# THE EVALUATION OF THE ARP-VARNUM RESPIRATOR AS AN ANETHESIA VENTILATOR WHILE DELIVERING THREE PERCENT HALOTHANE AND AIR MIXTURE

by

Jon Heath Betts

Thesis Submitted to the Graduate Faculty of the

Virginia Polytechnic Institute

in candidacy for the degree of

MASTER OF SCIENCE

in

INDUSTRIAL ENGINEERING

APPROVED: ______________________

Chairman, L. J. Arp

______________________

P. E. Torgersen

______________________

S. G. Gilbreath

June, 1967

Blacksburg, Virginia

# TABLE OF CONTENTS

# CHAPTER I

## INTRODUCTION[1]

"Respiratory distress syndrome (R.D.S.) also called hyaline membrance disease, and recently described as "The Pulmonary Hypoperfusion Syndrome" is responsible for the deaths of more newborn infants (neonates) than any other disease.

R.D.S. is characterized by pulmonary insufficiency which occurs most often in premature infants, infants of diabetic mothers, those born by cesarean section, and infants born of mothers who experienced intrauternia bleeding.

Clinically, the infants are often resuscitative problems at birth and soon develop the classic symptoms of R.D.S., labored breathing with a dramatic increase in rate from the normal 30 to 40 breaths per minute to as high as 100 to 120 breaths per minute. Inspiratory retractions of the sternum and rib cage and expiratory grunting are additional clinical manifestations of the severly distressed infant. Physical examination reveals harsh breath sounds, often with fine rales on deep inspiration. The general impression is that there is very poor air exchange. Progressive cyanosis and periods of apnea usually indicate impending death. The cause of respiratory distress is unknown.

---

[1] Unpublished, Copyrighted, Doctoral Dissertation, L. J. Arp, Iowa State University, 1966. By permission of the Author.

It is known that the compliance of the lung is drastically reduced by the hyaline-like membrane which sometimes covers the alveoli. This membrane causes atelectasis of many of the alveloli, thus reducing, and in some instances, preventing normal gaseous exchange with the blood.

The decrease in the number of alveoli actively involved in gaseous exchange with the blood, as well as the decrease of active surface area of the partially functioning alveoli, causes an increase in the carbon dioxide content of the blood and a decrease in pH. The reduced compliance and associated atelectasis may increase the amount of pulmonary work required to maintain a normal gas flow in and out of the lungs by as much as 400 per cent (1).

# CHAPTER II

## EXPERIMENTAL METHOD

The Experimental Method involves two considerations. The Procedure will be discussed first followed by the Characteristics of the Respirator.

### Procedure

A respirator is needed to assume the work load required of the infants. The respirator, triggered by the infant, should maintain proper $P_aCO_2$, $P_aO_2$ and pH levels in the blood of the infant.

Therefore, the purpose of this thesis will be to evaluate the Arp-Varnum Respirator's ability to ventilate and oxygenate a patient adequately while delivering an air oxygen mixture and while delivering three percent Halothane with an air oxygen mixture to induce deep surgical anesthesia.

In order to prove that this respirator is an adequate ventilator and oxygenator, three blood samples were taken from each of seven test subjects. Rabbits were used in this experiment because they very closely approximate the breathing patterns of new babies with Respiratory Distress Syndrome. Partial pressure of $CO_2$ and $O_2$, and the pH, under normal living conditions (Spontaneous Respiration) were determined using Instrumentation Laboratory Ultra-Micro pH and Blood Gas Analyzing System Model 113-S1 (Figure 1). The rabbits were then placed on the Arp-Varnum Infant Respirator for three separate two hour intervals (Figure 2). At the end

Figure 1. Blood Gas Analyzing System

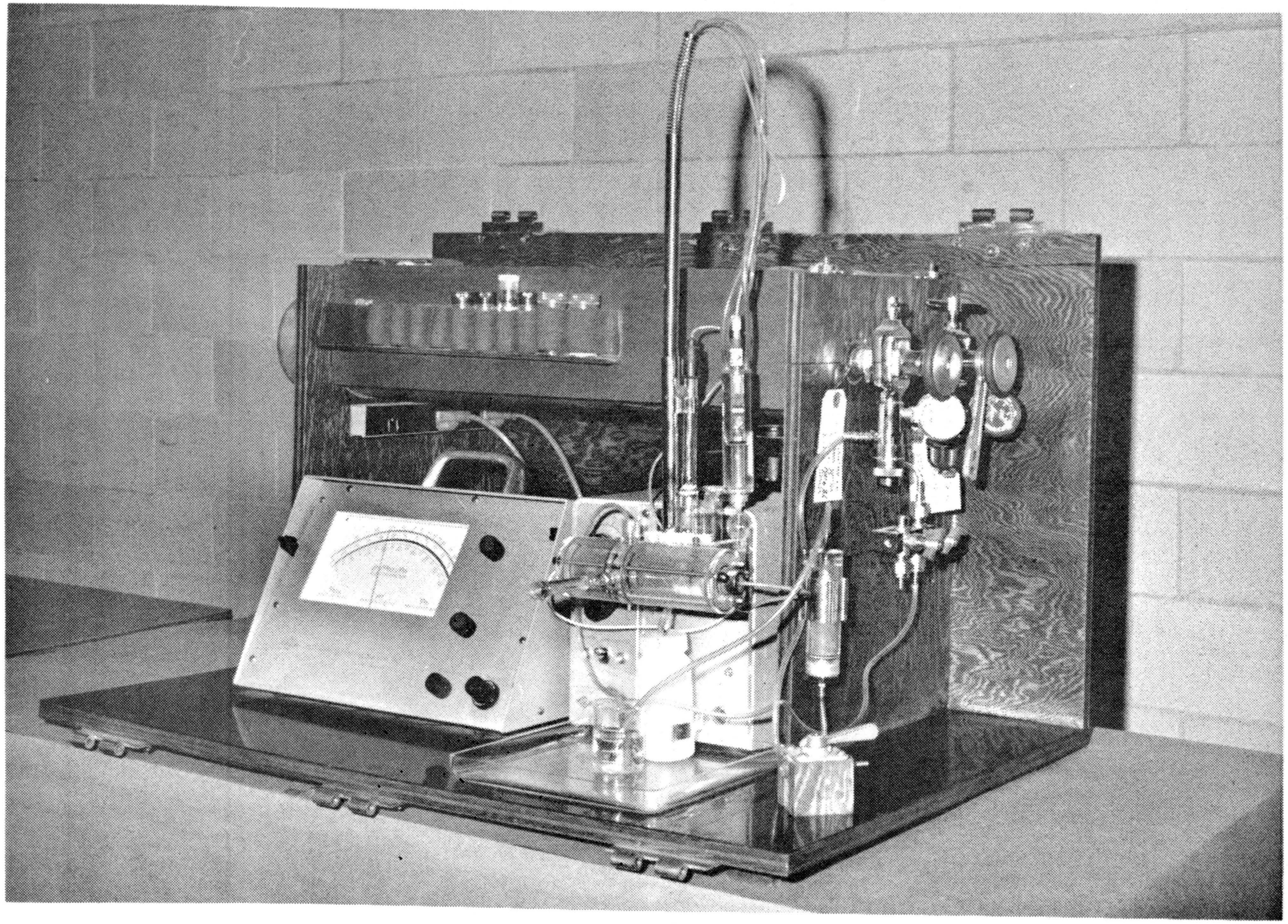
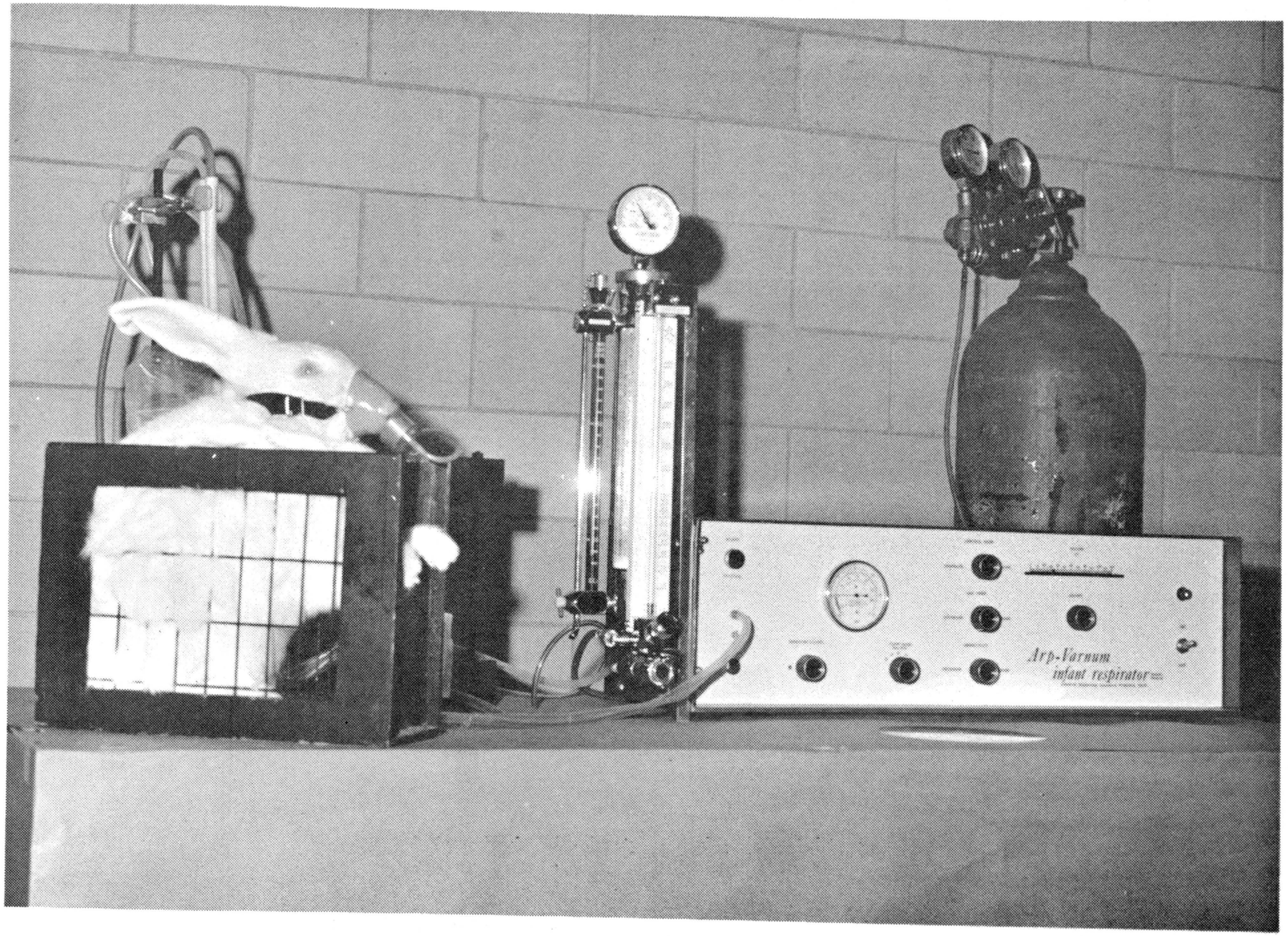


Figure 2. Rabbit on Assisted Respiration


Arp-Varnum
infant respirator

of each two hour interval an arterial blood sample was taken to measure the partial pressure of $CO_2$ and $O_2$, and the pH of the blood.

After these measurements were completed further testing was carried out using Halothane (Fluothane).[2] The rabbits were placed on the respirator for three two hour intervals (Figure 3). At the end of each two hour interval an arterial blood sample was taken to measure the partial pressure of $CO_2$ and $O_2$, and pH of the blood.

The Fluothane was vaporized using a "Side-Arm" Verni-Trol Vaporizer.[3]

---

[2]Fluothane, was donated to us for this research by the Veterinary Medical Division, Ayerst Laboratories, Inc., 685 3rd Avenue, New York, N.Y. 10017.

[3]The "Side-Arm" Vaporizer was donated to us for this research by Ohio Chemical and Surgical Equipment Co., 1400 E. Washington Ave., Madison, Wisconsin.

Figure 3. Rabbit on Assisted Respiration With Halothane


Arp-Varnum
infant respirator

## Characteristics of Respirator

"The performance characteristics built into the Arp-Varnum Respiratory are:

1. A system that can accurately and reliably sense the onset of inspiration.

2. The ability to provide controlled respiration should the patient become apneic.

3. The ability to deliver a predetermined volume to the patient at a constant average flow rate adjustable from 0 to 20 liters per minute.

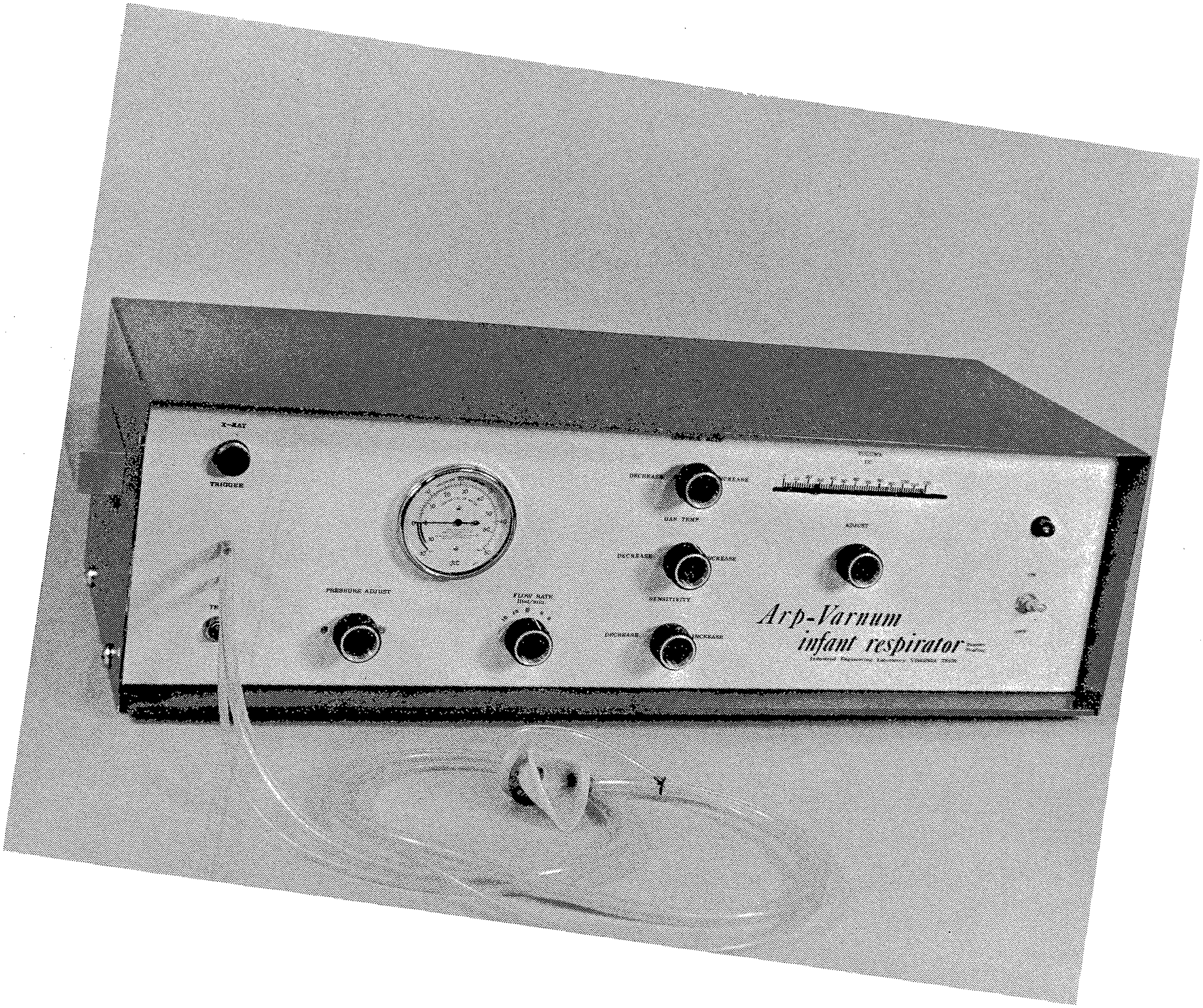
4. A satisfactory method of delivering the output of the respirator to the patient (in our case a rabbit) through a nasal mask.

The special nasal mask developed for this experiment was strapped on the face of the rabbit. Figure 4 shows the nasal mask used with the respirator described in this study.

The Arp-Varnum Respirator described in this study utilizes a negative pressure sensing switch, which has been designed to reliably trigger on a negative pressure of 0.5 mm. of $H_2O$. Artifact transient negative pressures of 12 cm. of $H_2O$ are rejected by this switch and do not cause false triggering of the respirator. However, if 0.1 $cm.^3$ of air is inhaled by the patient the required 0.5 mm. of $H_2O$ negative pressure is secured and the respirator is immediately switched on. Gas begins to flow to the patient not more than 20 ms. after onset of inspiration.

Controlled respiration may be supplied to the patient by the respirator simply by setting the controlling rate desired. Controlling

Figure 4. The Arp-Varnum Infant Respirator


X-RAY
TRIGGER
PRESSURE ADJUST
FLOW RATE
DECREASE
GAS TEMP.
SENSITIVITY
ADJUST
Arp-Varnum
infant respirator

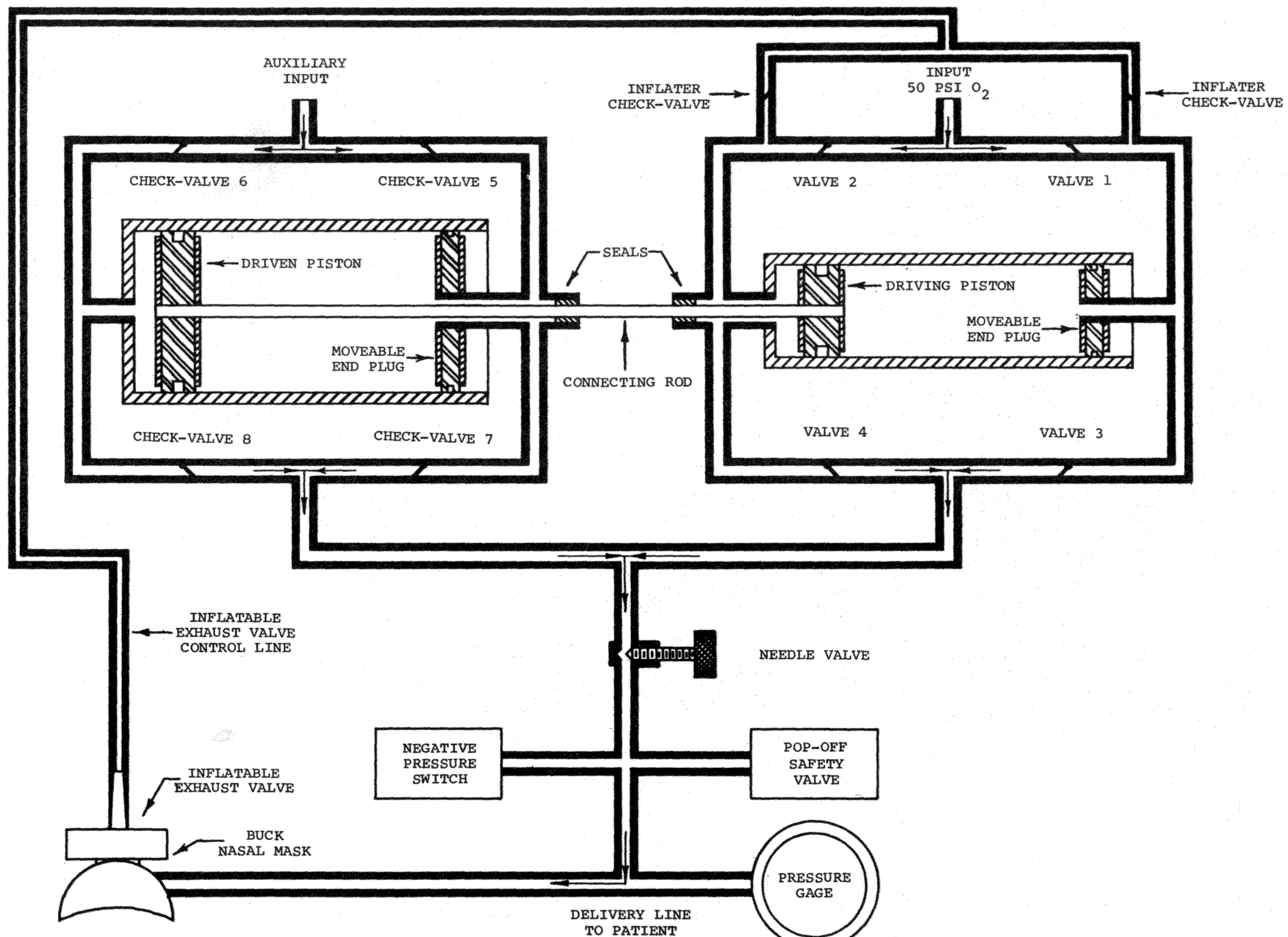
rates may vary from zero where the respirator is triggered by the patient's inspiratory efforts to 170 breaths per minute.

The Arp-Varnum Respirator described in this thesis will deliver an adjustable preset volume of gas (from 0 $cm.^3$ to 120 $cm.^3$) and mix any two gases to any concentration desired. Flow rates to the patient are continuously adjustable from 0 to 20 liters per minute.

The patient must pull a slight negative pressure (0.5 mm. of $H_2O$) at the beginning of the inspiratory phase in order to turn the respirator on. However, in order to eliminate the work being done by the infant during inspiration the pressure in the thorax and lungs must not be allowed to remain negative. Therefore, after the respirator is turned on, air flow must be great enough to keep the length of time that the thorax and lungs are at a negative pressure to a minimum. In general, gas flow to the infant should begin not later than 25 ms. after onset of inspiration. Since the thorax and lungs are at a negative pressure until the flow of gas has caught up with the demand it is imperative that the lag be made up as quickly as possible to maximize the assistance provided by the respirator.

The respirator is electronically controlled and pneumatically powered. Note that the pneumatic circuit (Figure 5) for the respirator is actually a bifurcation; the input side for delivery of gas from the respirator to the patient and the exhalation side. The inflatable exhaust valve at the end of the nasal mask, is normally closed. The respirator begins a delivery cycle with the patient tripping the negative pressure on the delivery line of 0.5 mm. of $H_2O$. For the sake of

Figure 5. Respirator Pneumatic Block Diagram


AUXILIARY INPUT
INPUT 50 PSI $O_2$
INFLATER CHECK-VALVE
INFLATER CHECK-VALVE
CHECK-VALVE 6
CHECK-VALVE 5
VALVE 2
VALVE 1
DRIVEN PISTON
SEALS
DRIVING PISTON
MOVEABLE END PLUG
MOVEABLE END PLUG
CONNECTING ROD
CHECK-VALVE 8
CHECK-VALVE 7
VALVE 4
VALVE 3
INFLATABLE EXHAUST VALVE CONTROL LINE
NEEDLE VALVE
NEGATIVE PRESSURE SWITCH
POP-OFF SAFETY VALVE
INFLATABLE EXHAUST VALVE
BUCK NASAL MASK
PRESSURE GAGE
DELIVERY LINE TO PATIENT

illustration, assume the pistons in cylinders one and two are at the position shown in Figure 5 at the beginning of the inspiratory cycle. Each time the respirator is tripped on, a control line delivers high pressure (30 to 50 cm. of $H_2O$) gas to the inflatable exhaust valve located at the end of the nasal mask to make sure that the gas to be delivered to the patient by the respirator does not escape from the exhaust part. At the end of the delivery stroke the exhaust valve control line is quickly dropped to atmospheric pressure; therefore, the pressure in the delivery line to the patient pops the exhaust valve open so that the patient may freely exhale from the open exhaust part. This sequence positively eliminates any chance of the inflatable valve sticking shut and impeding expiration. The tripping of the negative pressure switch energizes and opens valves two and three. Driving gas, usually $O_2$ at a pressure of 50 psi., flows into the left end of the driving cylinder one forcing the piston to move from left to right. The driving piston is attached to the driven piston contained in cylinder two by a connecting rod which passes through seals at the right end cylinder two and the left end of cylinder one. As the two pistons move from left to right the $O_2$ which moved the pistons from right to left during the previous delivery stroke and which still remains in cylinder one is forced out of cylinder one through the open valve three. At the same time the gas from the auxiliary input which was drawn into the right side of cylinder two through the one-way valve five during the previous delivery stroke is forced out through the one-way flow valve seven where it is mixed with the $O_2$ being expelled from cylinder one and delivered to the patient. As the piston in cylinder two moves from left to right, a new supply of gas for the next stroke is drawn into the left end of cylinder two through the one way valve six. Knowing the concentration of the driving gas and the gas supplied to the auxiliary input as well as the volumes of cylinders one and two make it possible to deliver a uniform and known concentration of gas to the patient regardless of the pressure variations which may occur in the delivery line. The volume of gas delivered to the patient is varied by moving end plugs in both cylinders to limit the distance the pistons may travel. Limit switches located in the end plugs of cylinder two sense the approach of the pistons near the end of travel. The limit switch at the right end of cylinder two de-energizes valves one and two. The limit switches are adjusted so as to start shut-down of the system before the pistons come to rest against the end plugs thus preventing a transient shock wave from reaching the patient. Inertia of the moving piston and accumulated driving gas in cylinder one causes the piston to continue to the end of travel. Complete closure of the valves coincides with the end of travel of the pistons, giving a smooth shut-down at the end of the delivery stroke. Upon shut-down valve one exhausts the left end of cylinder one to atmospheric pressure.

The next time the machine is tripped on, valves one and four are energized and opened thus causing the pistons to move from right to left. Gas from the auxiliary input is drawn into cylinder two through the one-way valve five and delivered to the patient through the one way valve eight. As in the previous cycle, gas from the two cylinders is again mixed and delivered to the patient. A limit switch located in the left end plug of cylinder two again shuts the system down near its end of travel. Delivery pressure is monitored on a gage on the front panel of the respirator. Maximum delivery pressure to the patient is selected by adjusting the safety pop-off valve also located on the front panel (1).

# CHAPTER III

# STATISTICAL ANALYSIS OF TEST DATA

Test Data

| Rabbit Number | Spontaneous Respiration | | | Assisted Respiration | | | Assisted Respiration With Halothane | | |
|---|---|---|---|---|---|---|---|---|---|
| | $P_aCO_2$ | $P_aO_2$ | pH | $P_aCO_2$ | $P_aO_2$ | pH | $P_aCO_2$ | $P_aO_2$ | pH |
| 84 | 27.4 | 62.4 | 7.461 | 27.1 | 73.3 | 7.475 | 30.0 | 83.8 | 7.412 |
| | 31.6 | 69.5 | 7.426 | 32.2 | 68.0 | 7.449 | 35.4 | 67.0 | 7.443 |
| | 30.1 | 66.5 | 7.463 | 31.8 | 68.8 | 7.443 | 33.7 | 62.0 | 7.431 |
| 86 | 24.3 | 71.5 | 7.453 | 29.2 | 67.5 | 7.433 | 37.2 | 60.5 | 7.420 |
| | 31.2 | 61.3 | 7.482 | 27.7 | 78.8 | 7.420 | 35.8 | 57.5 | 7.433 |
| | 27.2 | 71.0 | 7.483 | 31.6 | 63.5 | 7.434 | 30.7 | 62.0 | 7.449 |
| 87 | 31.8 | 61.8 | 7.497 | 31.1 | 62.5 | 7.421 | 35.1 | 81.4 | 7.464 |
| | 33.5 | 66.3 | 7.413 | 35.1 | 67.5 | 7.434 | 35.2 | 73.6 | 7.409 |
| | 31.9 | 68.5 | 7.416 | [illegible] | 67.4 | 7.435 | 36.8 | 72.8 | 7.446 |
| 94 | 31.7 | 65.7 | 7.487 | 27.3 | 72.3 | 7.439 | 30.5 | 70.3 | 7.437 |
| | 31.9 | 70.3 | 7.487 | 31.2 | 71.8 | 7.426 | 34.6 | 67.9 | 7.440 |
| | 28.8 | 63.0 | 7.493 | 30.0 | 69.9 | 7.449 | 31.7 | 83.3 | 7.434 |
| 117 | 32.9 | 67.3 | 7.493 | 35.4 | 71.0 | 7.414 | 32.8 | 69.5 | 7.432 |
| | 32.4 | 61.1 | 7.485 | 33.3 | 65.5 | 7.404 | 36.8 | 66.8 | 7.477 |
| | 31.5 | 63.4 | 7.481 | 30.7 | 79.0 | 7.376 | 36.3 | 73.1 | 7.470 |
| 123 | 32.4 | 59.8 | 7.463 | 33.1 | 69.3 | 7.468 | 32.0 | 60.8 | 7.436 |
| | 33.5 | 73.5 | 7.418 | 31.6 | 78.4 | 7.464 | 38.9 | 64.9 | 7.423 |
| | 30.5 | 70.9 | 7.462 | 30.3 | 72.1 | 7.476 | 32.8 | 54.8 | 7.443 |
| 127 | 29.9 | 73.3 | 7.435 | 34.4 | 69.0 | 7.433 | 36.0 | 62.8 | 7.418 |
| | 33.5 | 70.5 | 7.518 | 37.3 | 64.0 | 7.413 | 36.7 | 56.5 | 7.409 |
| | 29.2 | 71.5 | 7.491 | 34.0 | 68.3 | 7.437 | 39.8 | 65.4 | 7.415 |

All units are in mm. of Hg. except for pH which has no units.

Analysis of Variance

Analysis of Variance

| Factors | Abbreviation | Subscript | Levels | Type |
|---|---|---|---|---|
| Rabbits | H | i | 7 | R |
| Breathing Condition | B | j | 3 | F |
| Replication | R | k | 3 | R |

Breathing Conditions
Measuring $P_aCO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | Assisted Respiration With Halothane | Total |
|---|---|---|---|---|
| 84 | 27.4 | 27.1 | 30.0 | |
| | 31.6 | 32,2 | 35.4 | |
| | 30.1 | 31.8 | 33.7 | |
| | 89.1 | 91.1 | 99.1 | 279.3 |
| 86 | 24.3 | 29.2 | 37.2 | |
| | 31.2 | 27.7 | 35.8 | |
| | 27.2 | 31.6 | 30.7 | |
| | 82.7 | 88.5 | 103.7 | 274.9 |
| 87 | 31.8 | 31.1 | 35.1 | |
| | 33.5 | 35.1 | 35.2 | |
| | 31.9 | 35.9 | 36.8 | |
| | 97.2 | 102.1 | 107.1 | 306.4 |
| 94 | 31.7 | 27.3 | 30.5 | |
| | 31.9 | 31.2 | 34.6 | |
| | 28.8 | 30.0 | 31.7 | |
| | 92.4 | 88.5 | 96.8 | 277.7 |
| 117 | 32.9 | 35.4 | 32.8 | |
| | 32.4 | 33.3 | 36.8 | |
| | 31.5 | 30.7 | 36.3 | |
| | 96.8 | 99.4 | 105.9 | 302.1 |
| 123 | 32.4 | 33.1 | 32.0 | |
| | 33.5 | 31.6 | 38.9 | |
| | 30.5 | 30.3 | 32.8 | |
| | 96.4 | 95.0 | 103.7 | 295.1 |
| 127 | 29.9 | 34.4 | 36.0 | |
| | 33.5 | 37.3 | 36.7 | |
| | 29.2 | 34.0 | 39.8 | |
| | 92.6 | 105.7 | 112.5 | 310.8 |
| Total | 647.2 | 670.3 | 728.8 | 2046.3 |

All units are in mm. of Hg.

## $P_aCO_2$

### Analysis Of Variance

| Source | Sum of Squares | df | Mean Square Formula | Mean Square | F Test | Critical F | Conclusion |
|---|---|---|---|---|---|---|---|
| H | 147.762 | 6 | $\sigma_e^2 + 9\,\sigma_H^2$ | 24.627 | 1.76 | $F_{.05,6,42} = 2.32$ | Not Significant |
| B | 168.483 | 2 | $\sigma_e^2 + 3\,\sigma_{HB}^2 + 21\,\sigma_B^2$ | 84.242 | 6.00 | $F_{.05,3,42} = 2.83$ | Significant |
| HB | 53.826 | 12 | $\sigma_e^2 + 3\,\sigma_{HB}$ | 4.486 | 0.32 | $F_{.05,12,42} = 2.80$ | Not Significant |
| R(HB) | 589.298 | 42 | $\sigma_e^2$ | 14.031 | | | |

95 percent Confidence Interval On The Sample Means For Breathing Conditions

$$\bar{\bar{X}} \pm t_{0.025}\sqrt{\frac{S^2}{n}} = 32.500 \pm 2.019\sqrt{\frac{14.031}{21}}$$

$$= 32.500 \pm 2.019\ (.82)$$

$$= 32.500 \pm 1.650$$

30.850 $\bar{\bar{X}}$ 34.150

Spontaneous Respiration $\bar{X} = \frac{647.2}{21} = 30.82$

Assisted Respiration $\bar{X} = \frac{670.3}{21} = 31.92$

Assisted Respiration With Halothane $\bar{X} = \frac{728.8}{21} = 34.70$

Breathing Conditions
Measuring $P_aO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | Assisted Respiration With Halothane | Total |
|---|---|---|---|---|
| 84 | 62.4 | 73.3 | 83.8 | |
| | 69.5 | 68.0 | 67.0 | |
| | 66.5 | 68.8 | 62.0 | |
| | 198.4 | 210.1 | 212.8 | 621.3 |
| 86 | 71.5 | 67.5 | 60.5 | |
| | 61.3 | 78.8 | 57.5 | |
| | 71.0 | 63.5 | 62.0 | |
| | 203.8 | 209.8 | 180.0 | 593.6 |
| 87 | 61.8 | 62.5 | 81.4 | |
| | 66.3 | 67.5 | 73.6 | |
| | 68.5 | 67.4 | 72.8 | |
| | 196.6 | 197.4 | 227.8 | 621.8 |
| 94 | 65.7 | 72.3 | 70.3 | |
| | 70.3 | 71.8 | 67.9 | |
| | 63.0 | 69.9 | 83.3 | |
| | 199.0 | 214.0 | 221.5 | 634.5 |
| 117 | 67.3 | 71.0 | 69.5 | |
| | 61.1 | 65.5 | 66.8 | |
| | 63.4 | 79.0 | 73.1 | |
| | 191.8 | 215.5 | 209.4 | 616.7 |
| 123 | 59.8 | 69.3 | 60.8 | |
| | 73.5 | 78.4 | 64.9 | |
| | 70.9 | 72.1 | 54.8 | |
| | 204.2 | 219.8 | 180.5 | 604.5 |
| 127 | 73.3 | 69.0 | 62.8 | |
| | 70.5 | 64.0 | 56.5 | |
| | 71.5 | 68.3 | 65.4 | |
| | 215.3 | 201.3 | 184.7 | 601.3 |
| Total | 1409.1 | 1467.9 | 1416.7 | 4293.7 |

All units are in mm. of Hg.

## $P_aO_2$

### Analysis Of Variance

| Source | Sum of Squares | df | Mean Square Formula | Mean Square | F Test | Critical F | Conclusion |
|---|---|---|---|---|---|---|---|
| H | 134.08 | 6 | $\sigma_e^2 + 9\sigma_H^2$ | 22.35 | 0.407 | $F_{0.05,6,42} = 2.32$ | Not Significant |
| B | 97.41 | 2 | $\sigma_e^2 + 3\sigma_{HB}^2 + 21\sigma_B^2$ | 48.71 | 0.887 | $F_{0.05,3,42} = 2.83$ | Not Significant |
| HB | 924.14 | 12 | $\sigma_e^2 + 3\sigma_{HB}$ | 77.01 | 1.402 | $F_{0.05,12,42} = 2.80$ | Not Significant |
| R(HB) | 2306.62 | 42 | $\sigma_e^2$ | 54.92 | | | |

Breathing Conditions
Measuring pH

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | Assisted Respiration With Halothane | Total |
|---|---|---|---|---|
| 84 | 7.461 | 7.475 | 7.412 | |
| | 7.426 | 7.449 | 7.443 | |
| | 7.463 | 7.443 | 7.431 | |
| | 22.350 | 22.367 | 22.286 | 67.003 |
| 86 | 7.453 | 7.433 | 7.420 | |
| | 7.482 | 7.420 | 7.433 | |
| | 7.483 | 7.434 | 7.449 | |
| | 22.418 | 22.287 | 22.302 | 67.007 |
| 87 | 7.497 | 7.421 | 7.464 | |
| | 7.413 | 7.434 | 7.409 | |
| | 7.416 | 7.435 | 7.446 | |
| | 22.326 | 22.290 | 22.319 | 66.935 |
| 94 | 7.487 | 7.439 | 7.437 | |
| | 7.487 | 7.426 | 7.440 | |
| | 7.493 | 7.449 | 7.434 | |
| | 22.467 | 22.314 | 22.311 | 67.092 |
| 117 | 7.493 | 7.414 | 7.432 | |
| | 7.485 | 7.404 | 7.477 | |
| | 7.481 | 7.376 | 7.470 | |
| | 22.459 | 22.194 | 22.379 | 67.032 |
| 123 | 7.463 | 7.468 | 7.436 | |
| | 7.418 | 7.464 | 7.423 | |
| | 7.462 | 7.476 | 7.443 | |
| | 22.343 | 22.408 | 22.302 | 67.053 |
| 127 | 7.435 | 7.433 | 7.418 | |
| | 7.518 | 7.413 | 7.409 | |
| | 7.491 | 7.437 | 7.415 | |
| | 22.444 | 22.283 | 22.242 | 66.969 |
| Total | 156.807 | 156.143 | 156.141 | 469.091 |

## Analysis Of Variance

| Source | Sum of Squares | df | Mean Square Formula | Mean Square | F Test | Critical F | Conclusion |
|---|---|---|---|---|---|---|---|
| H | 0.0018 | 6 | $\sigma_e^2 + 9\sigma_H^2$ | 0.00030 | 0.2459 | $F_{.05,6,42} = 2.32$ | Not Significant |
| B | 0.0141 | 2 | $\sigma_e^2 + 3\sigma_{HB}^2 + 21\sigma_B^2$ | 0.00149 | 5.7780 | $F_{.05,3,42} = 2.83$ | Significant |
| HB | 0.0179 | 12 | $\sigma_e^2 + 3\sigma_{HB}$ | 0.00149 | 1.2210 | $F_{.05,12,42} = 2.80$ | Not Significant |
| R(HB) | 0.0511 | 42 | $\sigma_e^2$ | 0.00122 | | | |

95 percent Confidence Interval On The Sample Means For Breathing Conditions

$$\bar{\bar{X}} \pm t_{0.025}\sqrt{\frac{s^2}{n}} = 7.446 \pm 2.019\sqrt{\frac{0.00122}{21}}$$

$$= 7.446 \pm 2.019\ (0.007623)$$

$$= 7.446 \pm 0.015391$$

7.4306 $\bar{\bar{X}}$ 7.4614

Spontaneous Respiration $\bar{X} = \frac{156.807}{21} = 7.467$

Assisted Respiration $\bar{X} = \frac{156.143}{21} = 7.435$

Assisted Respiration With Halothane $\bar{X} = \frac{156.141}{21} = 7.435$

Student's $t$ Test

Breathing Conditions
Measuring $P_aCO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | d |
|---|---|---|---|
| 84 | 27.4 | 27.1 | -0.3 |
| | 31.6 | 32.2 | 0.6 |
| | 30.1 | 31.8 | 1.7 |
| 86 | 24.3 | 29.2 | 4.9 |
| | 31.2 | 27.7 | -3.5 |
| | 27.2 | 31.6 | 4.4 |
| 87 | 31.8 | 31.1 | -0.7 |
| | 33.5 | 35.1 | 1.6 |
| | 31.9 | 35.9 | 4.0 |
| 94 | 31.7 | 27.3 | -4.4 |
| | 31.9 | 31.2 | -0.7 |
| | 28.8 | 30.0 | 1.2 |
| 117 | 32.9 | 35.4 | 2.5 |
| | 32.4 | 33.3 | 0.9 |
| | 31.5 | 30.7 | -0.8 |
| 123 | 32.4 | 33.1 | 0.7 |
| | 33.5 | 31.6 | -1.9 |
| | 30.5 | 30.3 | -0.2 |
| 127 | 29.9 | 34.4 | 4.5 |
| | 33.5 | 37.3 | 3.8 |
| | 29.2 | 34.0 | 4.8 |

$\Sigma d = 23.1$ $\bar{d} = 1.100$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aCO_2$ levels for Spontaneous Respiration and Assisted Respiration.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{168.87 - \frac{533.61}{21}}{20}}$$

$$s_d = \sqrt{7.173}$$

$$s_d = 2.6783$$

$$t_c = \frac{1.1}{\frac{2.6783}{\sqrt{21}}}$$

$$t_c = 1.881$$

Critical Region for a significance level of 0.05 is

$$t \geq 2.080 \quad \text{or} \quad t < -2.080$$

Since $t_c$ fails to fall in the critical region, we fail to reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration when measuring $P_aCO_2$.

Breathing Conditions
Measuring $P_aCO_2$

| Rabbit Number | Assisted Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| 84 | 27.1 | 30.0 | 2.9 |
| | 32.2 | 35.4 | 3.2 |
| | 31.8 | 33.7 | 1.9 |
| 86 | 29.2 | 37.2 | 8.0 |
| | 27.2 | 35.8 | 8.6 |
| | 31.6 | 30.7 | -0.9 |
| 87 | 31.1 | 35.1 | 4.0 |
| | 35.1 | 35.2 | 0.1 |
| | 35.9 | 36.8 | 0.9 |
| 94 | 27.3 | 30.5 | 3.2 |
| | 31.2 | 34.6 | 3.4 |
| | 30.0 | 31.7 | 1.7 |
| 117 | 35.4 | 32.8 | -2.6 |
| | 33.3 | 36.8 | 3.5 |
| | 30.7 | 36.3 | 5.6 |
| 123 | 33.1 | 32.0 | -1.1 |
| | 31.6 | 38.9 | 7.3 |
| | 30.3 | 32.8 | 2.5 |
| 127 | 34.4 | 36.0 | 1.6 |
| | 37.3 | 36.7 | -0.6 |
| | 34.0 | 39.8 | 5.8 |

$\Sigma d = 59.0$ $\bar{d} = 2.8095$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aCO_2$ levels for Assisted Respiration and Assisted Respiration with Halothane.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{m}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom

$$s_d = \sqrt{\frac{350.22 - \frac{3481.00}{21}}{20}}$$

$$s_d = \sqrt{9.223}$$

$$s_d = 3.0369$$

$$t_c = \frac{2.8095}{\frac{3.0369}{\sqrt{21}}}$$

$$t_c = 4.2371$$

Critical Region for a significance level of 0.05 is

$$t > 2.080 \quad \text{or} \quad t < -2.080$$

Since $t_c$ falls into the critical region, we reject the null hypothesis that there is no difference between Assisted Respiration and Assisted Respiration with Halothane when measuring $P_aCO_2$.

Breathing Conditions
Measuring $P_aCO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| | 27.4 | 30.0 | 2.6 |
| 84 | 31.6 | 35.4 | 3.8 |
| | 30.1 | 33.7 | 3.6 |
| | 24.3 | 37.2 | 12.9 |
| 86 | 31.2 | 35.8 | 4.6 |
| | 27.2 | 30.7 | 3.5 |
| | 31.8 | 35.1 | 3.3 |
| 87 | 33.5 | 35.2 | 1.7 |
| | 31.9 | 36.8 | 4.9 |
| | 31.7 | 30.5 | -1.2 |
| 94 | 31.9 | 34.6 | 2.7 |
| | 28.8 | 31.7 | 2.9 |
| | 32.9 | 32.8 | -0.1 |
| 117 | 32.4 | 36.8 | 4.4 |
| | 31.5 | 36.3 | 4.8 |
| | 32.4 | 32.0 | -0.4 |
| 123 | 33.5 | 38.9 | 5.4 |
| | 30.5 | 32.8 | 2.3 |
| | 29.9 | 36.0 | 6.1 |
| 127 | 33.5 | 36.7 | 3.2 |
| | 29.2 | 39.8 | 10.6 |

$\Sigma d = 81.6 \qquad \bar{d} = 3.886$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aCO_2$ level for Spontaneous Respiration and Assisted Respiration with Halothane.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where
$$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n-1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{525.74 - \frac{6658.56}{21}}{20}}$$

$$s_d = \sqrt{10.434}$$

$$s_d = 3.23$$

$$t_c = \frac{3.886}{\frac{3.23}{\sqrt{21}}}$$

$$t_c = 5.5102$$

Critical Region for a significance level of 0.05 is

$$t > 2.080 \quad \text{or} \quad t < -2.080$$

Since $t_c$ falls into the critical region, we reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration With Halothane when measuring $P_aCO_2$.

Breathing Conditions
Measuring $P_aO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | d |
|---|---|---|---|
| 84 | 62.4 | 73.3 | 10.9 |
| | 69.5 | 68.0 | -1.5 |
| | 66.5 | 68.8 | 2.3 |
| 86 | 71.5 | 67.5 | -4.0 |
| | 61.3 | 78.8 | 17.5 |
| | 71.0 | 63.5 | -7.5 |
| 87 | 61.8 | 62.5 | 0.7 |
| | 66.3 | 67.5 | 1.2 |
| | 68.5 | 67.4 | -1.1 |
| 94 | 65.7 | 72.3 | 6.6 |
| | 70.3 | 71.8 | 1.5 |
| | 63.0 | 69.9 | 6.9 |
| 117 | 67.3 | 71.0 | 3.7 |
| | 61.1 | 65.5 | 4.4 |
| | 63.4 | 79.0 | 15.6 |
| 123 | 59.8 | 69.3 | 9.5 |
| | 73.5 | 78.4 | 4.9 |
| | 70.9 | 72.1 | 1.2 |
| 127 | 73.3 | 69.0 | -4.3 |
| | 70.5 | 64.0 | -6.5 |
| | 71.5 | 68.3 | -3.2 |

$\Sigma d = 58.8$ $\qquad \bar{d} = 2.800$

Student's t Test

$H_o$ : $\delta = 0$

$H_a$ : $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aO_2$ levels for Spontaneous Respiration and Assisted Respiration.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{1064.50 - \frac{3457.44}{21}}{20}}$$

$$s_d = \sqrt{44.993}$$

$$s_d = 6.7077$$

$$t_c = \frac{2.800}{\frac{6.707}{\sqrt{21}}}$$

$$t_c = 1.9141$$

Critical Region for a significance level of 0.05 is

$t > 2.080$ or $t < -2.080$

Since $t_c$ fails to fall in the critical region, we fail to reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration when measuring $P_aO_2$.

Breathing Conditions
Measuring $P_aO_2$

| Rabbit Number | Assisted Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| | 73.3 | 83.8 | 10.5 |
| 84 | 68.0 | 67.0 | -1.0 |
| | 68.8 | 62.0 | -6.8 |
| | 67.5 | 60.5 | -7.0 |
| 86 | 78.8 | 57.5 | -21.3 |
| | 63.5 | 62.0 | -1.5 |
| | 62.5 | 81.4 | 18.9 |
| 87 | 67.5 | 73.6 | 6.1 |
| | 67.4 | 72.8 | 5.4 |
| | 72.3 | 70.3 | -2.0 |
| 94 | 71.8 | 67.9 | -3.9 |
| | 69.9 | 83.3 | 23.4 |
| | 71.0 | 69.5 | -1.5 |
| 117 | 65.5 | 66.8 | 1.3 |
| | 79.0 | 73.1 | -5.9 |
| | 69.3 | 60.8 | -8.5 |
| 123 | 78.4 | 64.9 | -13.5 |
| | 72.1 | 54.8 | -17.3 |
| | 69.0 | 62.8 | -6.2 |
| 127 | 64.0 | 56.5 | -7.5 |
| | 68.3 | 65.4 | -2.9 |

$\Sigma d = -41.2$ $\bar{d} = -1.9619$

## Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aO_2$ levels for Assisted Respiration and Assisted Respiration with Halothane.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{2348.42 - \frac{1697.44}{21}}{20}}$$

$$s_d = \sqrt{113.3795}$$

$$s_d = 10.6480$$

$$t_c = \frac{-1.9619}{\frac{10.648}{\sqrt{21}}}$$

$$t_c = -0.84387$$

Critical Region for a significance level of 0.05 is

$$t > 2.080 \quad \text{or} \quad t < -2.080$$

Since $t_c$ fails to fall in the critical region, we fail to reject the null hypothesis that there is no difference between Assisted Respiration and Assisted Respiration With Halothane when measuring $P_aO_2$.

Breathing Conditions
Measuring $P_aO_2$

| Rabbit Number | Spontaneous Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| 84 | 62.4 | 83.8 | 21.4 |
| | 69.5 | 67.0 | -2.5 |
| | 66.5 | 62.0 | -4.5 |
| 86 | 71.5 | 60.5 | -11.0 |
| | 61.3 | 57.5 | -3.8 |
| | 71.0 | 62.0 | -9.0 |
| 87 | 61.8 | 81.4 | 19.6 |
| | 66.3 | 73.6 | 7.3 |
| | 68.5 | 72.8 | 4.3 |
| 94 | 65.7 | 70.3 | 4.6 |
| | 70.3 | 67.9 | -2.4 |
| | 63.0 | 83.3 | 20.3 |
| 117 | 67.3 | 69.5 | 2.2 |
| | 61.1 | 66.8 | 5.7 |
| | 63.4 | 73.1 | 9.7 |
| 123 | 59.8 | 60.8 | 1.0 |
| | 73.5 | 64.9 | -8.6 |
| | 70.9 | 54.8 | -16.1 |
| 127 | 73.3 | 62.8 | -10.5 |
| | 70.5 | 56.5 | -14.0 |
| | 71.5 | 65.4 | -6.1 |

$\Sigma d = 7.6$ $\quad \bar{d} = 0.3619$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the $P_aO_2$ levels for Spontaneous Respiration and Assisted Respiration With Halothane.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{2404.90 - \frac{57.76}{21}}{20}}$$

$$s_d = \sqrt{120.108}$$

$$s_d = 10.9594$$

$$t_c = \frac{0.3619}{\frac{10.9594}{\sqrt{21}}}$$

$$t_c = 0.15124$$

Critical Region for a significance level of 0.05 is

$t > 2.080$ or $t < -2.080$

Since $t_c$ fails to fall in the critical region, we fail to reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration With Halothane when measuring $p_aO_2$.

Breathing Conditions
Measuring pH

| Rabbit Number | Spontaneous Respiration | Assisted Respiration | d |
|---|---|---|---|
| 84 | 7.461 | 7.475 | 0.014 |
| | 7.426 | 7.449 | 0.023 |
| | 7.463 | 7.443 | -0.020 |
| 86 | 7.453 | 7.433 | -0.020 |
| | 7.482 | 7.420 | -0.062 |
| | 7.483 | 7.434 | -0.049 |
| 87 | 7.497 | 7.421 | -0.076 |
| | 7.413 | 7.434 | 0.021 |
| | 7.416 | 7.435 | 0.019 |
| 94 | 7.487 | 7.439 | -0.048 |
| | 7.487 | 7.426 | -0.061 |
| | 7.493 | 7.449 | -0.044 |
| 117 | 7.493 | 7.414 | -0.079 |
| | 7.485 | 7.404 | -0.081 |
| | 7.481 | 7.376 | -0.105 |
| 123 | 7.463 | 7.468 | 0.005 |
| | 7.418 | 7.464 | 0.046 |
| | 7.462 | 7.476 | 0.014 |
| 127 | 7.435 | 7.433 | -0.002 |
| | 7.518 | 7.413 | -0.105 |
| | 7.491 | 7.437 | -0.054 |

$\sum d = -0.664$ $\bar{d} = -0.03162$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the pH levels for Spontaneous Respiration and Assisted Respiration.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

where $$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{0.062418 - \frac{0.440896}{21}}{20}}$$

$$s_d = \sqrt{0.00207115}$$

$$s_d = 0.04551$$

$$t_c = \frac{-0.03162}{\frac{(0.04551)}{\sqrt{21}}}$$

$$t_c = -3.18215$$

Critical Region for a significance level of 0.05 is

$t > 2.080$ or $t < -2.080$

Since $t_c$ falls into the critical region, we reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration when measuring pH.

Breathing Conditions
Measuring pH

| Rabbit Number | Assisted Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| 84 | 7.475 | 7.412 | -0.063 |
| | 7.449 | 7.443 | -0.006 |
| | 7.443 | 7.431 | -0.012 |
| 86 | 7.433 | 7.420 | -0.013 |
| | 7.420 | 7.433 | 0.013 |
| | 7.434 | 7.449 | 0.015 |
| 87 | 7.421 | 7.464 | 0.043 |
| | 7.434 | 7.409 | -0.025 |
| | 7.435 | 7.446 | 0.011 |
| 94 | 7.439 | 7.437 | -0.002 |
| | 7.426 | 7.440 | 0.014 |
| | 7.449 | 7.434 | -0.015 |
| 117 | 7.414 | 7.432 | 0.018 |
| | 7.404 | 7.477 | 0.073 |
| | 7.376 | 7.470 | 0.094 |
| 123 | 7.468 | 7.436 | -0.032 |
| | 7.464 | 7.423 | -0.041 |
| | 7.476 | 7.443 | -0.033 |
| 127 | 7.433 | 7.418 | -0.015 |
| | 7.413 | 7.409 | -0.004 |
| | 7.437 | 7.415 | -0.022 |

$\Sigma d = -0.002$ $\quad\quad$ $\bar{d} = -0.00009524$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the pH levels for Assisted Respiration and Assisted Respiration With Halothane.

$$t_c = \frac{\frac{\bar{d} - \delta}{s_d}}{\sqrt{n}}$$

where

$$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{0.02674 - \frac{0.000004}{21}}{20}}$$

$$s_d = \sqrt{0.001337}$$

$$s_d = 0.036566$$

$$t_c = \frac{\frac{-0.00009524}{0.036566}}{\sqrt{21}}$$

$$t_c = -0.0119291$$

Critical Region for a significance level of 0.05 is

$t > 2.080$ or $t < -2.080$

Since $t_c$ fails to fall in the critical region, we fail to reject the null hypothesis that there is no difference between Assisted Respiration and Assisted Respiration With Halothane.

Breathing Conditions
Measuring pH

| Rabbit Number | Spontaneous Respiration | Assisted Respiration With Halothane | d |
|---|---|---|---|
| 84 | 7.461 | 7.412 | -0.049 |
| | 7.426 | 7.443 | 0.017 |
| | 7.463 | 7.431 | -0.032 |
| 86 | 7.453 | 7.420 | -0.033 |
| | 7.482 | 7.433 | -0.049 |
| | 7.483 | 7.449 | -0.034 |
| 87 | 7.497 | 7.464 | -0.033 |
| | 7.413 | 7.409 | -0.004 |
| | 7.416 | 7.446 | 0.030 |
| 94 | 7.487 | 7.437 | -0.050 |
| | 7.487 | 7.440 | -0.047 |
| | 7.493 | 7.434 | -0.059 |
| 117 | 7.493 | 7.432 | -0.061 |
| | 7.485 | 7.477 | -0.008 |
| | 7.481 | 7.470 | -0.011 |
| 123 | 7.463 | 7.436 | -0.027 |
| | 7.418 | 7.423 | 0.005 |
| | 7.462 | 7.443 | -0.019 |
| 127 | 7.435 | 7.418 | -0.017 |
| | 7.518 | 7.409 | -0.109 |
| | 7.491 | 7.415 | -0.076 |

$\Sigma d = -0.6660$ $\bar{d} = -0.0317$

Student's t Test

$H_o$: $\delta = 0$

$H_a$: $\delta \neq 0$

where $\delta$ is equal to the mean of the true differences in the pH levels for Spontaneous Respiration and Assisted Respiration With Halothane.

$$t_c = \frac{\bar{d} - \delta}{\frac{s_d}{\sqrt{n}}}$$

$$s_d = \sqrt{\frac{\Sigma d_i^2 - \frac{(\Sigma d_i)^2}{n}}{n - 1}}$$

with 20 degrees of freedom.

$$s_d = \sqrt{\frac{0.0415 - \frac{0.4436}{21}}{20}}$$

$$s_d = \sqrt{0.00102}$$

$$s_d = 0.03194$$

$$t_c = \frac{-0.0317}{\frac{0.03194}{\sqrt{21}}}$$

$$t_c = -4.5456$$

Critical Region for a significance level of 0.05 is

$$t > 2.080 \quad \text{or} \quad t < -2.080$$

Since $t_c$ falls into the critical region, we reject the null hypothesis that there is no difference between Spontaneous Respiration and Assisted Respiration With Halothane when measuring pH.

# Setting of Tolerance Limits

## Setting of Tolerance Limits Under Assumption of Normality (2)

### Sample Calculations for $P_aCO_2$ without respirator

Tolerance limits $L_1$ and $L_2$ such that the probability is $\beta$ that at least $\alpha$ of the population falls between $L_1$ and $L_2$ are given by the following:

$$L_1 = \overline{X} - \lambda S$$

$$L_2 = \overline{X} + \lambda S$$

$X$ = measured partial pressure for $CO_2$, $O_2$, or the pH.

$\overline{X}$ = mean of the partial pressures for $CO_2$, $O_2$ or the pH.

$S$ = Sample standard error

$n$ = number of samples

$\alpha = 0.99$

$\beta = 0.95$

$$\lambda = \left( \sqrt{\frac{n-1}{\chi^2_{n-1,\ \beta}}} \right) r$$

$\chi^2_{n-1,}$ = value of chi square with n-1 degrees of freedom which will be exceeded $\beta$ of the times.

$r$ = a number such that:

$$\int_{\frac{1}{\sqrt{n}} - r}^{\frac{1}{\sqrt{n}} + r} N(0,1) = \alpha$$

N(0,1) = value from a table of normal distribution with a mean value of zero, ± one standard deviation.

$$\Sigma X = 647.2$$

$$(\Sigma X)^2 = 418867.84$$

$$\Sigma X^2 = 20057.72$$

$$\bar{X} = \frac{647.2}{21}$$

$$\bar{X} = 30.819$$

$S^2$ = sample variance

$$S^2 = \frac{\Sigma x^2}{n-1}$$

where $$\Sigma x^2 = \Sigma X^2 - \frac{(\Sigma X)^2}{n}$$

$$\Sigma x^2 = 20057.72 - \frac{418867.84}{21}$$

$$\Sigma x^2 = 111.63$$

$$S^2 = \frac{111.63}{20}$$

$$S^2 = 5.5815$$

S = sample standard error

$$S = 2.3626$$

$$\sqrt{\frac{1}{21}} \cong 0.218$$

Find r for the following equation

$$\int_{\sqrt{\frac{1}{21}} - r}^{\sqrt{\frac{1}{21}} + r} N(0,1) = \alpha = 0.99$$

Using the preceding integral, by successive approximations choose

r = 2.58

$$\int_{-2.36}^{2.80} N(0,1) = 0.98830 \qquad \begin{array}{r} 0.49086 \\ \underline{0.49744} \\ 0.98830 \end{array} \quad \text{table values}$$

r = 2.70

$$\int_{-2.48}^{2.98} N(0,1) = 0.99199 \qquad \begin{array}{r} 0.49343 \\ \underline{0.49856} \\ 0.99199 \end{array}$$

r = 2.64

$$\int_{-2.42}^{2.86} N(0,1) = 0.99012 \qquad \begin{array}{r} 0.49224 \\ \underline{0.49788} \\ 0.99012 \end{array}$$

r = 2.63

$$\int_{-2.41}^{2.85} N(0,1) = 0.98983 \qquad \begin{array}{r} 0.49202 \\ \underline{0.49781} \\ 0.98983 \end{array}$$

When r equals 2.64, $\alpha$ approaches very closely its desired value of 0.99. Therefore, the value to be used in the following calculations will be 2.64.

From a table of chi square, the $X^2_{n-1,\beta}$ $(X^2_{20,95})$ value equals 10.851.

From the following equation:

$$\lambda = \left(\sqrt{\frac{n-1}{X^2_{n-1}}}\right) r$$

$$\lambda = \left(\sqrt{\frac{20}{10.851}}\right) 2.64$$

$$= 3.5851$$

Compute the limits $L_1$, and $L_2$

$$L_1 = \overline{X} - \lambda S$$

$$L_2 = \overline{X} + \lambda S$$

$$L_1 = \left[30.819 - (3.5881)(2.3626)\right]$$

$$L_1 = 22.349$$

$$L_2 = \left[30.819 + (3.5851)(2.3626)\right]$$

$$L_2 = 39.289$$

In view of the calculations, the following statement may be made of the experimental test:

The probability is 0.95 that 0.99 of the observations will fall between 22.349 mm. of Hg. and 39.289 mm. of Hg. when measuring $P_aCO_2$ without the respirator. Another way of making this statement is to say that the probability is 0.95 that 99 of every 100 observations will fall between 22.349 mm. of Hg. and 39.289 mm. of Hg. when measuring $P_aCO_2$ without the respirator.

Summary of statistical results

The following statements may be made of the experimental tests:

The probability is 0.95 that 0.99 of the observations will fall between 51.393 mm. of Hg. and 82.807 mm. of Hg. when measuring $P_aO_2$ without the respirator.

The probability is 0.95 that 0.99 of the observations will fall between 7.359 and 7.575 when measuring pH without the respirator.

The probability is 0.95 that 0.99 of the observations will fall between 21.784 mm. of Hg. and 42.054 mm. of Hg. when measuring $P_aCO_2$ with the respirator.

The probability is 0.95 that 0.99 of the observations will fall between 53.133 mm. of Hg. and 86.667 mm. of Hg. when measuring $P_aO_2$ with the respirator.

The probability is 0.95 that 0.99 of the observations will fall between 7.349 and 7.522 when measuring pH with the respirator.

The probability is 0.95 that 0.99 of the observations will fall between 24.909 mm. of Hg. and 44.501 mm. of Hg. when measuring $P_aCO_2$ with the respirator while administering Halothane (Fluothane).

The probability is 0.95 that 0.99 of the observations will fall between 37.598 mm. of Hg. and 97.326 mm. of Hg. when measuring $P_aO_2$ with the respirator while administering Halothane (Fluothane).

The probability is 0.95 that 0.99 of the observations will fall between 7.367 and 7.504 when measuring pH with the respirator while administering Halothane (Fluothane).

# CHAPTER IV

## RESULTS AND CONCLUSIONS

### Results

Upon completion of the experiments the data was subjected to an analysis of variance to determine if the $CO_2$, the $O_2$ or the pH levels were affected by the three breathing conditions. The null hypotheses for the analyses of variance were that the mean $CO_2$, $O_2$, and pH levels for spontaneous respiration are equal to the mean $CO_2$, $O_2$, and pH levels respectively for breathing with the respirator are equal to the mean $CO_2$, $O_2$, and pH levels respectively for breathing with the respirator while administering 3 percent Halothane.

The results of these tests rejected the null hypotheses, indicating that there was significant difference in response among the three breathing conditions.

Further analyses were carried out to determine the source of the significant differences among the three breathing conditions.

Student's t Tests for paired differences were conducted to test the hypotheses that the $CO_2$, $O_2$, and the pH levels are unaffected by the respirator when compared to spontaneous respiration. The results of these tests indicated that at the 5 percent level there was no significant difference between these two breathing conditions when comparing $CO_2$ and $O_2$ levels. However, there was a small significant decrease in the pH levels when breathing was assisted. The paired differences tested the hypotheses that the $CO_2$, $O_2$, and the pH levels were unaffected by the respirator when compared to the respirator while administering 3 percent Halothane. The results of these tests rejected the null hypotheses indicating that there was a small but significant increase in the $CO_2$ level when Halothane was administered. On the other hand, the results of the test brought about acceptance of the null hypotheses that there were no significant differences in the $O_2$ and pH levels. The reason for the significant increase in the $CO_2$ level is attributed to the presence of Halothane in the breathing gas which resulted in a slightly higher blood tension of $CO_2$. The Student's $t$ Test did not result in rejection of the null hypothesis that the pH level is unaffected by the respirator as compared to the respirator while administering Halothane. This may be attributed to three possibilities. One, a possible time lag for the higher $CO_2$ tension to reflect in a lowered pH. Another possibility is that the body is able to maintain a relatively stable pH regardless of a slight increase in the blood tension of $CO_2$ over the two hour test period. This last possibility suggests a need for additional research to observe the pH levels while the patient is under the affects of Halothane for longer periods of time. Finally, the small shift in the $CO_2$ and pH levels may have been caused by experimental errors.

Further use of the Student's $t$ Tests for paired differences tested the hypotheses that the $CO_2$, $O_2$, and the pH levels were unaffected by the respirator while administering 3 percent Halothane when compared to spontaneous respiration. The results of this test rejected the null hypotheses indicating that there was a small but significant increase in the $CO_2$ level and decrease in the pH level when Halothane was administered. On the other hand, the result of the test accepted the null hypothesis that there was no significant difference in the $O_2$ level.

The Student's t Tests have indicated that there was no significant difference between spontaneous respiration and assisted respiration, using the Arp-Varnum infant respirator, however, a small but significant difference does exist between assisted respiration and assisted respiration with Halothane. The presence of Halothane in the breathing gas appears to cause a small increase in the $CO_2$ level and has led to a statistical rejection of the null hypothesis that the mean $CO_2$ levels are equal. The medical meaning of this small increase in $CO_2$ is another question. The small increase in $CO_2$ has told us statistically that there is a significant difference between the two breathing conditions. However, from a medical viewpoint an increase in the arterial blood tension of $CO_2$ of several mm. of Hg. may be completely acceptable and a normal reaction when using Halothane. In other words, statistically it has been shown the $CO_2$ has increased between the two breathing conditions (assisted respiration and assisted respiration delivering 3 percent Halothane). However, medically this slight increase in $CO_2$ may not significantly change the patient's pH.

All statistical analyses completed at this time have been concerned with averages for the data obtained. This thesis also establishes a Confidence Interval in which there is a 95 percent probability that 99 percent of all observations will fall within the following ranges:

Spontaneous Respiration

| | |
|---|---|
| $CO_2$ Range | 22.349 mm. of Hg. to 39.289 mm. of Hg. |
| $O_2$ Range | 51.393 mm. of Hg. to 82.807 mm. of Hg. |
| pH Range | 7.359 to 7.575 |

Assisted Respiration With Respirator

| | |
|---|---|
| $CO_2$ Range | 21.784 mm. of Hg. to 42.054 mm. of Hg. |
| $O_2$ Range | 53.133 mm. of Hg. to 86.667 mm. of Hg. |
| pH Range | 7.349 to 7.522 |

Assisted Respiration With Respirator Delivering Halothane

| | |
|---|---|
| $CO_2$ Range | 24.909 mm. of Hg. to 44.501 mm. of Hg. |
| $O_2$ Range | 37.598 mm. of Hg. to 97.326 mm. of Hg. |
| pH Range | 7.367 to 7.504 |

These ranges indicate the same general trends as found in the Analysis of Variance and The Student's t Tests.

## Conclusions

Therefore it is believed that from a medical viewpoint the Arp-Varnum respirator can adequately ventilate and oxygenate a patient. This is accomplished by delivering an air oxygen mixture or by delivering three percent Halothane with an air oxygen mixture to induce deep surgical anesthesia.

## ACKNOWLEDGMENTS

The author wishes to express his appreciation to the many people who have assisted and advised in this Research. I especially wish to thank the following:

Doctor L. J. Arp, my major advisor, for his advice, and unfaltering cooperation and encouragement.

R. E. Dillon, C. L. Gray, R. W. Henderson, B. G. Simmers, and M. K. Smith, members of the Industrial Engineering Laboratory, all of whom have been active and enthusiastic co-workers in the clinical use and evaluation of the various instruments included in the system.

Special thanks goes to Doctor D. F. Watson and other members of Veterinary Science for their many contributions to this project. Without their assistance and cooperation this research would not have been possible.

Many people contributed to the Research Project including:

Doctor W. B. Harrison, Dean of the Research Division, for his recognition of the need for the Blood-Gas Analyzing Equipment.

Doctor S. G. Gilbreath and Doctor P. M. Ghare of the Industrial Engineering Department, and Doctor W. Cobb of the Statistics Department, for their assistance in the Statistical Analysis of the Test Data.

Members of the Departments of Bio-Chemistry, Mechanical Engineering, and Doctor Nathan Waldman of Chemical Engineering.

Mr. E. F. Fullwood, Vice-President of Research and Development of Ohio Chemical and Surgical Equipment Co. who donated the "Side-Arm" vaporizer.

Mr. R. J. Nuttall, D.V.M., Director of Clinical Research Veterinary Medical Division, Ayerst Laboratories, Inc., who donated the Halothane (Fluothane).

# LITERATURE CITED

1. Arp, L. J., Development of a System For Respiratory Augmentation, Unpublished, Copyrighted, Doctoral Disseration, Iowa State University of Science and Technology, Ames, Iowa. 1966.

2. Wäld, A. and Walfowitz, J., Tolerance limits for a normal distribution. Annals of Mathematical Statistics 17:208-215. 1946.

# APPENDIX

## MISCELLANEOUS CALCULATIONS

Figure 6 shows the schematic diagram of the system delivering 21 percent oxygen to the rabbit.

Sample calculation for delivering 3 percent Halothane to patient (see Figure 7).

(X percent Concentration of Halothane in Re-Breathing Bag) (Volume of Large Cylinder) + (0 percent Halothane in Small Cylinder) (Volume of Small Cylinder) = (3 percent Halothane to be delivered to the Patient) (Total Volume of Cylinders)

(X percent Halothane) (1 liter) + (0 percent Halothane) (0.3167 Liter)

= (3 percent Halothane) (1.3167 Liters)

$$X = \frac{0.0395 \text{ Liter}}{1 \text{ Liter}}$$

X = 3.95 percent Concentration of Halothane

is required in the Re-Breathing Bag in order to deliver 3 percent Halothane to the patient.

Total Volumes of Gases flowing into Re-Breathing Bag.

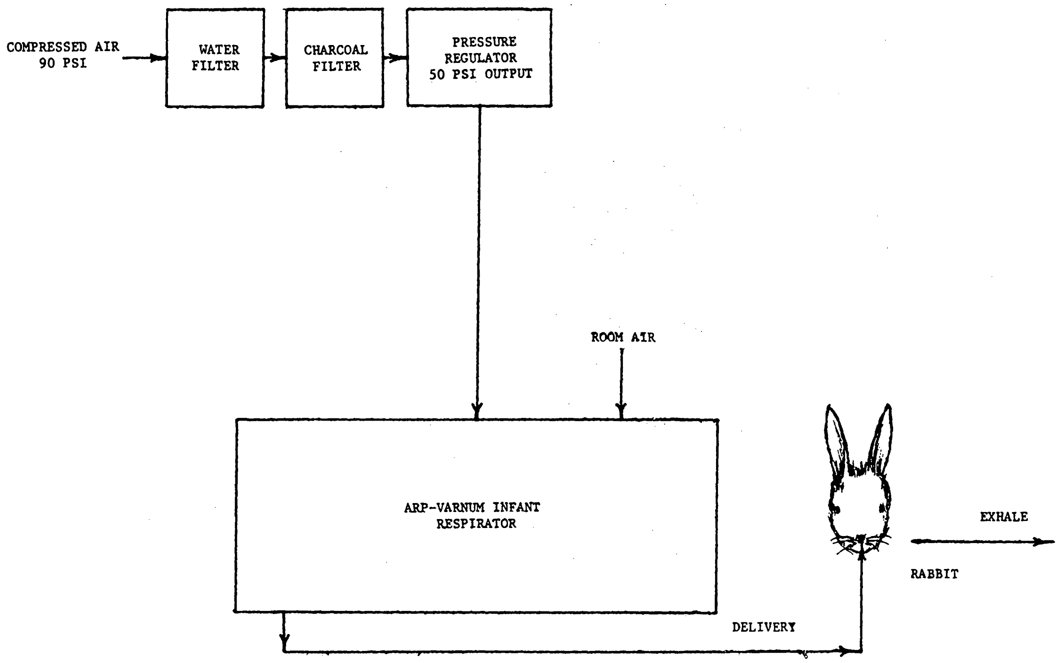
Closed Circuit - Recirculating the exhaled gas through the soda lime to the Re-Breathing Bag.

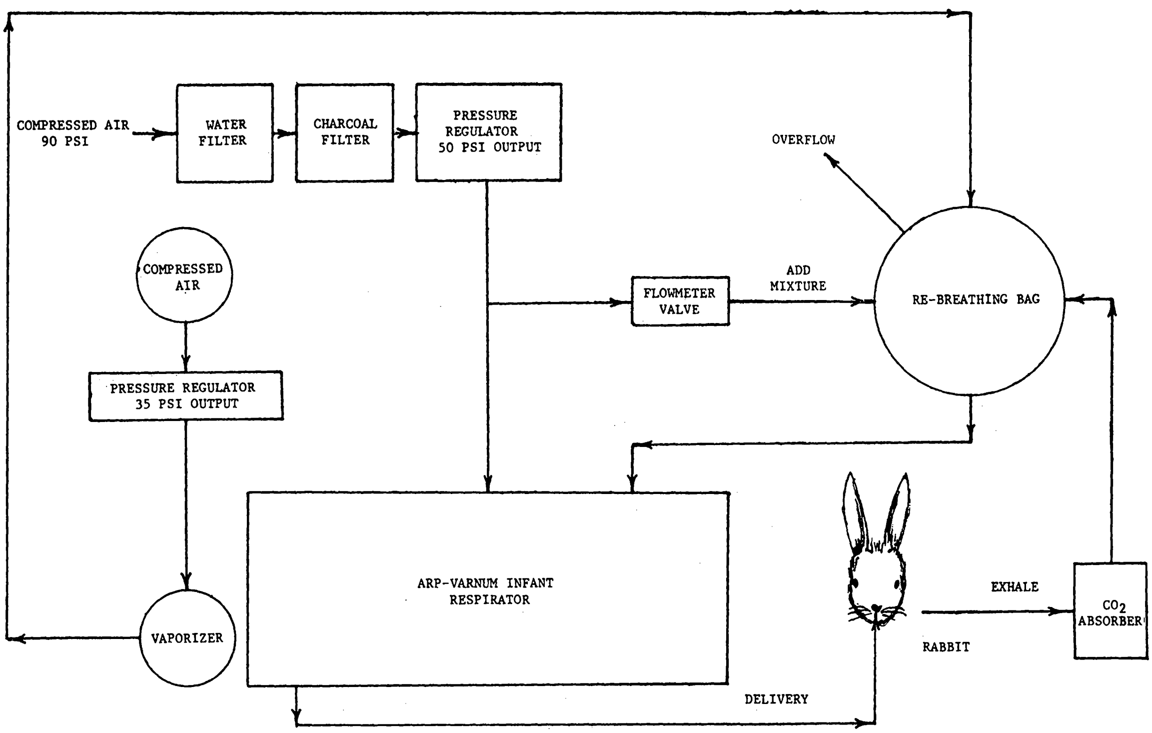
Requirements:

1) 3 percent Halothane to patient
2) 3.95 percent Halothane concentration in Re-Breathing Bag.

Figure 6. System Schematic For Assisted Respiration

Figure 7. System Schematic For Assisted Respiration With Halothane


COMPRESSED AIR
90 PSI
WATER FILTER
CHARCOAL FILTER
PRESSURE REGULATOR 50 PSI OUTPUT
ROOM AIR
ARP-VARNUM INFANT RESPIRATOR
EXHALE
RABBIT
DELIVERY


COMPRESSED AIR
90 PSI
WATER FILTER
CHARCOAL FILTER
PRESSURE REGULATOR 50 PSI OUTPUT
OVERFLOW
COMPRESSED AIR
FLOWMETER VALVE
ADD MIXTURE
RE-BREATHING BAG
PRESSURE REGULATOR 35 PSI OUTPUT
ARP-VARNUM INFANT RESPIRATOR
EXHALE
$CO_2$ ABSORBER
VAPORIZER
RABBIT
DELIVERY

3) Assume

   a) Rabbit breathing rate not in excess of 100 breaths per minute.

   b) Tidal Volume being delivered to the rabbit - 50 cc.

4) The minimum volume of gas flowing into the Re-Breathing Bag must be greater than or equal to the volume of gas delivered to the rabbit per unit of time.

   Flow of gas from Re-Breathing bag = (100 Breaths per minute) (50 cc. of gas delivered)

   Flow of gas from Re-Breathing Bag = 5000 cc./min.

   Gas flow required into Re-Breathing Bag $\geq$ 5000 cc./min.

5) Because of leakage around the nasal mask and oxygen consumed an Add Mixture of air is necessary to meet the gas flow requirements into the Re-Breathing Bag. Assume that upon each delivery, 4.5 cc. of gas escapes to the atmosphere.

6) Sample calculation for determining flow meter setting on the Verni-Trol Vaporizer.

   Setting of Vaporizer's Flowmeter = (Add Mixture Volume) (Percent of Concentration required in Re-Breathing Bag) (Saturation Ratio).

   The Saturation Ratio is the ratio of the vehicle gas flow delivered to the vaporizer to the vapor flow which the vehicle gas carried out of the vaporizer. The chart in Figure 3 page 5 of Ohio-Chemical Operation and Repair Manual for a

"Side-Arm" Verni-Trol Vaporizer shows this ratio for several anesthetic agents together with vapor pressure plotted as a function of temperature.

Setting of Vaporizer's Flowmeter = (1000 cc./min. - Add Mixture Volume) (3.95 percent Halothane Concentration in Re-Breathing Bag) (2 - Saturation Ratio for 21.1° C)

Flowmeter Setting = 105.3 cc./min.

The vehicle gas flowmeter would be set to 105.3 cc./min., and this flow would deliver 52.7 cc./min. of saturated Halothane vapor from the vaporizer.

In summation, the total volumes delivered to the Re-Breathing Bag are as follows:

| | |
|---|---|
| Recirculation of exhaled gas | 4550.0 cc./min. |
| Add mixture | 1000.0 cc./min. |
| Gas flow from vaporizer | 105.3 cc./min. |
| Halothane vapor from vaporizer | 52.7 cc./min. |
| Total gas flow to Re-Breathing Bag | 5738.0 cc./min. |

Flow in excess of the rabbit's requirements is released through the overflow port shown in Figure 7.

Chemical reaction when $CO_2$ is removed from the exhaled gas by Soda Lime - $Ca(OH)_2$.

$$C_a(OH)_2 + CO_2 \longrightarrow C_aCO_3 + H_2O$$

$$C_aCO_3 + 6H_2O \longrightarrow C_aCO_3 \cdot 6H_2O$$

The vita has been removed from the scanned document

THE EVALUATION OF THE ARP-VARNUM RESPIRATOR AS AN ANETHESIA VENTILATOR WHILE DELIVERING THREE PERCENT HALOTHANE AND AIR MIXTURE

by Jon Heath Betts


ABSTRACT

This study presents the evaluation of the Arp-Varnum Respirator as an anethesia ventilator while delivering three percent Halothane and air mixture. The system is designed for neonates suffering from Respiratory Distress Syndrome (R.D.S.). This disease, which is also called hyaline membrane disease, causes the death of an estimated 25,000 newborn infants each year.

The respirator is a volume limited assister-controller type respirator capable of delivering volumes from 5 ml. to 250 ml. Flow rate is adjustable from 1 liter per minute to 20 liters per minute. The patient may trigger the respirator to deliver a preset volume of air by exerting as little as 0.5 mm. $H_2O$ negative pressure. Any two gases may be mixed and delivered to a patient in any ratio or concentration desired.

The respirator described in this study has been used to deliver three percent Halothane to seven rabbits for twenty one test runs.

From this study it is believed that the Arp-Varnum respirator can adequately ventilate and oxygenate a patient while delivering three percent Halothane.