 2							
PVR [a]	2	314.31	35.00	289.56	339.06	21	00
"	1	359.13	00.00	359.13	359.13	22	30
"	1	300.10	00.00	300.10	300.10	22	60
GROUP 3							
PVR	4	356.25	126.41	185.53	490.50	31	00
"	5	375.11	166.88	235.36	562.99	32	30
"	5	470.37	182.91	271.63	686.71	32	60
GROUP 4							
PVR	3	217.30	32.31	180.15	238.79	41	00
"	3	284.64	52.00	250.00	344.44	42	30
"	3	330.02	83.94	275.08	426.64	42	60
GROUP 5							
PVR	9	300.61	102.97	180.15	490.50	AIR	00
"	9	343.18	128.66	235.36	563.00	OXY	30
"	9	404.67	156.99	271.63	686.71	OXY	60

[a] Pulmonary vascular resistance.

Table A16. Mean values of systemic vascular resistance (dynes.s/cm^5) by treatment and time in all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREAT	TIME
GROUP 2							
SVR[a]	5	3713	1019	2740	5216	21	00
"	5	3924	750	3233	4785	22	30
"	5	4502	800	3711	5674	22	60
GROUP 3							
SVR	5	4161	1142	2789	5886	31	00
"	5	5047	1567	3354	7465	32	30
"	5	5997	1467	4178	8026	32	60
GROUP 4							
SVR	6	4189	1391	2335	6097	41	00
"	6	5471	1786	2768	7306	42	30
"	6	6312	2212	3192	9479	42	60
GROUP 5							
SVR	16	4032	1149	2335	6097	AIR	00
"	16	4855	1518	2768	7465	OXY	30
"	16	5648	1741	3191	9479	OXY	60

[a] Systemic vascular resistance.

Table A17. Mean values of total (general), cerebral, and hindlimb oxygen consumption (ml/min) by treatment for all groups

VARIABLE	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	TREATMENT
GROUP 2						
GENVO2 [a]	5	54.98/62.63	18.84/30.89	38.29/41.34	85.12/117.2	21/22
CARVO2 [b]	5	2.14/2.19	1.04/0.86	1.02/0.93	3.68/3.30	21/22
FEMVO2 [c]	5	1.80/1.82	0.77/0.89	0.66/0.58	2.39/3.04	21/22
GROUP 3						
GENVO2	5	58.37/68.37	8.36/20.36	47.78/46.56	70.30/101.8	31/32
CARVO2	5	3.18/3.65	1.50/1.87	1.78/2.11	5.35/6.69	31/32
FEMVO2	5	1.59/1.84	0.48/0.29	1.12/1.41	2.19/2.23	31/32
GROUP 4						
GENVO2	6	60.52/66.87	22.75/31.24	34.20/38.24	93.81/122.5	41/42
CARVO2	7	2.48/2.93	1.93/0.81	0.56/1.90	6.49/3.98	41/42
FEMVO2	7	1.29/1.54	0.38/0.40	0.71/1.00	1.77/2.11	41/42
GROUP 5						
GENVO2	16	58.12/66.02	17.07/26.38	34.20/38.24	93.81/122.5	AIR/OXY
CARVO2	17	2.59/2.92	1.55/1.28	0.56/0.93	6.49/6.69	AIR/OXY
FEMVO2	17	1.53/1.71	0.56/0.55	0.66/0.58	2.39/3.04	AIR/OXY

[a] Oxygen consumption, total.
[b] Oxygen consumption, cerebral.
[c] Oxygen consumption, hindlimb.