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RELATIVE DECOMPRESSION RISKS OF SPACECRAFT CABIN ATMOSPHERES: COMPARISON OF GASES USING MINIATURE PIGS

by

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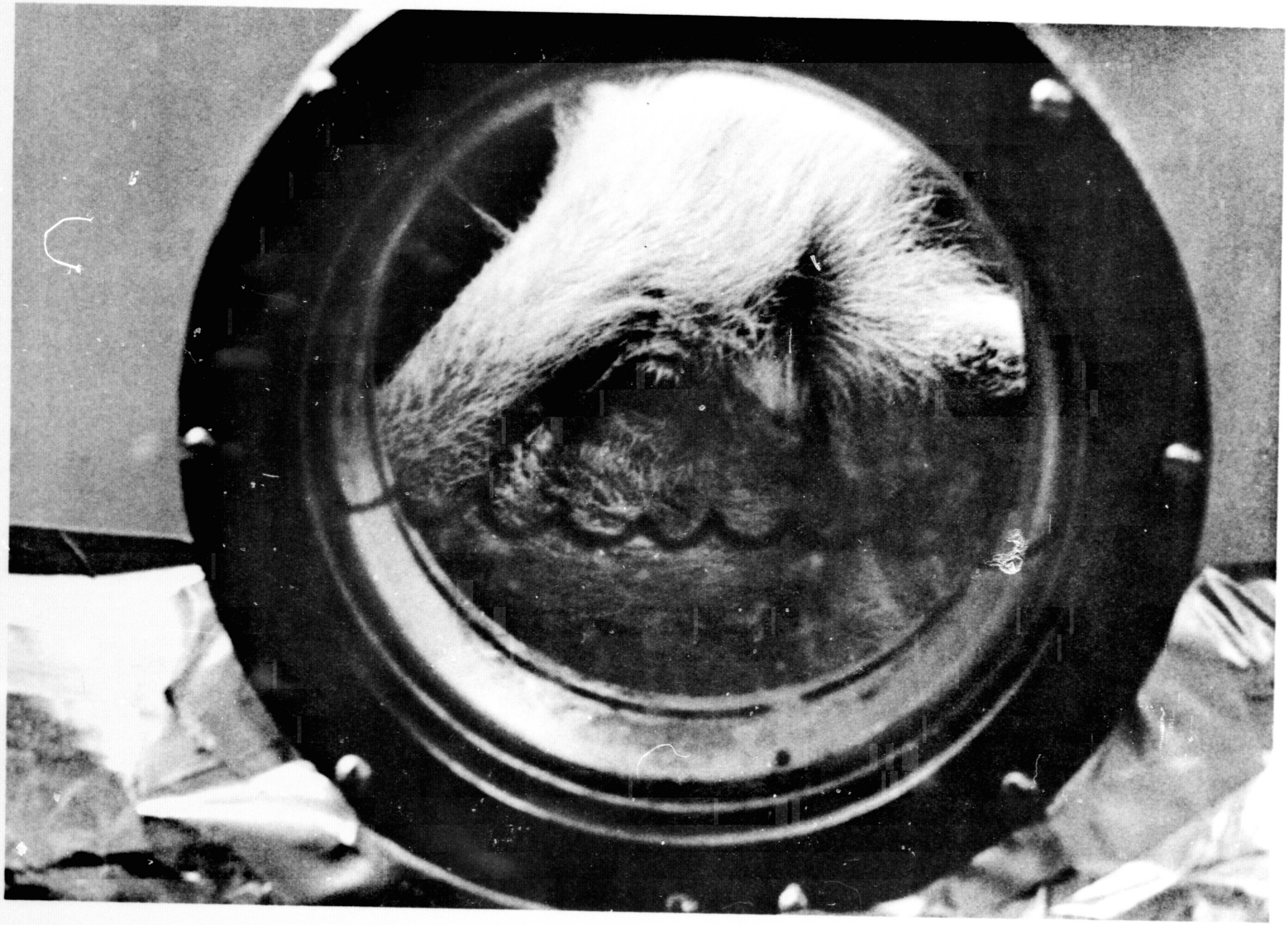

Frontispiece. The experiments reported here were performed according to the standards reccommended by the National Society for Medical research for the humane treatment of experimental animals, and in conformity with the laws of the United States and the State of New York.

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I. SUMMARY

The miniature pig has been demonstrated in this study to be a useful animal model for the analysis of altitude decompression sickness and for determining the relative decompression hazards of various potential space-cabin atmospheres. By replicate decompressions of individual pigs after saturation exposure in the same and in different inert gas environments a relative ranking of five inert gas mixtures in terms of increasing severity of decompression hazard was made. The order of increasing risk for the gases studied was:

Neon < Crude Neon < Helium < Nitrogen < Argon

In these experiments we saturated miniature pigs for 22 hours in a controlled environmental chamber at a pressure slightly greater than atmospheric (900 mm Hg). Individual pigs were decompressed in an oxygen environment to 105 mm Hg (46,000 feet altitude equivalent). Gases used were nitrogen, helium, neon, argon, and crude neon (a mixutre of 75% neon and 25% helium obtained from air separation plants). Signs of decompression sickness were analyzed in terms of severity, time of occurrence, individual animal response, and reproducibility of response. Results were analyzed in terms of both a supersaturation limiting concept of decompression risk and the correlation of observed decompression risk for each gas with parameters of bubble growth characteristic of the gases. Maximum Haldane ratios and Haldane ratios for various inert gas transport compartments at the time of symptom occurrence do not appear to correlate with the observed symptom incidence or severity among the five gases. Reasonably good correlation between some bubble growth parameters and decompression sickness scores for the gases was found.

To the extent the pig resembles man in inert gas transport, neon or neon mixtures with helium may be a better gas for use as a diluent in a two-gas spacecraft environment than nitrogen or helium.

II. INTRODUCTION

A. Background

The recent loss of three Russian cosmonauts in an operation which had come to be routine points out with tragic forcefulness the fact that there are still many unsolved problems in manned space flight. Decompression sickness may well have played a role in their death (1).

As the pace of space operations slows down and spectacular events become less frequent, attention is being turned to the long-range goals of manned space flight to the neighboring planets. Among the many factors which make a long flight a different ball game from current short ones is the choice of the breathing atmosphere of the spacecraft cabin.

Biologically there are two major considerations involved in the choice of the best inert gas for this application: physiological consequences of living in the synthetic atmosphere, and risks of decompression sickness. Other properties such as weight, storage volume, leak rate, engineering complexities, fire safety, and cost are of course important, but they do not represent areas where vital information is lacking.

For the immediate post-Apollo flights the National Aeronautics and Space Administration has chosen nitrogen as the oxygen diluent, and both laboratory and operational experience indicate that the missions can be accomplished accordingly. It is of course well established that nitrogen is safe to breathe and its fire, decompression and engineering characteristics are well understood, but the possibility exists that some other inert gas may offer considerable overall operational advantages over that gas, especially in the case of a long flight. A comprehensive literature review and theoretical analysis completed in 1967 by Dr. E. M. Roth of the Lovelace Foundation (2, 3, 4, 5,) suggests that neon may be a better choice.

Helium is also a viable candidate, having been chosen by the U.S. Air Force for the now-defunct Manned Orbiting Laboratory project.

Both the long and short term habitability data and available information on relative decompression risks of the various possible inert gases have been reviewed in the report covering the first year's work under this contract (6) and in an earlier report along the same lines (7). A theoretical approach slightly different from that of Roth has been advocated by Schreiner (8). The conclusions are that although there is scanty support by experimental or operational data it appears that any one of the gases nitrogen, helium or neon would pose no significant biological limitations, surely for short flights and possibly for long ones. But as far as decompression is concerned, there are probably differences and these might be substantial in terms of relative safety.

Tests which have been conducted before in attempts to rank various gases with respect to their decompression risk have been limited to experiments on small rodents(7, 9, 10, 11) or on men exposed for relatively short times to the gas in question before decompression (12, 13, 14). The experiments reported here have attempted to bridge the gap by using an animal more similar to man, the pig, have involved virtual saturation and have made side-by-side comparisons of nitrogen, neon, helium and argon. (These are the only gases in serious consideration for spacecraft use, other possibilities being either flammable or otherwise unsuitable without regard to decompression characteristics.)

B. Neon

One special aspect of this project is the attention given to the gas neon. Roth's analyses (4) give neon a slight edge over its competitors in terms of the probabilities involved in decompression problems, and neon stacks up well in other aspects relating to its use in a spacecraft. It is our feeling that this gas merits serious consideration.

The element neon was discovered in 1898 by Ramsay and Travers as a component of the inert or "argon" fraction of air that remains after nitrogen and oxygen are chemically removed (15). Having an atomic number of 10 and an atomic weight of 20.2, neon is the second member of the helium group of elements. It is found in atmospheric air at the level of 18.18 parts per million; it is somewhat more abundant in the universe, being the fourth most common element. By contrast, helium is found in the atmosphere at 5.25 parts per million and is the second most common element in the universe. Hydrogen, the most common element in the universe, appears in our atmosphere at a basic concentration of 0.5 parts per million, but may be somewhat higher in the vicinity of some types of industry. All neon used today is obtained from atmospheric distillation processes. (For a thorough review of this topic, see Ref. 16.)

In the air separation plant essentially all the incoming air is liquefied in the first distillation column. The bottom liquid from this column is enriched in oxygen. The liquid removed from the top of this column is essentially pure liquid nitrogen. Neon, along with helium and hydrogen, remains in an uncondensed nitrogen fraction above the liquid nitrogen. Partial condensation against boiling nitrogen removes most of the nitrogen, resulting in a mixture containing roughly 1/2 neon, 1/3 nitrogen, 1/6 helium and 1 to 2% hydrogen. Further condensation using vacuum pumped liquid nitrogen reduces the nitrogen to less than 10%. The remaining nitrogen is removed by adsorption and the hydrogen is removed by catalytic oxidation, leaving a mixture of neon and helium essentially free of all contamination.

The ratio of neon to helium in the atmosphere, 18.2 to 5.25, is equivalent to a 77.7% neon, 22.3% helium mixture. The exact ratio of a Ne-He product depends on the specific equipment and operating technique but is normally found in the range of 72-78% neon, 28-22% helium. This is the material which we call "crude neon".

These experiments involved both crude neon and the far more expensive research grade, 99.9 or more percent pure. There are reasons for both. The crude is cheap enough to use freely with minimal regard for the cost of the gas. It is being used in diving, and is the "neon" used in many literature references. Being in a mixture with helium may give it special decompression advantages, and we seek the optimal gas system.

Pure neon on the other hand must be tried, because it is the gas that is relevant to space travel. Any flight long enough to be concerned about the economies afforded by neon will most likely employ a cryogenic storage system, with the gas in liquid or some transitional form. Once the liquid phase is obtained then there is no need to maintain the mixture we call crude neon--separation of neon and helium then becomes relatively simple. Here, incidently, is another advantage of neon· its thermodynamic properties make it much easier to store in liquid form than helium.

One further aspect of neon which may be relevant is a series of experiments recently conducted in our laboratory and as yet reported only in a preliminary way (17). The main theme of the experiments was to study performance while using crude neon as a diving gas, but in order to do this human subjects were exposed to neon at pressures equivalent to 200, 300, 400, 500 and 600 feet of sea water. Comparable experiments were performed with helium, and with nitrogen to the 400 foot level. "Bottom time" was 30 to 35 minutes for each dive; oxygen levels were 10% for the 200, 300 and 400 foot dives, and 7% for the deeper ones. The experiments were not designed to make precise comparisons of decompression risk, but the conditions were generally comparable. The essential point is that there was a substantially lower incidence of bends in the neon dives than in those using either helium or nitrogen.

C. Miniature Pigs in Decompression

Although experiments on rats may very well permit a distinct ranking of inert gas diluents with respect to their degree of decompression risk, it must be recognized that these data will apply best to rats, and although certain aspects of the behavior of the gases will be applicable to the human situation it is not likely that the overall results can be transposed directly to astronauts. Schreiner (8) has pointed out the inconsistencies which arise in dealing with the poorly perfused tissues in a small animal. Likewise, it would be inappropriate for a variety of reasons to conduct initial screening on exotic gas mixtures with human subjects. To be most meaningful we felt the experiment should use a model which resembles man as much as possible, yet be of manageable scope. We considered several criteria in the selection of the animal to be used in these studies of altitude decompression sickness:

1. A minimum tissue perfusion rate very close to that of man.
2. Control of regional blood flow (i.e. neurological, hormonal, and pharmacologic responses similar to that of man.
3. Predictable susceptibility to altitude decompression sickness and display of objectively assessable signs thereof.
4. Fat-lean ratios and lipid chemistry similar to man's.
5. Ease of handling and convenient size.

The medium-sized domestic animals, i.e. dog, goat, sheep, and pig, are probably more physiologically similar to man than many of the species (e.g. rodents) usually found in the research laboratory. Some of the similarities between these animals and man are body weight, respiratory rate, heart rate, systemic blood pressure, etc., with the seeming similarity between two species usually being a function of body size.

The variety of species previously employed in decompression studies has been very limited; of these, the goat has been most often used, although only in diving decompressions. It is said that the onset and type of symptoms observed are like those observed in man. Certain physiologic and metabolic parameters of the goat differ distinctly, however. One anatomic difference which inevitably introduces many physiologic differences is the compound structure of the ruminant digestive tract. The microbiological acitivity and consequent voluminous gas production would probably make this species unsuitable for altitude decompression studies. Sheep, on the other hand, have been used with considerable success in diving studies employing Doppler ultrasonic detectors (18).

The dog is a well-established laboratory animal for many physiological investigations, and has been used quite successfully in diving decompression work (19). However, we were not satisfied that the dog is endowed with the same quantitative and qualitative physiological characteristics which are in the end responsible for man's susceptibility to decompression sickness. Also, several practical factors (i.e. availability, handling, variability) make the conduct of this type of experiment on dogs a difficult matter.

No small and easily handled non-human primates are available that have enough fat to suggest that they might be suitable.

When comparing various domestic, non-primate, simple stomached mammals to man, the one most physiologically similar is the pig. Recent increases in the application of this species to laboratory usage support this statement. New strains of miniature swine have been developed (20) and are finding increasing use in the field of cardiovascular physiology. Withstanding certain obvious phenotypic variations, the similarity between the pig and man is not limited to the cardiovascular system (21). Because of the lack of much experimental data, it will be necessary to speculate on the relative merits of the pig as a model for studying altitude decompression sickness. One recent report showing successful use of the pig in diving is that of Gillis (22).

Pigs, particularly the miniature varieties, have a vascular distribution, lean body mass, and adipose tissue content and distribution much like man. If adipose tissue content is a limiting factor, one could assume that the minimum perfusion rate of the pig would approximate that of man. (The importance of perfusion and tissue fat content in decompression is reviewed in Ref. 8.) The amount of fat on the small pigs can be controlled over a wide range by adjusting the diet.

Known pharmacological differences between pigs and man are no greater than individual variations in a normal human population.

The thoracic cavity of the pig is smaller when comparing total lung capacity to body size than in most other animals. The residual volume of the pig is relatively the same as that of other animals. Nevertheless, as a direct result of smaller expiratory and inspiratory reserve volumes, the vital capacity of the pig is smaller. In effect, there is less compensatory capacity of the respiratory system.

Relative heart size of the pig is smaller than that of either the dog or the goat, resulting in less reserve capacity of the cardiovascular system.

Miniature swine should have both perfusion and diffusion limitations more severe than dogs, goats, or sheep, and we felt would be more suitable subjects for this study.

Work accomplished during the first year of this contract (6) gave us further confidence in the use of the pig specifically for altitude decompression studies, but showed likewise that there would be some problems. Pigs are tolerant of altitudes sufficient to induce bends (when pure oxygen is breathed) but they are not unaffected by the relative hypoxia. The conclusion that we reached in the earlier experiments and the basis for this contract was that individual pigs had to be "calibrated" for the profiles to be used and distinctions established for each one between the effects of hypoxia and of decompression sickness.

III. EXPERIMENTAL METHODS

The purpose of the experiment was to provide a quantitative separation of the inert gases, nitrogen, helium, crude neon, neon and argon, as possible oxygen diluents, with respect to the degree of decompression to reduced pressures from a saturated condition. Our approach to this problem was in effect to saturate an animal in an atmosphere containing the necessary oxygen and the inert gas in question, then to purge with oxygen and reduce the pressure low enough to cause bends. Miniature pigs were maintained for 20-24 hours in a controlled environmental system having a total pressure of 900 mm of mercury and an oxygen partial pressure of 120 mm mercury and subsequently were decompressed to 106 mm of mercury, equivalent to an altitude of 46,000 feet, and were monitored for up to 40 minutes for signs of decompression sickness. This regime was repeated on several animals and in each gas in question. A number of preliminary experiments were run to establish profiles and individual susceptibility.

A. Miniature Pigs

All animals were obtained from Vita Vet Laboratories, Merion, Indiana. Four young females arrived in January, 1970, and were maintained on a restricted diet for about one year. Their diet was increased at the beginning of this experiment to allow the development of body fat. These pigs were named Kitty, Sally, Lucy and Fran. All are white, and all have pleasant dispositions and are easy to handle.

Four male pigs were obtained in April of 1971. These are nearly hairless, dark brown in color and are less docile than the females. These were named Fenimor, Rupert, Donald and Morgan.

Weights of the animals at the times they were used for experiments can be found in the summary tables. Morgan and Fenimor were too small to be used routinely in this experiment.

Some special characteristics deserve mention. Lucy became, apparently, deficient in some essential nutrient during the past winter and had to be treated with injections of vitamins and minerals. She developed ataxia and partial paralysis to the extent that she could not eat and drink. We did not determine the specific deficiency but began at this time a routine use of Vita Vet supplement No. 1, and had no further problems of this nature.

Sally has a remarkable resistance to the standard signs of decompression sickness which we saw in other pigs. We therefore chose not to use her for many comparative exposures. Our two most susceptible subjects were Fran and Rupert, but unfortunately both were lost during initial experiments in which a suitable profile was being established. Fran died following respiratory and perhaps neurocirculatory problems, the treatment for which was delayed too long. Rupert was the victim of a malfunction of the control system.

Kitty seems to have a persistent case of vertigo which resulted from vestibular damage during rapid purging of the chamber, and this has been considered in judging her response to decompression.

B. Equipment

All exposures were carried out in a controlled environmental system designated CES-2 and used in previous experiments of this type in our laboratory (6, 7,). CES-2 has been used for exposing rats and rabbits to simulated altitude conditions and spacecraft atmosphere conditions for periods of up to one week and for similar exposures for shorter periods of animals which were to be used for decompression studies (23). This system consists of an 800-liter chamber fitted with a plexiglass dome and a semi-closed, recirculating atmosphere and environmental control system (Figures 1 and 2). The unique features of CES-2 are the gas partial-pressure control system which is conservative of inert gas and the use of liquid scrubbers (Figure 3). Pressure is controlled by a simple diaphragm pressure switch which responds to deviations in pressure by a call for either venting or addition of gas. The choice of whether to add oxygen or inert gas is determined by the setting of a meter relay which can be adjusted to maintain desired oxygen tension. This meter relay replaces the standard meter supplied with a Beckman 777 polarographic oxygen analyzer, the probe of which is in the circulating gas stream.

Certain modifications were made on CES-2 especially for this experiment. The major one was the removal of a small animal cage and replacement with a rotating table which can be used as a treadmill for animals being examined for decompression sickness (Figure 4). The circular table was cut from a sheet of half-inch plywood. It rests on furniture casters attached around the periphery of the chamber and is driven by a reversible motor through reducing gears. A wooden baffle or gate is attached inside the chamber vertically along a radius from the center to the wall. With this in place when the table is rotating it is necessary for an animal to walk in order to keep from being pushed into this baffle (Figure 4). Previous experience in decompressing pigs on a small belt-type treadmill suggested

Figure 1. CES-2 in operation during a decompression. One technician monitors pressure control system while observer records signs of decompression sickness.

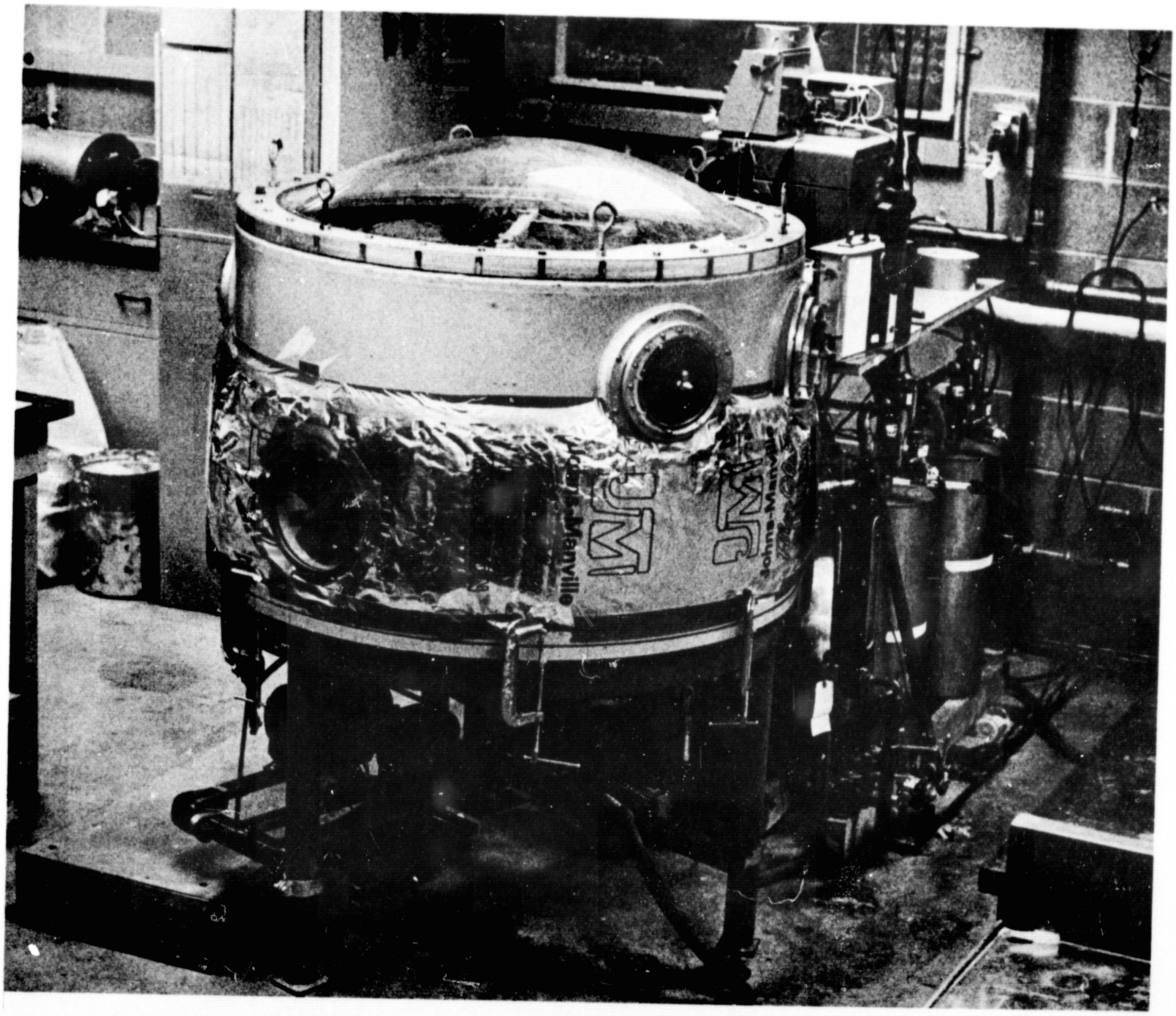
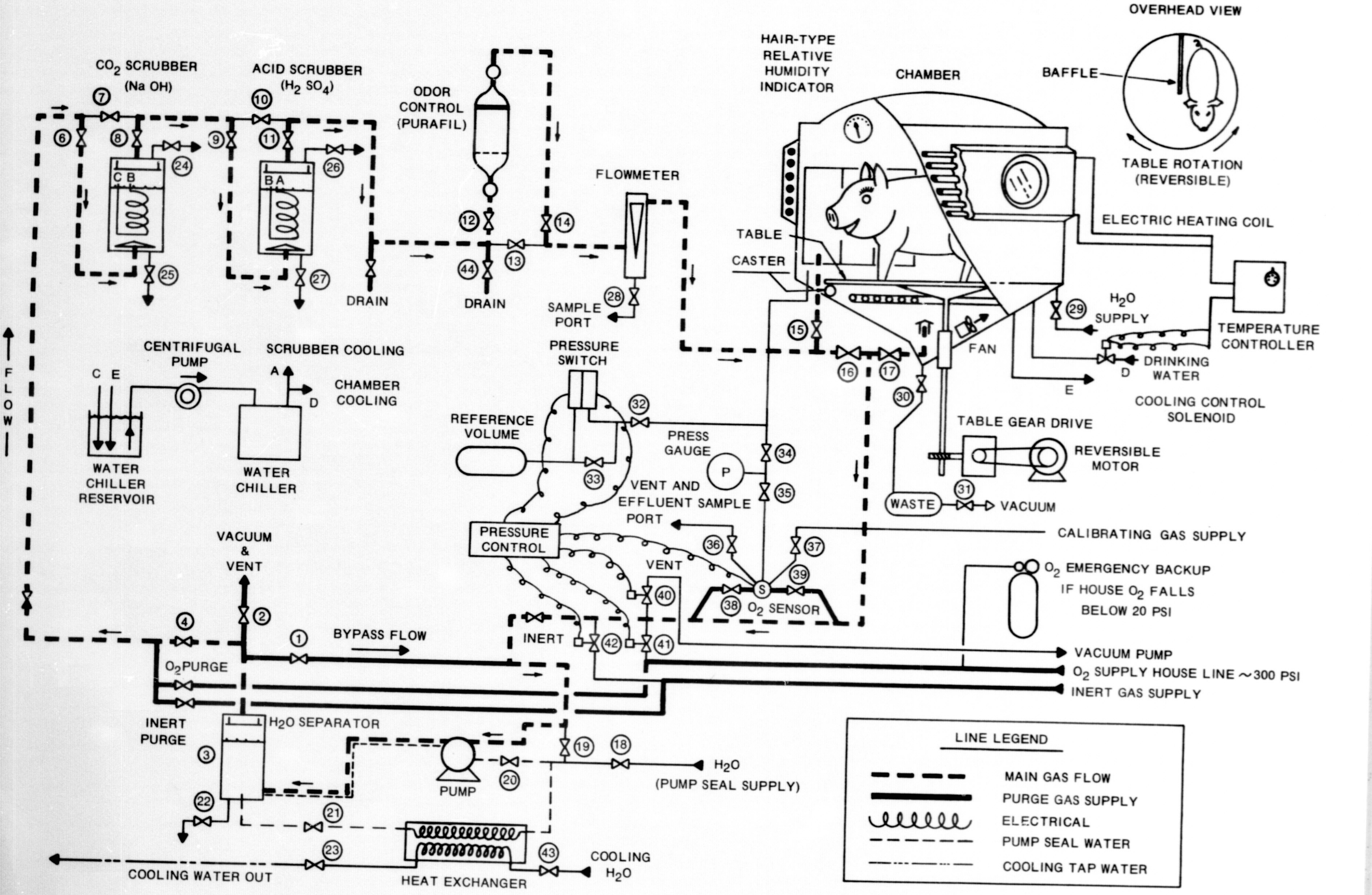


Figure 2. CES-2 system showing gear drive mechanism below floor. Working through a vertical shaft the motor turns the floor of the chamber forcing the pig to walk.

Figure 3. Closed Environmental System - 2



CO$_2$ SCRUBBER
(Na OH)
ACID SCRUBBER
(H_2 SO$_4$)
ODOR CONTROL
(PURAFIL)
HAIR-TYPE RELATIVE HUMIDITY INDICATOR
CHAMBER
OVERHEAD VIEW
BAFFLE
TABLE ROTATION
(REVERSIBLE)
ELECTRIC HEATING COIL
FLOWMETER
TABLE
CASTER
C B
B A
DRAIN
DRAIN
SAMPLE PORT
H_2O SUPPLY
TEMPERATURE CONTROLLER
FAN
DRINKING WATER
D
E
COOLING CONTROL SOLENOID
TABLE GEAR DRIVE
REVERSIBLE MOTOR
WASTE
VACUUM
FLOW
CENTRIFUGAL PUMP
SCRUBBER COOLING
A
D
C E
CHAMBER COOLING
WATER CHILLER RESERVOIR
WATER CHILLER
PRESSURE SWITCH
REFERENCE VOLUME
PRESS GAUGE
P
VENT AND EFFLUENT SAMPLE PORT
PRESSURE CONTROL
CALIBRATING GAS SUPPLY
VENT
S
O_2 SENSOR
O_2 EMERGENCY BACKUP
IF HOUSE O_2 FALLS
BELOW 20 PSI
VACUUM
&
VENT
BYPASS FLOW
INERT
VACUUM PUMP
O_2 SUPPLY HOUSE LINE ~300 PSI
INERT GAS SUPPLY
O_2PURGE
INERT PURGE
H_2O SEPARATOR
PUMP
H_2O
(PUMP SEAL SUPPLY)
COOLING WATER OUT
HEAT EXCHANGER
COOLING H_2O
① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨ ⑩ ⑪ ⑫ ⑬ ⑭ ⑮ ⑯ ⑰ ⑱ ⑲ ⑳ ㉑ ㉒ ㉓ ㉔ ㉕ ㉖ ㉗ ㉘ ㉙ ㉚ ㉛ ㉜ ㉝ ㉞ ㉟ ㊱ ㊲ ㊳ ㊴ ㊵ ㊶ ㊷ ㊸ ㊹
LINE LEGEND
MAIN GAS FLOW
PURGE GAS SUPPLY
ELECTRICAL
PUMP SEAL WATER
COOLING TAP WATER

CES-2 Valve Legend

1. Pump Bypass
2. Main Vent and Vacuum
3. Water Separator
4. System Isolate
5. Inert and Oxygen Purge
6. CO_2 Scrubber Inlet
7. CO_2 Scrubber Bypass
8. CO_2 Scrubber Outlet
9. Acid Scrubber Inlet
10. Acid Scrubber Bypass
11. Acid Scrubber Outlet
12. Odor Control Inlet
13. Odor Control Bypass
14. Odor Control Outlet
15. Chamber Inlet
16. Chamber Bypass
17. Chamber Outlet
18. Pump Seal Supply
19. Auxiliary Seal Inlet
20. Seal Inlet
21. Seal Recirculate
22. Separator Drain
23. Cooling Water Outlet
24. CO_2 Scrubber Vent
25. CO_2 Scrubber Drain
26. Acid Scrubber Vent
27. Acid Scrubber Drain
28. Influent Sample
29. Waste Removal Water Supply
30. Chamber Drain
31. Waste Flask Vent
32. Pressure Control Isolate
33. Reference Pressure Set
34. Vacuum Gauge to Chamber
35. Vacuum Gauge to Sensor
36. Sensor Vent and Effluent Sample
37. Calibrating Gas Inlet
38. Sensor Outlet
39. Sensor Inlet
40. Vent Solenoid
41. Oxygen Solenoid
42. Inert Gas Solenoid
43. Cooling Water Inlet

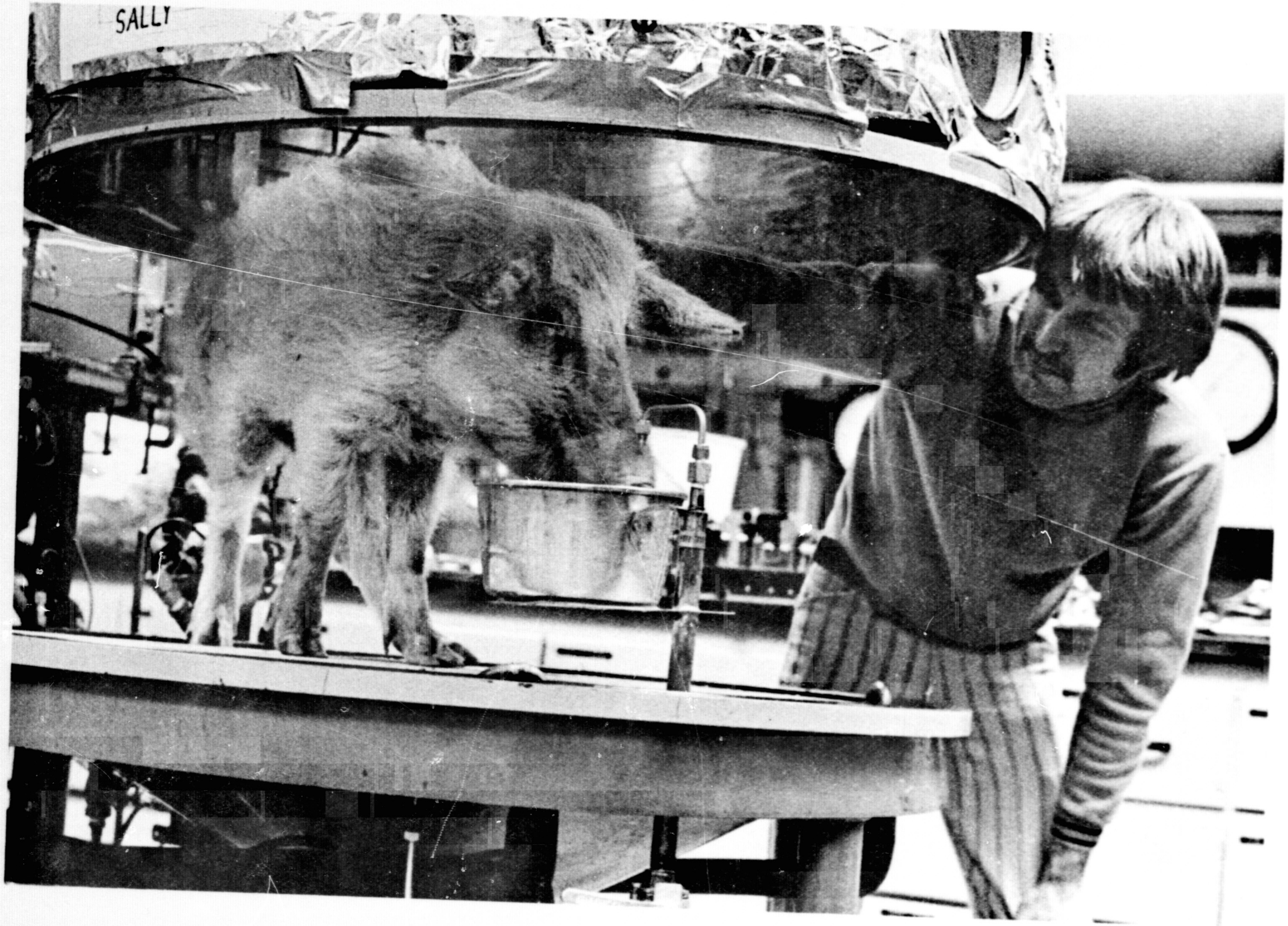


Figure 4. Sally and friend at beginning of equilibration run. Pigs were fed at this time about one-third of a day's ration, and were allowed water until the morning of the decompression.

the need for a method of shocking the animals when they refused to walk, so we installed lines from our fence charger along the baffle. In the present experiment we found this not to be necessary, the main reason probably being the fact that these pigs were provided with more adequate and stable oxygen levels than those used in the earlier experiments. The pigs were therefore less likely to become tired and refuse to walk. Initially the baffle was constructed as a folding gate which crossed the entire diameter of the chamber, forcing the pig to walk along on one side (Figure 5). When one of the more frisky pigs destroyed this gate we found that the baffle alone was adequate (Figure 6).

The routine consisted of placing a pig in the chamber around midday and feeding it about one-third its daily ration of Purina Sow Chow (one interesting problem one encounters in managing laboratory pigs is the fact that maintenance diets are not available--virtually all prepared pig feed is dedicated to some special purpose such as fattening or farrowing). Water was provided throughout the night. Because of the stress of the experiment, especially that due to hypoxia, we felt it was better not to fast the animals for almost 48 hours as would have been the case had we not fed them when they were put in the chamber. If they were given a full ration even 20 to 22 hours before decompression they would vomit during the exposure to simulated altitude. This was seldom a problem once we established the procedure described here.

After purging with oxygen and refilling with the proper inert gas to a total pressure of 900 mm mercury the chamber was allowed to stabilize and adjusted to the proper conditions; these were maintained until the beginning of the decompression procedure the following day.

During our "preliminary" runs (so designated because we could not get satisfactory signs of bends until we settled on the proper profile) we provided a stop at sea level near the beginning of the decompression

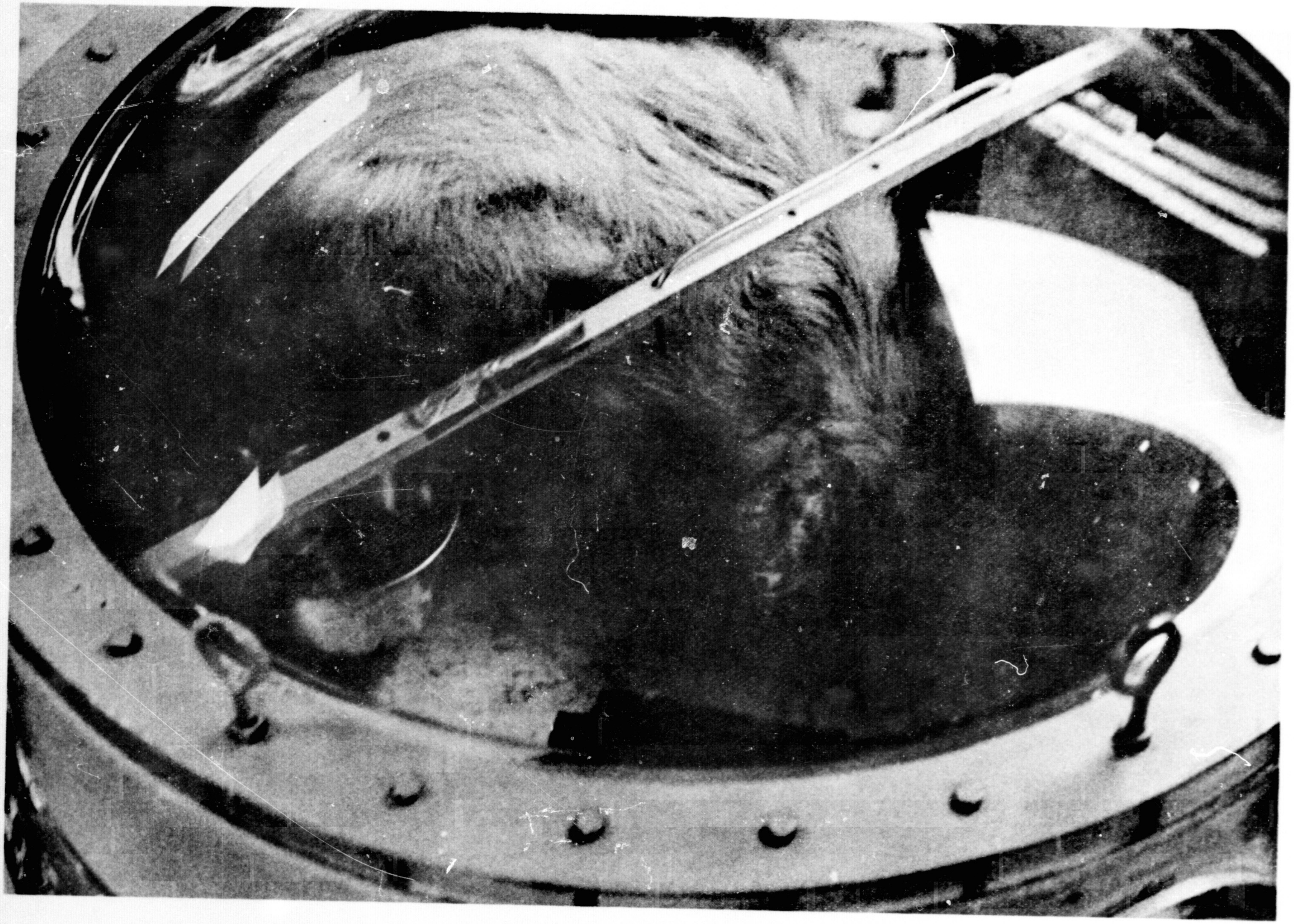


Figure 5. The folding gate is retracted, giving the pig ample room during his 20-hour equilibration. Gate was extended across the diameter of the chamber during a decompression, forcing the pig to walk as the table rotated.

Figure 6. The single baffle covering half the diameter of the chamber worked just as well as the folding gate and was much less trouble. It was left in place at all times.

profile in order to close the "gate". This was accomplished through the dry-box gloves attached to chamber portholes, but these gloves could be used only when the chamber was at sea level. Later we found that half the gate would suffice, and from then on "sea level" stops were no longer needed.

Saturation conditions were the same for all animals, regardless of the decompression profile used, varying only in duration. Target conditions were 120 mm Hg PO_2, 900 mm Hg total pressure, humidity 50-75% and the approximate temperature. A summary of environmental conditions obtained is given in Table 1. Temperatures were chosen on the basis of calculations of forced convective heat loss (7) corroborated with experience on humans in a helium environment (24) or on observations of animals (6, 7), and on observations of the apparent comfort of the pigs. The following temperatures were set up as desired, but these were changed if the animals behavior (e.g. shivering) indicated:

Helium	29° C
Crude Neon	26° C
Neon	25° C
Nitrogen	24° C
Argon	23° C

TABLE I

Environmental Data

Date 1971	Time	Pig	lbs Wt	Inert Gas	°C Temp Mean	% Relative Humidity Mean	Gas Analysis %					
							O_2	N_2	He	Ne	Ar	CH_4
26 May	1314	Kitty	70	N_2	25.0	65	14	85	-	-	-	-
27 May	1321	Rupert	77	N_2	22.1	63	14	85	-	-	-	-
28 May	1315	Donald	60	N_2	24.1	58	14	85	-	-	-	-
01 June	0830	Fenimor	35	N_2	24.0	58	14	85	-	-	-	-
10 June	1016	Sally	68	N_2	20.5	62	14	85	-	-	-	-
11 June	0952	Lucy	69	N_2	24.2	54	14	85	-	-	-	-
14 July	1020	Donald	72	N_2	23.1	52	16.1	83.5	-	-	-	0.19
14 June	1139	Donald	61	He	28.5	59	14.2	1.5	81.9	-	-	0.13
15 June	1006	Kitty	73	He	28.8	56	14	1	84	-	-	0.5
16 June	1020	Sally	68	He	30.5	50	14	1	84	-	-	0.5
17 June	1050	Lucy	72	He	29.0	52	14	1	84	-	-	0.5
18 June	1442	Donald	62	He	30.2	53	14	1	84	-	-	0.5
21 June	1314	Kitty	75	He	30.0	56	14.1	0.39	82.4	-	-	0.12
22 June	0930	Lucy	78	He	29.1	58	13.8	0.22	85.8	-	-	0.14
23 June	1054	Donald	63	He	29.1	53	15.1	0.58	83.8	-	-	0.04
24 June	1001	Kitty	75	He	29.0	56	14.0	0.35	84.0	-	-	0.03
25 June	1106	Lucy	77	He	28.9	58	14.3	0.25	83.5	-	-	0.18

Table I Cont.

Date 1971	Time	Pig	lbs Wt	Inert Gas	°C Temp Mean	% Relative Humidity Mean	Gas Analysis %					
							O_2	N_2	He	Ne	Ar	CH_4
28 June	0948	Donald	62	Ne*	25.6	58	14.0	0.8	24.2	60.8	-	0.21
29 June	0814	Kitty	73	Ne*	25.0	80	14	1	25	60	-	0.5
30 June	1059	Lucy	76	Ne*	25.6	51	14.1	1.28	24	60.0	-	0.5
1 July	1059	Donald	64	Ne**	23.5	75	15.2	3.9	42	38.8	-	0.5
3 July	1358	Kitty	74	Ne*	24.3	68	14	1	25	60	-	0.5
4 July	1300	Lucy	75	Ne*	24.7	60	14	1	25	60	-	0.5
5 July	1015	Donald	65	Ne*	26.8	63	14	1	25	60	-	0.5
6 July	1021	Kitty	76	Ne*	26.2	62	14.9	0.12	27.2	57.1	-	0.19
7 July	1003	Lucy	83	Ne*	25.9	63	15.4	1.73	25.9	56.8	-	0.15
8 July	1046	Donald	64	Ne	26.1	68	14	0.5	-	85	-	-
9 July	1005	Kitty	76	Ne	24.5	60	14.2	0.33	-	84.2	-	-
10 July	1114	Lucy	81	Ne	25.1	57	14.1	0.30	-	86.0	-	-
11 July	1030	Donald	75	Ar	23.4	60	14.6	5.22	-	-	80.0	-
12 July	1000	Lucy	80	Ar	23.9	62	13.8	1.81	-	-	84.1	-
13 July	1000	Sally	69	Ar	20.1	61	14.9	2	-	-	83.3	-

* Crude Neon Mix

** Helium Neon Mix

C. Experimental Design

One of the surprising aspects of this experiment has been the resistance which these miniature pigs show to decompression sickness. We began decompressing saturated pigs on the assumption that they would show signs characteristic of decompression sickness on a profile in the same general range as would men. A recent summary by Allen (25) showed 74 to 91% of men developed bends at a pressure of 196 mm Hg (depending on the amount of body fat). These were exposed for up to 6 hours, and of course symptoms in a man are more easily noted than signs in an animal. We thought we would see bends with exposures to 187 mm Hg, or 155 or surely 128, but we were generally disappointed with these exposures.

Specifically, the first profile we tried is given in Figure 7A. The idea of this decompression was to expose each animal in stages to increasingly lower pressures, hoping to get a definite number for each animal in each gas. Each animal was allowed to equilibrate for 20 hours at 900 mm Hg, decompressed to sea level for a purge with pure oxygen (so the reduced pressures could be tolerated) then decompressed to the first pressure. Following a 30-minute run at, say, 187 mm Hg, the pig was decompressed to 900 mm Hg where hopefully he would restore the gas loadings in his tissues by the time of the next decompression. Then after 2 and 1/2 hours at 900 mm Hg a second decompression was begun, this one to a slightly lower pressure.

This design suffered from several defects. To begin with, neither the exposure time nor the re-equilibration time were long enough, but these were as long as could be tolerated within the structure of a working day. In effect, the first exposures were not stressful enough to cause bends but were very effective in allowing time for degassing before exposure to a still lower pressure. Because of the degassing of the earlier stop, this one now became tolerable and consequently allowed another

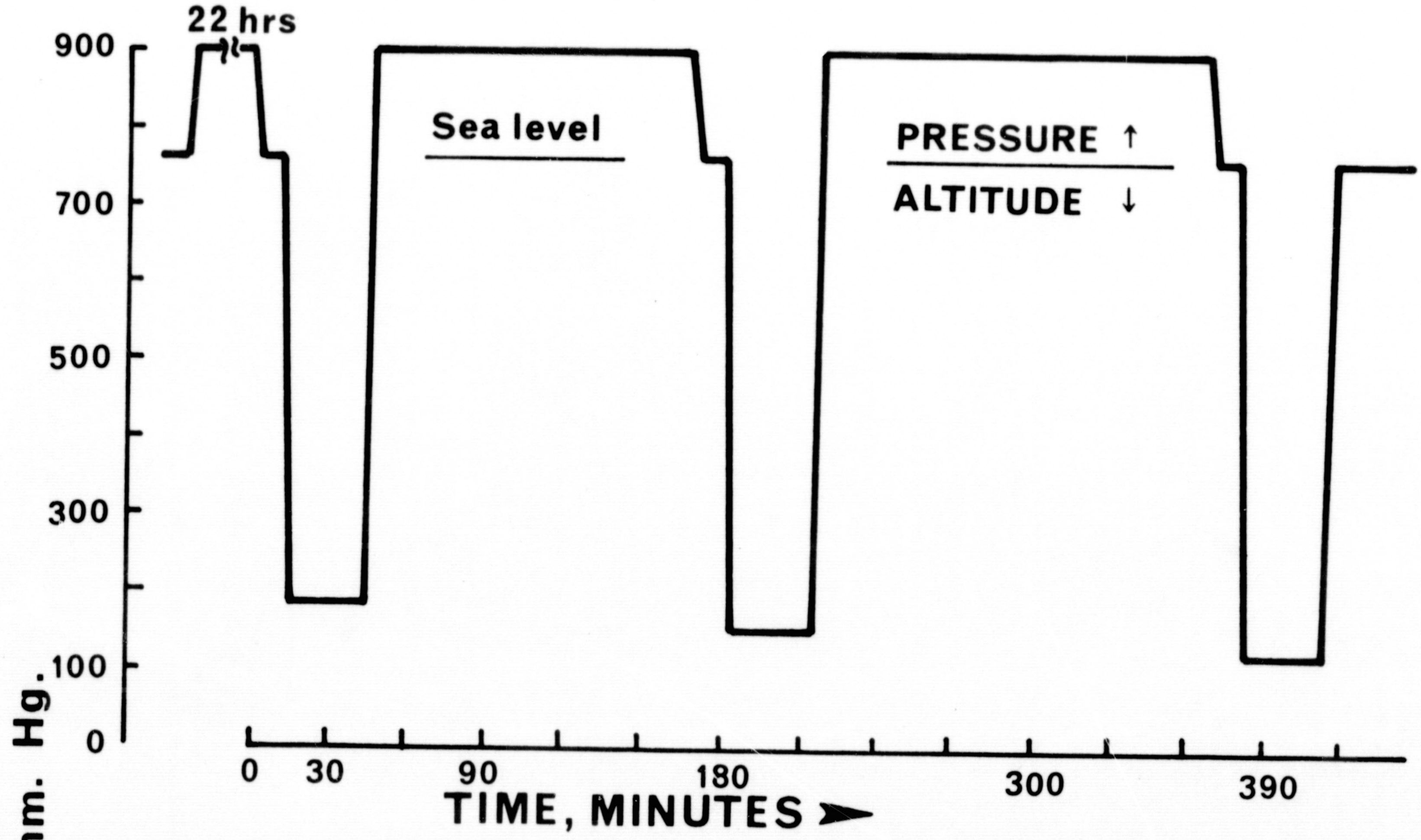


FIG. 7A PROFILE I

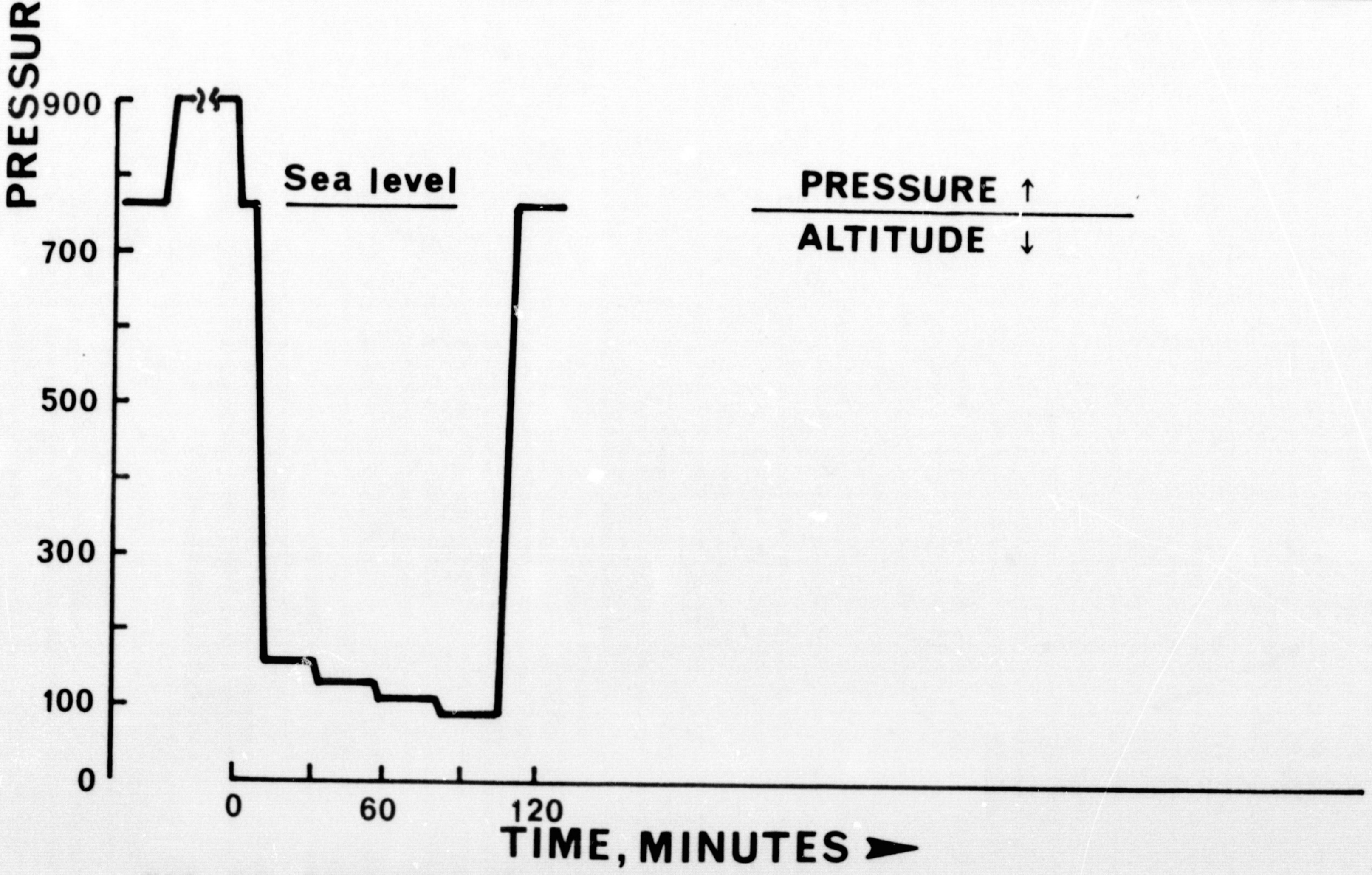


FIG. 7B PROFILE II

period of degassing. The result was that this profile produced very few bends and was certainly unsuitable for our purposes.

The next profile (II) we tried consisted of a stepwise increase in altitude (or decrease in pressure) as shown in Figure 7B. This approach suffers from the same problems as Profile I, in that effective degassing is allowed to take place before a stressful pressure is reached.

We next decided to settle on a rapid decompression to a single pressure in all cases, relying on differences in bends severity and incidence for our discrimination, rather than specific pressures. This is shown in Figure 8A. This profile (III) proved to be unsatisfactory because of hypoxic stress at the 91 Hg level. A summary of the experiences to this point is given in Table II.

It was clear by now that we were on the edge between pressures too high to cause dependable decompression signs and too low to allow proper oxygenation. The compromise was settled on 105 mm Hg, the equivalent to 46,000 feet. This profile, designated IV, is given in Figure 8B.

The routine used in each subsequent experiment was this. After a 22-hour equilibration a gas sample was taken, the scrubbers were bypassed and the pressure control system was turned off. At t=O an oxygen purge was started and at the same time decompression was begun. With the oxygen purge continuing, at 200 mm Hg decompression was stopped and the chamber was recompressed with oxygen to 800 mm Hg, at which point decompression was resumed until 105 mm Hg was reached. This procedure, from the moment the oxygen purge was begun until the pig arrived at 105 mm Hg, took seven minutes. Originally we tried to avoid fast decompressions, partially to avoid intestinal gas, but also to avoid stressing the very fastest tissues. Whether we succeeded is open to question. Bloating was seen in early experiments but seemed not to be a problem later on. Ernsting (26)

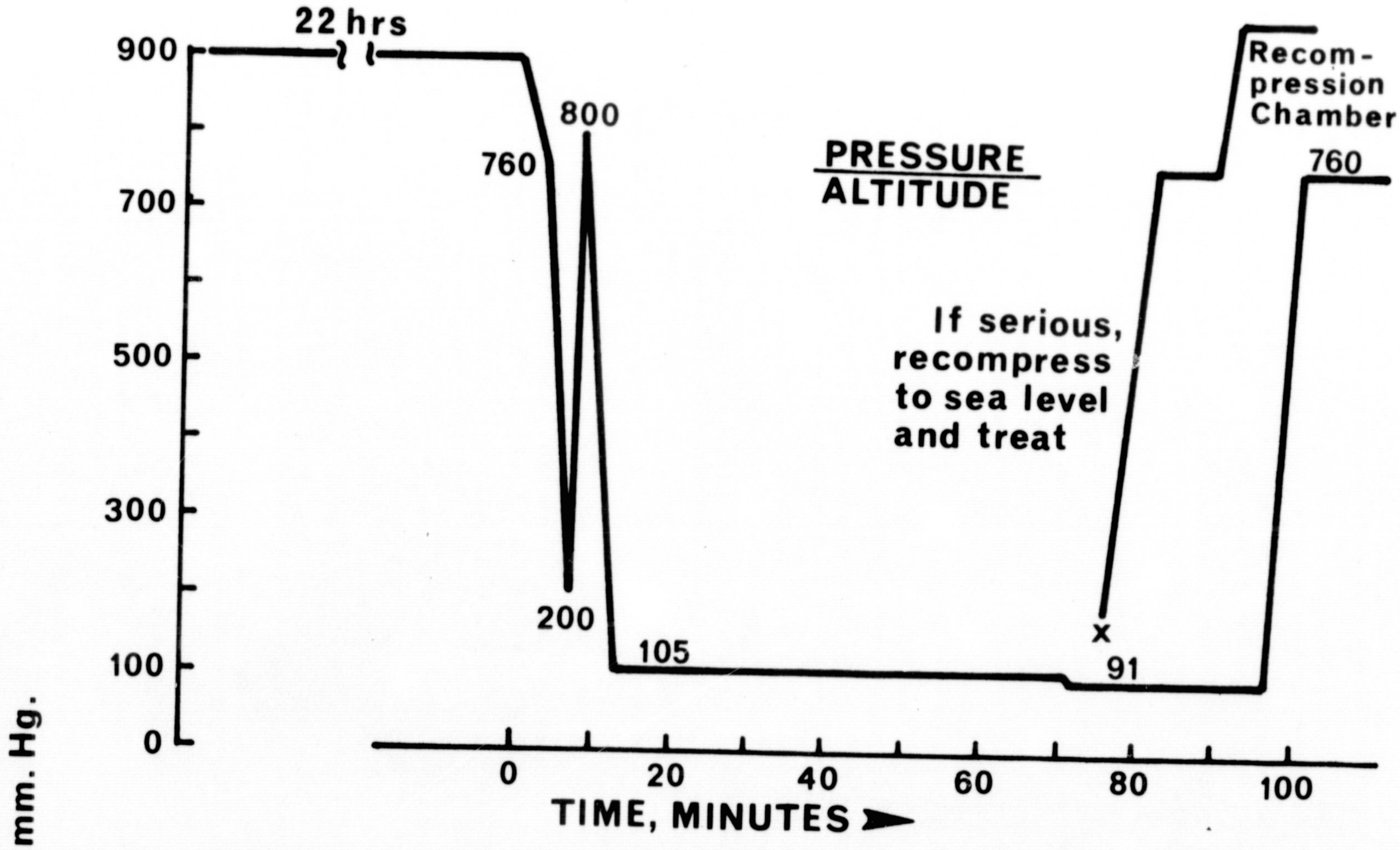


FIG. 8A PROFILE III

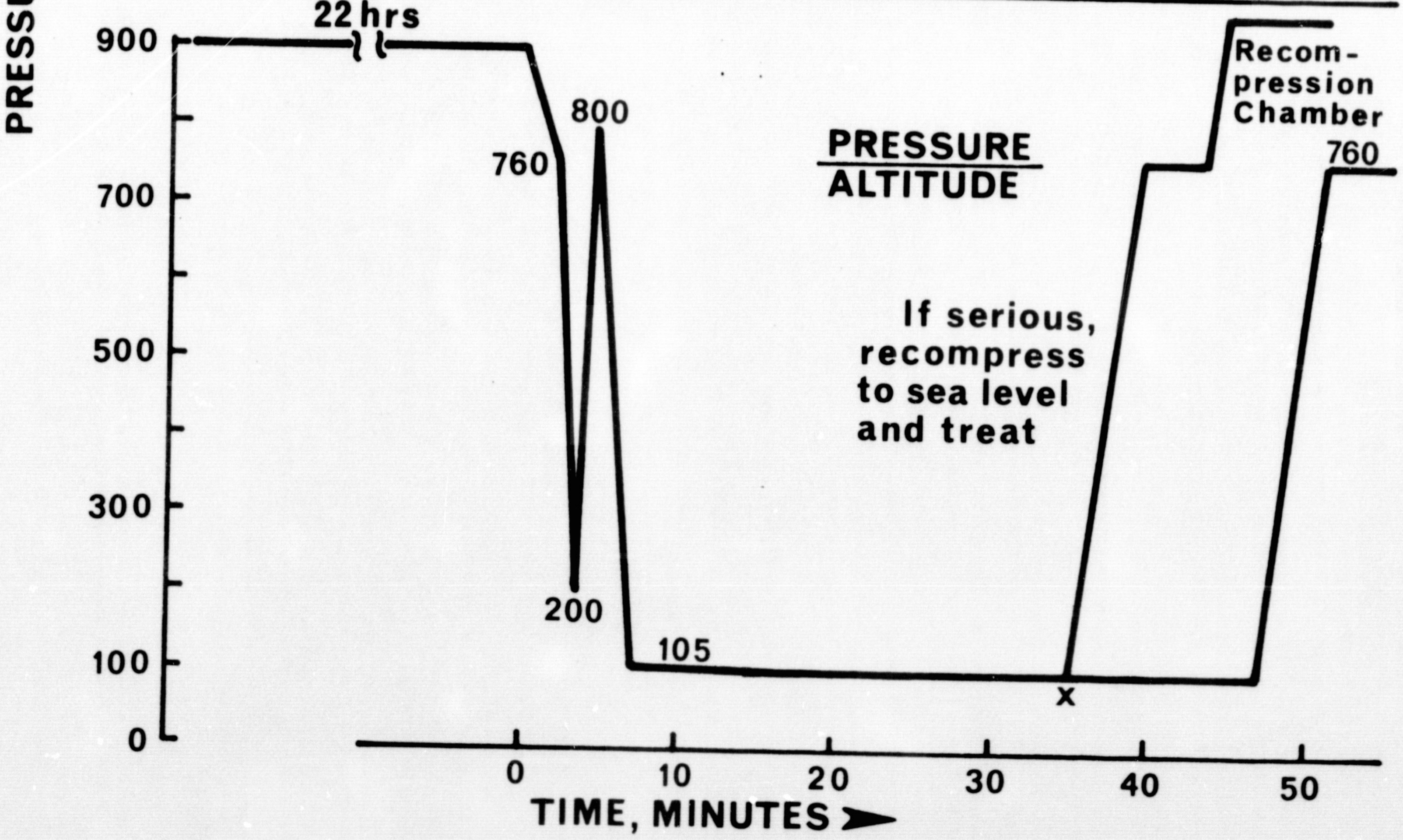


FIG. 8B PROFILE IV

TABLE II

Decompression Data Summary: Preliminary Experiments

Date	Pig	Weight	Gas	Profile Summary Min. Press. Reached Mm Hg	 Time to Reach Min.	 Time at Min. Press. Min.	Results and Remarks
(The following experiments follow Profile I)							
7 April	Sally	52	N_2	225	14	32	OK (Extra stop at 225, this experiment only)
7 April	Sally		N_2	187	7	30	Vomited, bloated, cyanotic, dizzy; probably hypoxia. No bends signs.
13 April	Lucy	53	N_2	187	26	30	Vomited. No bends
13 April	Lucy		N_2	155	7	30	Probable leg pain
13 April	Lucy		N_2	128	10	30	Treadmill failed after 13 minutes
16 April	Kitty	64	N_2	187	12	30	Vomited, bloated, no bends
16 April	Kitty		N_2	155	14	30	Droopy, distressed, coughing or "dry heaves". No bends. Ataxia on recompression.
21 April	Fran	44	N_2	187	16	4	By 250 mm Hg pig was very bloated, very distressed. Vomited. Coughed or choked continually. Treated at 55 psi on O_2, some relief but generally had severe respiratory distress. Died 6 hours after decompression and treatment began.
29 April	Sally	67	He	187	16	14	Vomited. Taken to 148 mm Hg from 187 directly
29 April	Sally		He	148	3	3	Vomited. Bloated. No limb bends. Fell down.

TABLE II (continued)

Decompression Data Summary: Preliminary Experiments

				Profile Summary			
Date	Pig	Weight	Gas	Min. Press. Reached Mm Hg	Time to Reach Min.	Time at Min. Press. Min.	Results and Remarks
4 May	Lucy	72	He	187	19	40	Ear distress: turned head, swallowed, coughed.
4 May	Lucy		He	158	15	28	Bloated but OK. No bends.
4 May	Lucy		He	128	16	30	Gasped, slid hind legs. Possible bends.
6 May	Kitty		N_2	187	17	30	Nervous. No bends
6 May	Kitty	68	N_2	155	15	31	Definite limb bends
10 May	Sally	64	N_2	187	15	30	Fell down four times. No bends
10 May	Sally		N_2	155	13	30	Difficulty walking. Went to knees. Tired.
10 May	Sally		N_2	128	13	30	Difficulty walking, favored hind leg, was hypoxic at first. Probably no bends.
12 May	Lucy	68	N_2	187	12	30	Scratched a lot; possible skin bends
12 May	Lucy		N_2	155	13	30	Very tired and droopy, but OK
12 May	Lucy		N_2	128	13	31	Walked with difficulty. No bends
13 May	Kitty	71	He				Pig got severe vertigo during purging
14 May	Rupert	73	N_2	187	14	30	No problem. Vertigo on recompression
14 May	Rupert		N_2	155	13	30	No problem.
14 May	Rupert		N_2	128	18	30	Walked on front knees. No bends.

TABLE II (continued)

Decompression Data Summary: Preliminary Experiments

				Profile Summary			
Date	Pig	Weight	Gas	Min. Press. Reached Mm Hg	Time to Reach Min.	Time at Min. Press. Min.	Results and Remarks
(The following experiments follow profile IA - modified to 60 minutes at each level.)							
17 May	Donald	58	N_2	155	22	60	Bloated, droopy. No bends
17 May	Donald		N_2	128	15	60	Tired, on front knees a lot. No bends
19 May	Kitty	70	He	155	15	60	No problems
19 May	Kitty		He	128	13	60	Favored right hind leg slightly.
(The following experiment followed Profile II)							
24 May	Sally	60	N_2	155	9	20	Walked on front knees
24 May	Sally		N_2	128	1/2	20	Vomited, was bloated. Coughed, shivered
24 May	Sally		N_2	105	1/2	20	Vomited. Cyanotic. Bloated.
24 May	Sally		N_2	87	1/2	3	Passed out, recovered, was severely hypoxic, had trouble walking and standing remained cyanotic, showed definite favoring and pain of left hind leg; limb bends.
(The following experiment followed Profile III)							
25 May	Lucy	70	N_2	105	9	58	Vomited. Walked with difficulty
25 May	Lucy		N_2	91	1	25	Favored right hind leg a little

suggests that rate of ascent is not likely to be an important factor.

Once at minimum pressure the pressure control was reset and a steady oxygen purge was maintained to assure over 95%oxygen (generally it was near 98%) and minimal chance of hypoxia. The animal was maintained at 105 mm and observed for 40 minutes, or 47 minutes total elapsed time to recompression, provided no signs of decompression were seen. As soon as a definite sign of decompression sickness was observed, whether a limb bend or neurocirculatory collapse, recompression was begun immediately. If there were any signs whatsoever remaining once sea level was reached the animal was rushed (1-2 min) to our hyperbaric facility and compressed with oxygen to 60 feet and given an oxygen treatment procedure sufficient for the conditions. These precautions--rapid recompression and treatment--were necessary to assure that no additional animals die as a result of the experiment, since they were by now irreplaceable.

During the observation period the treadmill was turned on for about one minute out of every four, for the purpose of forcing slow walking. Without the treadmill a pig might well stand still on a painful leg, but when forced to move he will favor the leg. Speed of treadmill at half its radius is 4.5 meters per minute.

During the decompression period a pig might show any of the following signs:

Vomit
Urinate
Defecate
Sit down
Close eyes
Scratch
Root or paw floor
Kick sides of chamber

Chew something
Have trouble walking
Go to knees
Walk on knees
Lie down
Have "hot-foot" syndrome
Have convulsions.
Fall down
Pass out
Appear droopy
Become cyanotic
Turn or twist head
Stagger
Break out in goose-pimples (hairless pigs only)

Signs which we determined were representive of decompression sickness are summarized in Table III. In addition to decompression sickness there are two complicating factors, hypoxia and vertigo. Both of these can be somewhat eliminated by experience of an observer with a given pig. Hypoxia can further be eliminated by recompression to 200 mm Hg at which point alveolar oxygen should be higher than at sea level, and signs of simple hypoxia should disappear.

Vertigo is a particularly serious problem with pigs. This seems to be due to pressure inequalities in the ear, and it occurs in nearly all rapid pressure changes. Gillis (22) feels that at least in diving it is only a problem on ascent (reduction in pressure--just the opposite problem as in most humans) but we seemed to observe it in both directions equally. We could not be completely sure collapse and inability to get up was due to decompression sickness or ear problems, except by the time it occurred. When it happened during a pressure change we attributed it to the ear, but if it happened several

TABLE III

Criteria For Scoring Decompression Signs

Category 1.	No signs ascribable to decompression sickness. (Except perhaps scratching)
Category 2.	Minor or possible signs of decompression sickness. Pig may occasionally (but not continually) favor one leg, or may act as if he is on a hot surface by rapid walking in place. Coughing and mild respiratory distress. Difficulty in walking. Occasionally going to knees.
Category 3.	Definite signs of decompression sickness. Favoring of a leg repeatedly. Refusal to walk, eliminated as hypoxia by a momentary recompression.
Category 4.	Serious signs of decompression sickness. Collapse, inability to walk (not due to vertigo or hypoxia). Severe respiratory distress, choking, and coughing, not due to intestinal bloating.

minutes after arrival at pressure and no signs of especially serious ear trouble were seen on ascent we attributed the disturbance to decompression sickness. There were in fact no cases where we had serious doubts as to the identity of this kind of problem. Whether or not vertigo (turning or twisting of the torso, staggering, walking sideways) occurred, our animals always responded to the pressure changes with shaking of the head, scratching, etc., to indicate ear discomfort.

IV. EXPERIMENTAL RESULTS

A. Decompression Results

After Profile IV (Figure 8B) was established in preliminary experiments to give observable signs of decompression sickness in pigs equilibrated in nitrogen all further studies with the various inert gases were done using this profile of exposure and decompression to altitude. Three pigs were run in replicate (up to three flights each) in nitrogen, helium, and crude neon and singly (one flight each) in pure neon and in argon. Three additional pigs were included in some gas mixtures. Overall data are summarized in Table IV.

Table IV lists the time in minutes (from the beginning of decompression) to the appearance of first signs of minor, definite, and serious symptoms of decompression sickness and scores each animal for each flight on a relative overall bends hazard scale (final category: 1 to 4). Thirty two overall flights were done: seven in nitrogen, ten in helium, eight in crude neon, three each in pure neon and argon, and an additional flight in a modified mixture of helium-neon. This last case is not included in our data analyses.

Grossly it was observed that argon was extremely hazardous in terms of severity of decompression sickness symptoms; nitrogen and helium were similar in behavior and somewhat hazardous and crude neon and neon were relatively safe. Individual differences between animals were seen in their behavior toward a given gas mixture and variability was sometimes noted for a given animal upon repeated decompression in the same gas mixture.

In order to better express the relative behavior of the different gas mixtures tested we have summarized in Figure 9 the decompression sickness category score (arrived at for each flight from an overall consideration of symptoms observed) as a function of gas mixture for each

TABLE IV

DECOMPRESSION DATA SUMMARY

Gas	Pig	Date	Wt Lbs	Time From Beginning of Decompression to the First Sign (MINUTES)			Total Time of RUN (MINUTES)	Final Category of Signs	Treated ?
				MINOR	DEFINITE	SERIOUS			
N_2	KITTY	26 MAY	70	19	21	-	23	3	YES
N_2	RUPERT	27 MAY	77	8	9	12	12	4	YES
N_2	DONALD	28 MAY	60	13	25	27	27	3	YES
N_2	FENIMOR	1 JUNE	35	25	-	-	40	2	NO
N_2	SALLY	10 JUNE	68	-	-	-	47	1	NO
N_2	LUCY	11 JUNE	69	14	15	16	18.5	4	YES
N_2	DONALD	14 JULY	72	21	24	-	32.3	3	NO
He	DONALD	14 JUNE	61	12	20	-	32	2.5	NO
He	KITTY	15 JUNE	73	13	14	-	19.5	3	YES
He	SALLY	16 JUNE	68	-	-	-	52	1	NO
He	LUCY	17 JUNE	72	10	14	-	33	3	YES
He	DONALD	18 JUNE	62	16	28	-	37	3	NO
He	KITTY	21 JUNE	75	15	18	-	30	2.5	NO
He	LUCY	22 JUNE	78	11	12	13	13	4	YES

TABLE IV (cont)

Gas	Pig	Date	Wt Lbs	Time From Beginning of Decompression to the First Sign (MINUTES)			Total Time of RUN (MINUTES)	Final Category	Treated ?
				MINOR	DEFINITE	SERIOUS			
He	DONALD	23 JUNE	63	27	30	-	34	2.5	NO
He	KITTY	24 JUNE	75	16	17.5	-	19	3	NO
He	LUCY	25 JUNE	77	12	-	-	42	2	NO
Ne*	DONALD	28 JUNE	62	21	-	-	43	2	NO
Ne*	KITTY	29 JUNE	73	-	-	-	21	1	NO
Ne*	LUCY	30 JUNE	76	42	-	-	47	2	NO
Ne**	DONALD	1 JULY	64	19	-	-	47	2	NO
Ne*	KITTY	3 JULY	74	28	-	-	47	2	NO
Ne*	LUCY	4 JULY	75	-	-	-	47	1	NO
Ne*	DONALD	5 JULY	65	33	-	-	47	2	NO
Ne*	KITTY	6 JULY	76	14	-	-	47	2	NO
Ne*	LUCY	7 JULY	83	21	-	-	47	2	NO

TABLE IV (cont)

Gas	Pig	Date	Wt Lbs	Time From Beginning of Decompression to the First Sign (MINUTES)			Total Time of RUN (MINUTES)	Final Category	Treated ?
				MINOR	DEFINITE	SERIOUS			
Neon	DONALD	8 JULY	64	24	-	-	47	1.5	NO
Neon	KITTY	9 JULY	76	14	-	-	47	2	NO
Neon	LUCY	10 JULY	83	-	-	-	47	1	NO
Ar	DONALD	11 JULY	75	9	10	11	11.5	4	YES
Ar	LUCY	12 JULY	80	9.5	10	10.5	10.5	4	YES
Ar	SALLY	13 JULY	69	7	7.5	8	8.6	4	YES

* CRUDE NEON MIX made up approximately of
60-75 Percent NEON
20-40 Percent HELIUM
00-05 Percent NITROGEN

** HELIUM - NEON MIX made up approximately of
42 Percent HELIUM
39 Percent NEON
4 Percent NITROGEN

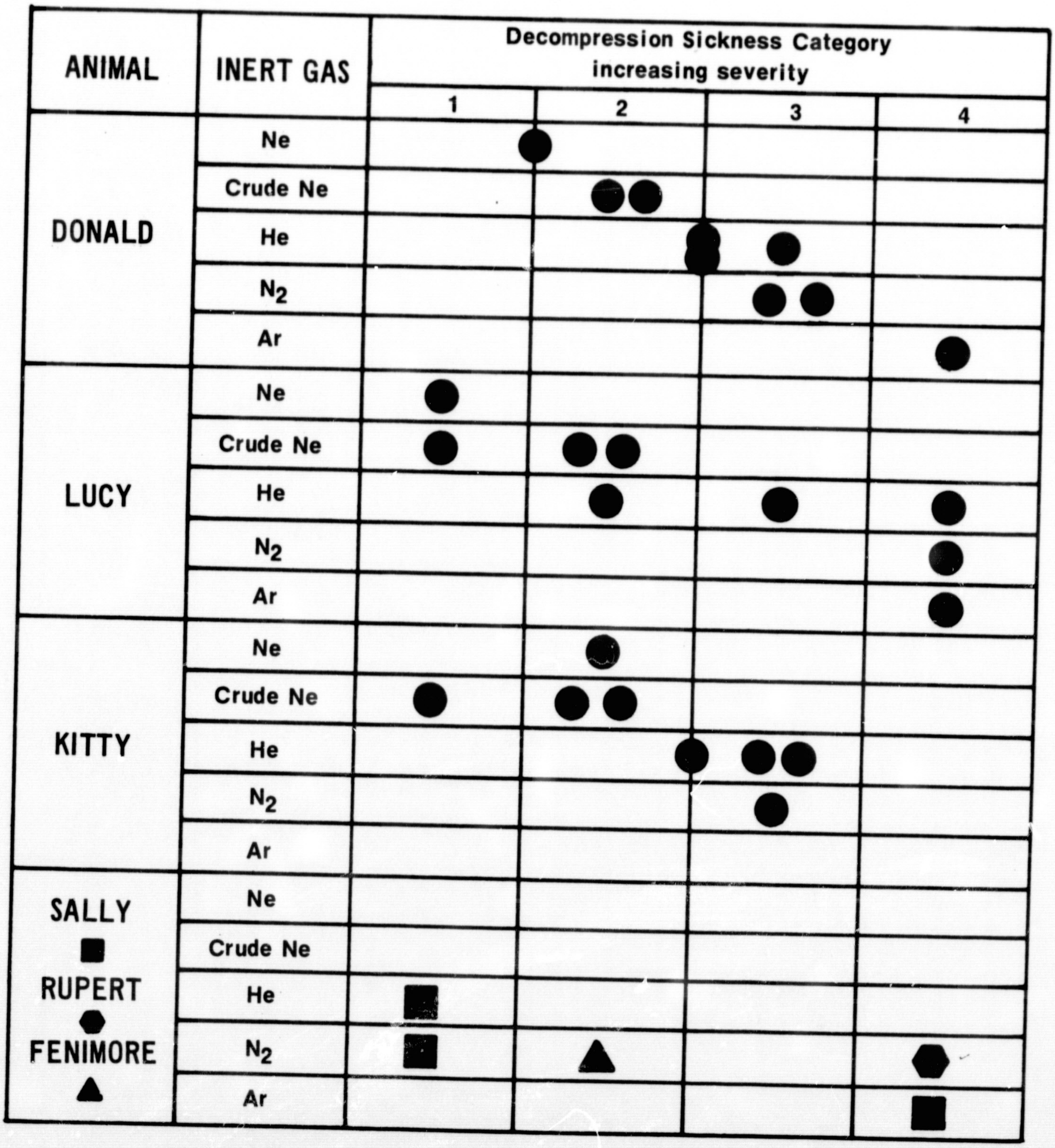


Figure 9. Distribution of Decompression Sickness Severity According to Animal and Inert Gas

individual pig. A definite trend among the several gases could be seen and the gases are listed in rank of increasing decompression hazard in Figure 9. The ranking remains the same in spite of relative differences in response of individual animals. Thus the order of increasing hazard is·

$$Ne < \text{Crude } Ne < He < N_2 < Ar$$

Individual pigs appear to differ somewhat in decompression susceptibility and in variability of response. This can be seen by taking average scores from Figure 9 for each of the multiply decompressed three pigs.

	Ne	Crude Ne	He	N_2	Ar
DONALD	1.5	2	2.7	3	4
LUCY	1	1.7	3	4	4
KITTY	2	1.7	2.8	3	-

Lucy appears to be least susceptible of the three pigs in neon but most susceptible in nitrogen. Donald appears to be quite constant in his repetitive response to a gas mixture while Lucy appears to be variable in repetitive response. Probably no sex dependence of decompression susceptibility exists since Donald (male) was essentially as susceptible as Kitty (female) or Lucy (female).

Without regard to the unequal involvement of individual pigs in repetitive flights on any one gas mixture, we have summarized the overall frequency of occurrence of decompression sickness symptoms as a function of gas mixture in Table V. Considering <u>serious</u> symptoms the ranking of gases is:

$$Ar \gg N_2 > He > \text{Crude } Ne = Ne$$

Considering <u>definite</u> symptoms the rank is:

$$Ar > He = N_2 > Ne > \text{Crude } Ne$$

On any basis the frequency of occurrence of observable evidence of decompression sickness suggests an advantage of neon and crude neon over the other gases.

TABLE V

Summary of Frequency of Occurrence of Decompression Sickness Symptoms

	Number of Hits / Total Flights (and %)		
Grade of Symptoms:	Minor	Definite	Serious
Argon	3/3 (100)	3/3 (100)	3/3 (100)
Nitrogen	7/8 (88)	6/8 (75)	2/8 (25)
Helium	9/10 (90)	8/10 (80)	1/10 (10)
Crude Neon	6/8 (75)	2/8 (25)	0/8 (0)
Neon	2/3 (66)	2/3 (66)	0/3 (0)

All flights (experiments) are included; therefore each individual animal may occur up to 3 times (3 separate flights) in a single gas; see text for details.

B. Analysis of Decompression Results

Two types of analysis of our decompression results have been made in an attempt to indicate the basis of the observed relative ranking of the inert gas mixtures in terms of decompression hazard. In one case we have considered the concept of relative tissue inert gas supersaturation and of a limiting supersaturation determining bubble formation probability. In the second approach we have looked for correlations between our experimental data and a parameter expressing relative bubble growth capacity--the bubble factors calculated by Roth (4) for various inert gases.

In one we have computed inert gas tensions for five compartments of our model of tissue inert gas transport for the flight profile used and for each gas mixture studied. Computations were made for the individual and sum of partial pressures of inert gases present and the relative supersaturation attained at altitude (ambient pressure=105 mm Hg), that is the Haldane ratios for times ranging from first reaching altitude (t=O) to about 20 minutes after arrival at altitude.

In our gas transport model discussed in Appendix A we assume exponential gas uptake and release from a series of theoretical parallel gas exchange compartments characterized by a spectrum of blood flows ($\dot{Q}$) and fat-like fractions (ranging from 0 to 100%fat-like). The fat-water composition of a compartment and corresponding fat and water solubilities for each inert gas determine the specific time constant for the kinetics of uptake and release of each inert gas.

Calculations for Haldane ratios for each compartment and each gas at three times after reaching altitude on Profile IV (Figure 8) are tabulated in Table IV.

The profile used is quite stressful in that high Haldane ratios occur for even very short half time compartments and extremely high

Haldane ratios occur for the slower compartments. In man one would not expect to deal with ratios much beyond 3 or 4 in the very slowest compartments. Rodents however will sustain ratios of perhaps 5 in limiting compartments without decompression sickness.

No obvious relation exists between the maximum Haldane ratios attained on arrival at altitude and the observed decompression hazard; indeed almost the reverse exists for slower compartments where one finds higher ratios for the safer gas mixtures.

We have considered the complicating factor of residual nitrogen in the slower compartments. Indeed nitrogen present initially is not completely lost during the 20-24 hour equilibration to another gas mixture without nitrogen. Table VII shows computed results for helium exposure and for crude neon exposure. After 20-24 hour saturation and decompression to 105 mm, one arrives at altitude with some 80 mm of nitrogen remaining in compartment 15. Because of the long half time for nitrogen this partial pressure barely declines during the observation period of residence at altitude. It is doubtful that this residual nitrogen could afford an advantage to neon mixtures compared to helium.

While computed Haldane ratios for all compartments at selected time intervals are shown in Table VI we have selected compartment 7 for further analysis in Figure 10. Haldane ratios are shown as the solid line versus time after arrival at altitudes. Superimposed are symbols indicating the actual times at which definite decompression sickness symptoms were observed in individual pigs. Hits over total flights are shown opposite each gas. From these curves one can determine the Haldane ratio prevailing for compartment No. 7 at the time a "hit" or symptom occurred. This is summarized in Figure 11.

It would appear that nitrogen and argon "hits" may occur at higher Haldane ratios than neon or helium "hits". Helium would appear to

TABLE VI

Computed Haldane Ratios for Dissolved Inert Gases in 5 Perfusion Limited Tissue Compartments at Various Times after Reaching Altitude (105 mm Hg)

Compartment	Time Mins	Ne	Crude Ne	He	N_2	Ar
1	0	2.64	2.64	2.65	3.82	3.81
1	9.4	0.35	0.35	0.35	1.08	1.07
1	19.4	0.08	0.08	0.03	0.31	0.31
5	0	4.97	4.92	4.79	5.74	5.78
5	9.4	2.44	2.36	2.16	3.74	3.87
5	19.4	1.16	1.10	0.94	2.37	2.52
7	0	5.71	5.63	5.45	6.48	6.48
7	9.4	3.73	3.57	3.20	5.39	5.44
7	19.4	2.37	2.21	1.83	4.43	4.52
11	0	6.62	6.59	6.55	6.91	6.88
11	9.4	5.81	5.72	5.55	6.55	6.52
11	19.4	5.05	4.93	4.66	6.18	6.17
15	0	7.62	7.61	7.66	6.84	6.74
15	9.4	7.35	7.33	7.34	6.73	6.64
15	19.4	7.08	7.04	7.01	6.62	6.54

TABLE VII

Computed Tissue Inert Gas Tensions (π-Values) for each Gas Present in Various Compartments at Times after Reaching Altitude

	Time	Helium		Crude Neon		
Compartment	Mins	N_2 mm	He mm	N_2 mm	Ne mm	He mm
1	0	2.3	276	4.6	188	85
	19.4	0.2	8.4	3.7	5.8	2.6
5	0	3.4	500	7.0	355	154
	19.4	1.4	97.4	2.9	82.6	30
7	0	3.9	569	7.9	408	175
	19.4	2.7	189	5.4	169	58
11	0	4.7	683	8.9	473	210
	19.4	4.2	485	7.9	360	150
15	0	81	723	85	492	223
	19.4	79	657	82	455	202

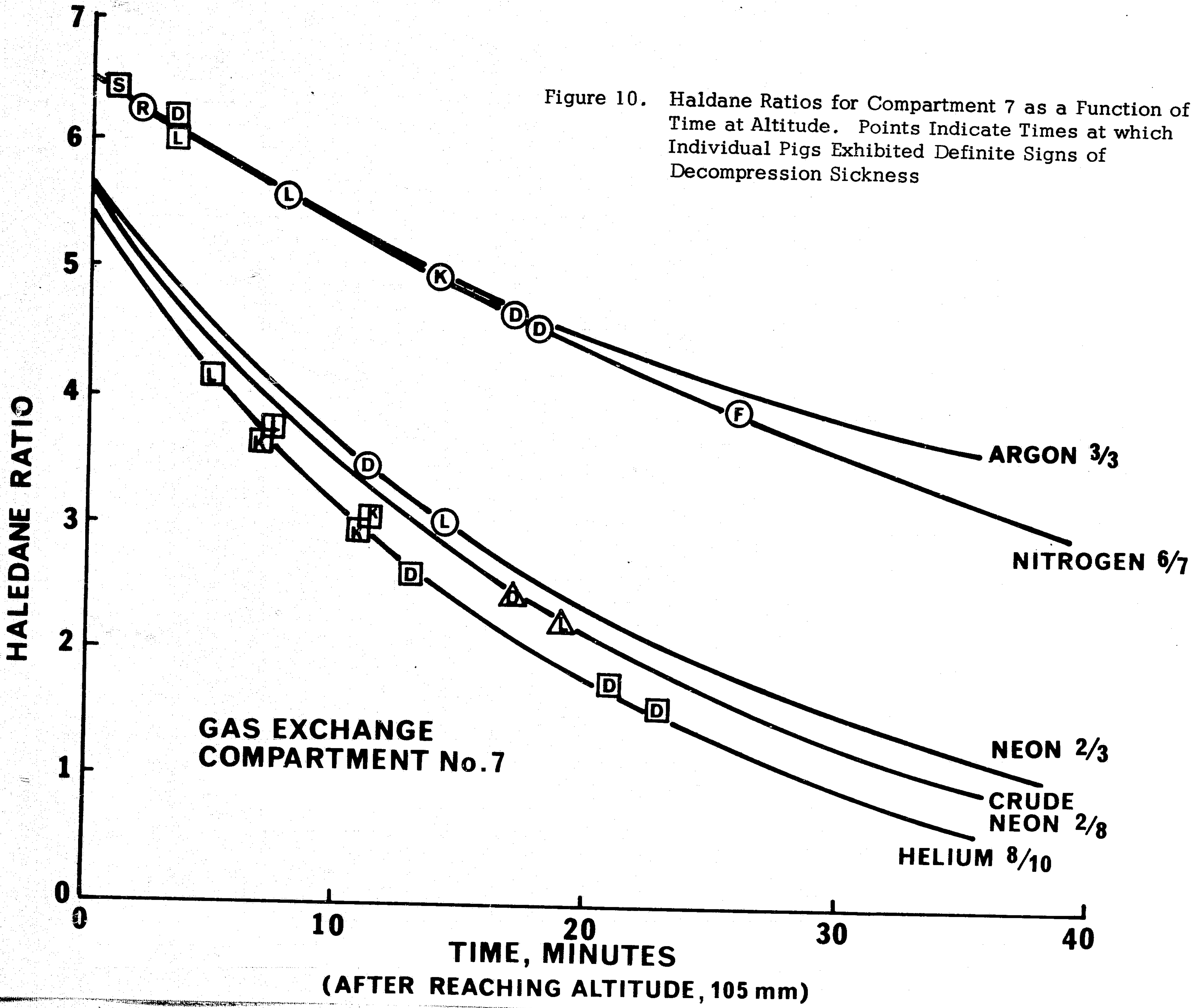


Figure 10. Haldane Ratios for Compartment 7 as a Function of Time at Altitude. Points Indicate Times at which Individual Pigs Exhibited Definite Signs of Decompression Sickness

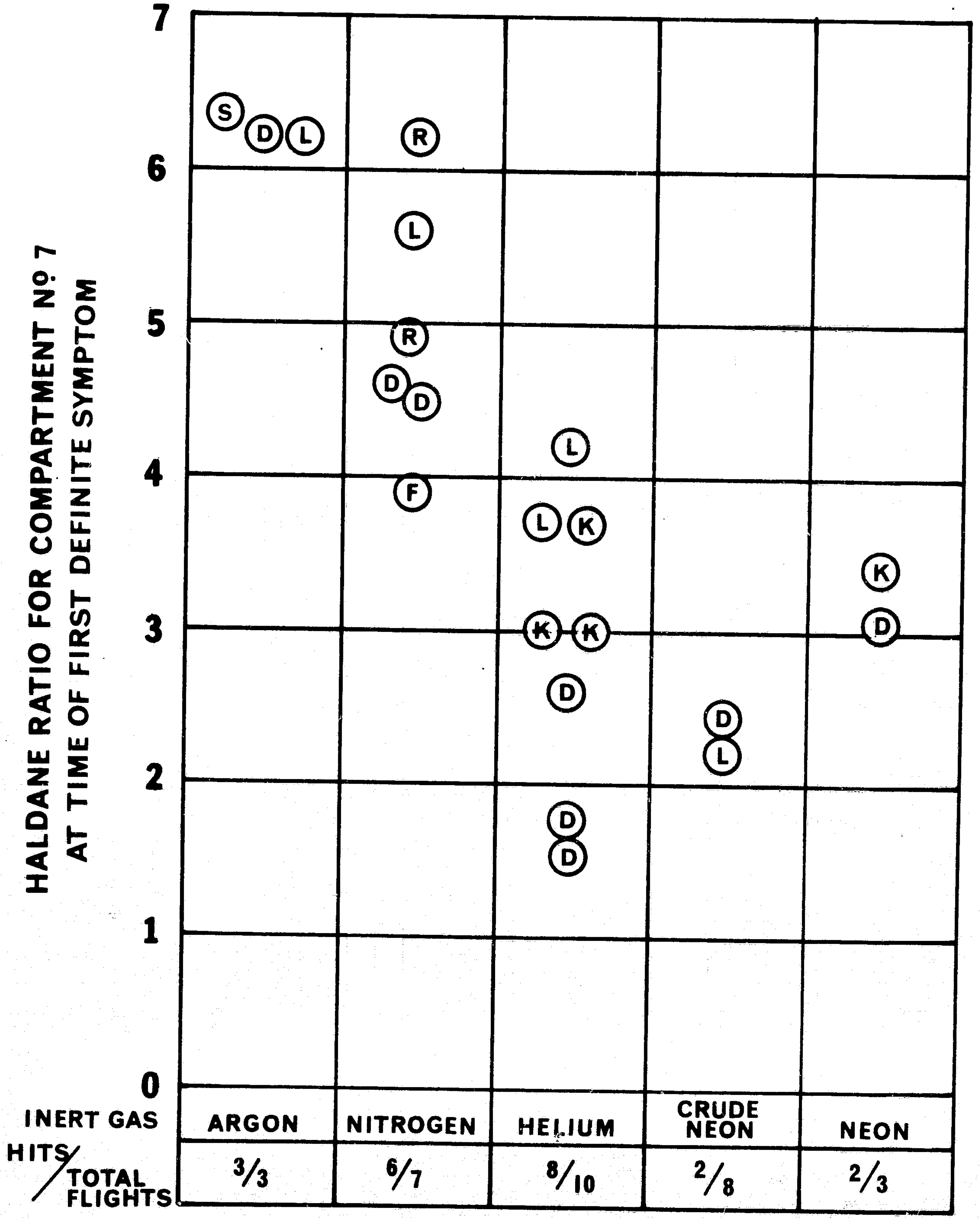


Figure 11. Haldane Ratios for Gas Exchange Compartment No. 7 at Time of First Definite Symptoms of Decompression Sickness

remain potentially hazardous even after the Haldane ratio has decreased markedly below its maximum value. This would suggest that even though the probability of getting bubbles to form had decreased markedly (assuming supersaturation concepts of decompression) significant and frequent hits will still occur in helium. Too few observations are available to say anything in this regard for pure neon; however, for crude neon, while hits appear to occur at Haldane ratios comparable to helium, the frequency is very much less. Similar conclusions were arrived at by corresponding analysis of other compartments.

In a second line of analysis of the decompression data we looked to a possible correlation between bubble growth determining parameters and the relative decompression hazard scores arrived at for the several gas mixtures. Roth (4) in his comprehensive discussion of physiological factors of inert gases in space-cabin atmospheres developed the concept of various classes of bubbles to be considered in decompression sickness. He calculated gas-specific bubble factors which would be determinants of peak bubble size. Roth considered the following classes of bubbles and their dependence for growth on solubility, α, and diffussivity, D, in fat, blood, and connective tissue:

<u>Type</u>	
1.	bubbles forming autochthonously in adipose tissue
2-1	bubbles forming intravascularly within adipose tissue and remaining <u>in situ</u> (early bubble)
2-2	bubbles forming intravascularly within adipose tissue and remaining <u>in situ</u> (late bubble)
3	bubbles forming intravascularly in adipose tissue or muscle and lodging in a vessel at a remote site
4	bubbles forming extravascularly as a gas pocket (eg. in connective tissue)

Calculated bubble factors (relative values) are tabulated in Appendix B and were used to plot Figure 12 and 13 in an attempt to observe any correlations between our relative decompression hazard scores for the various gases and a parameter related to bubble growth. Relatively poor or no correlation exists between decompression hazard score and bubble factors for type 1 or type 2-1 bubbles; reasonably good correlation exists between decompression hazard score and bubble factors for type 2-2 or types 3 or 4 bubbles. Bubble factors for crude neon were calculated by proportion from our gas compositions and factors for helium and neon.

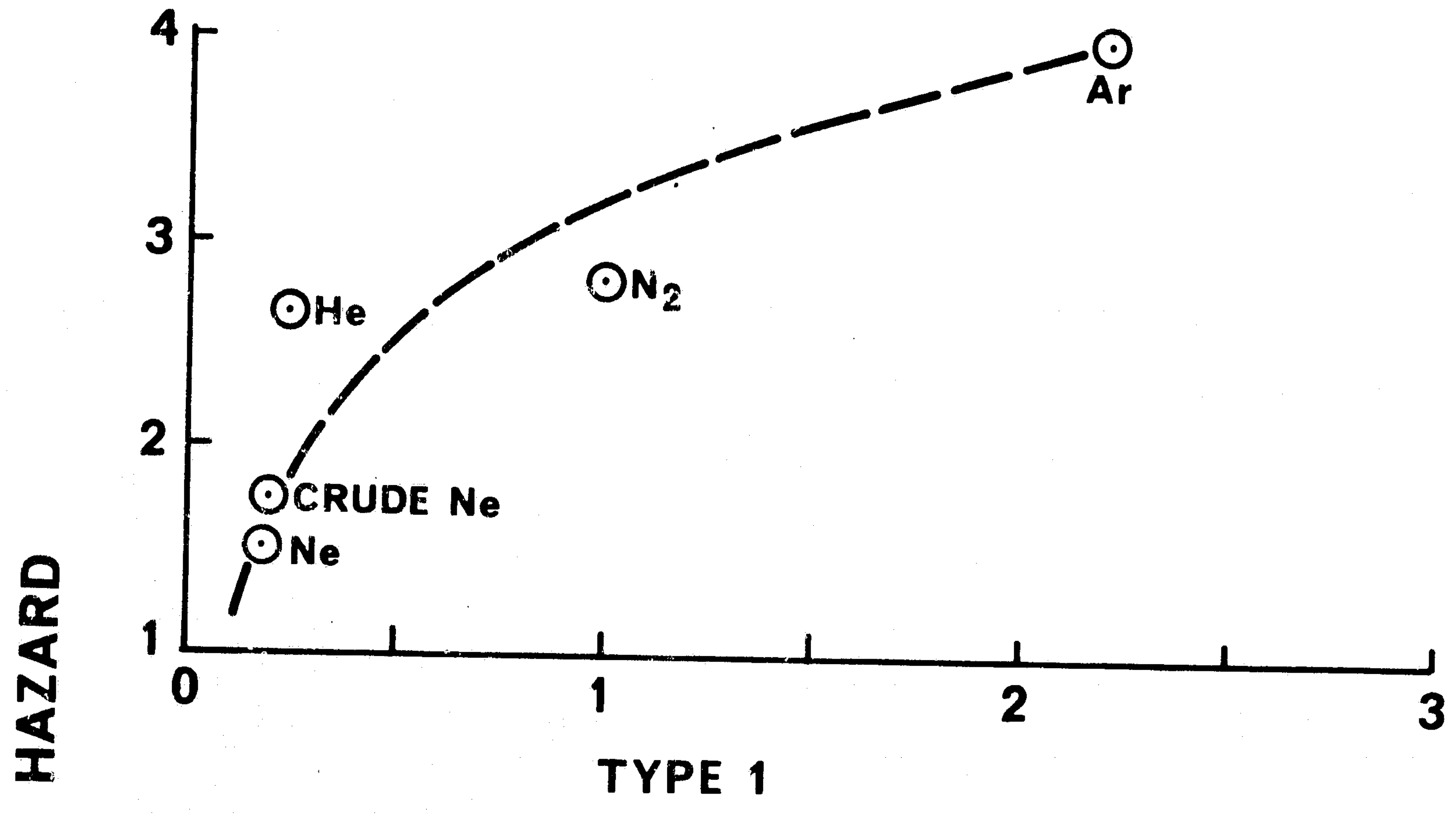


Figure 12A. Relation Between Decompression Hazard and Bubble Factors (Type 1) for Various Gas Mixtures

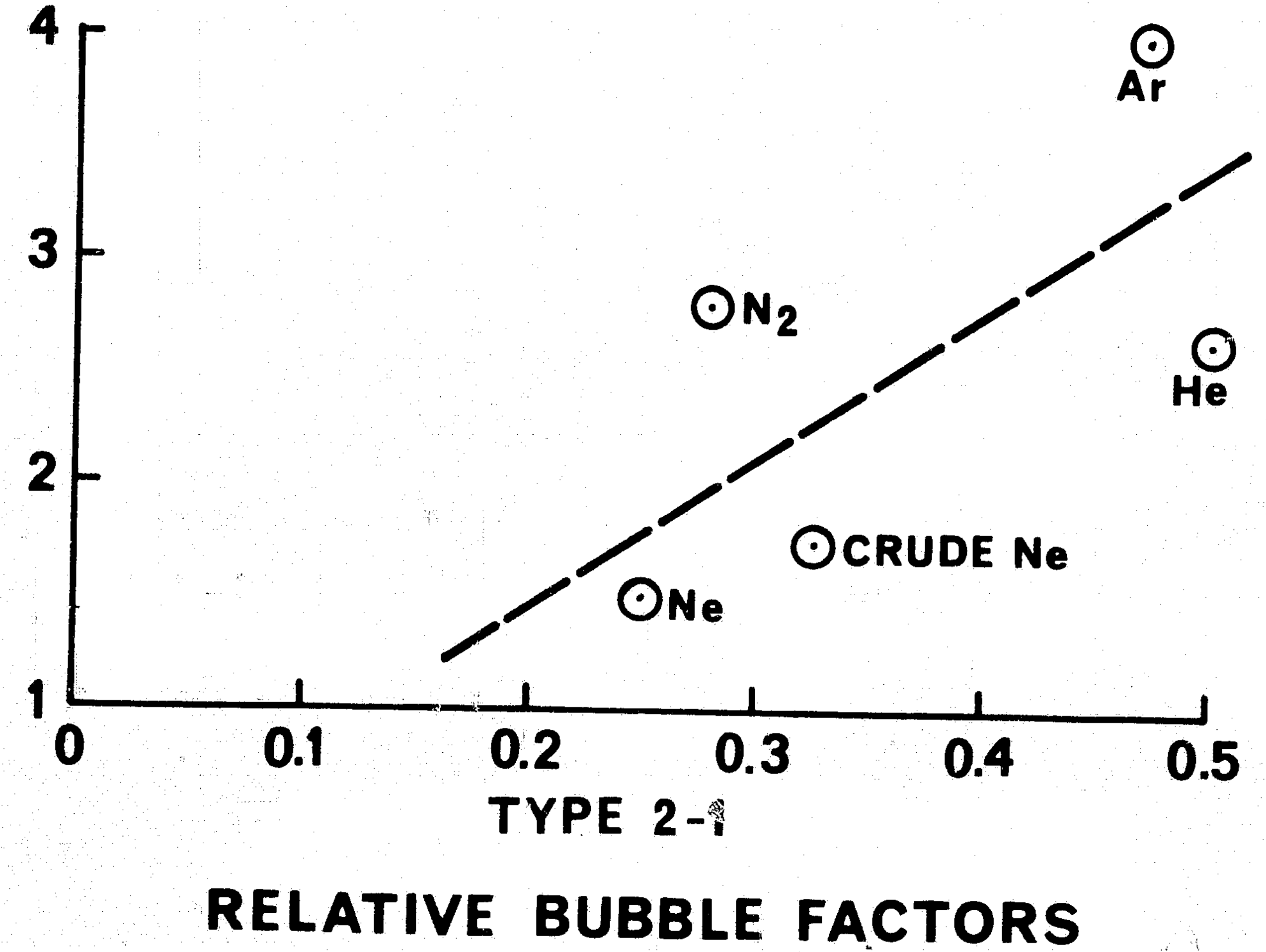


Figure 12B. Relation Between Decompression Hazard and Bubble Factors (Type 2-1)

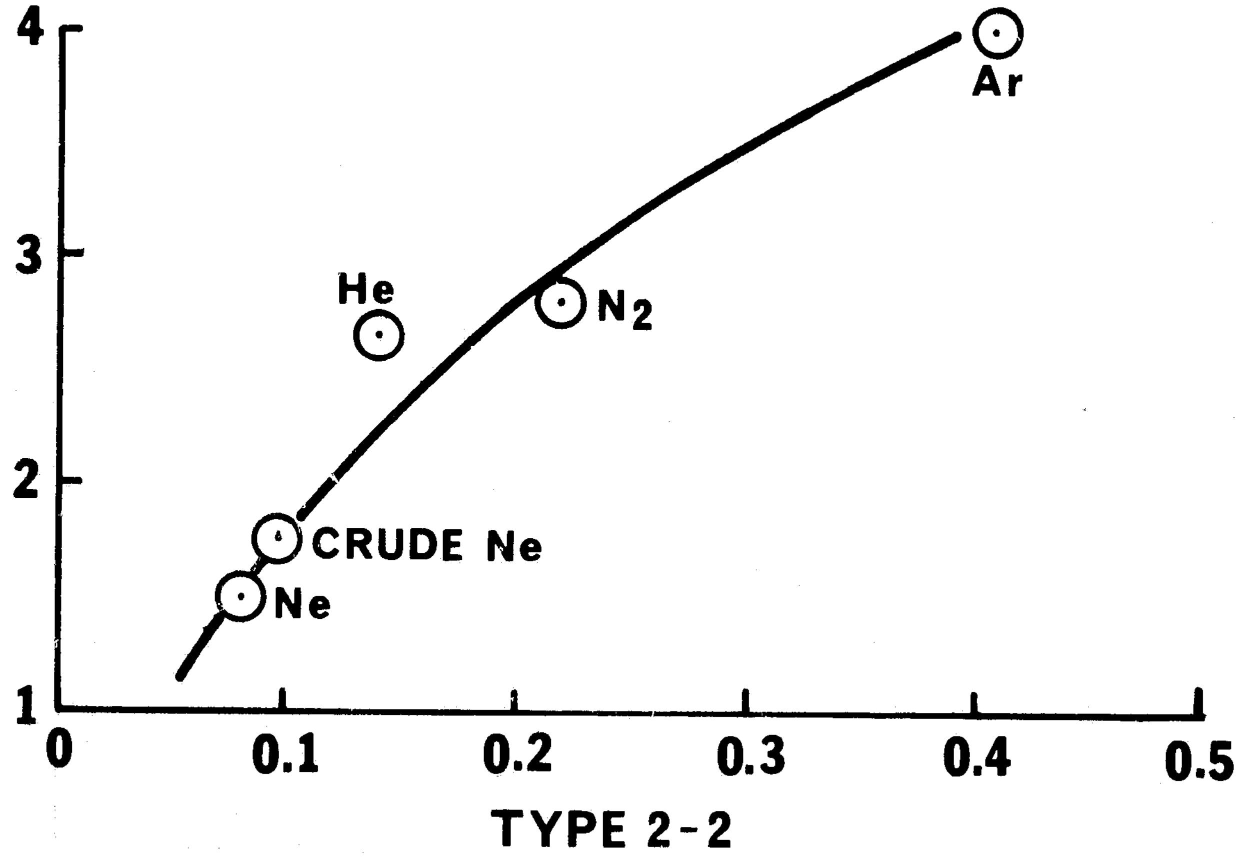


Figure 13A. Relation Between Decompression Hazard and Bubble Factors (Type 2-2)

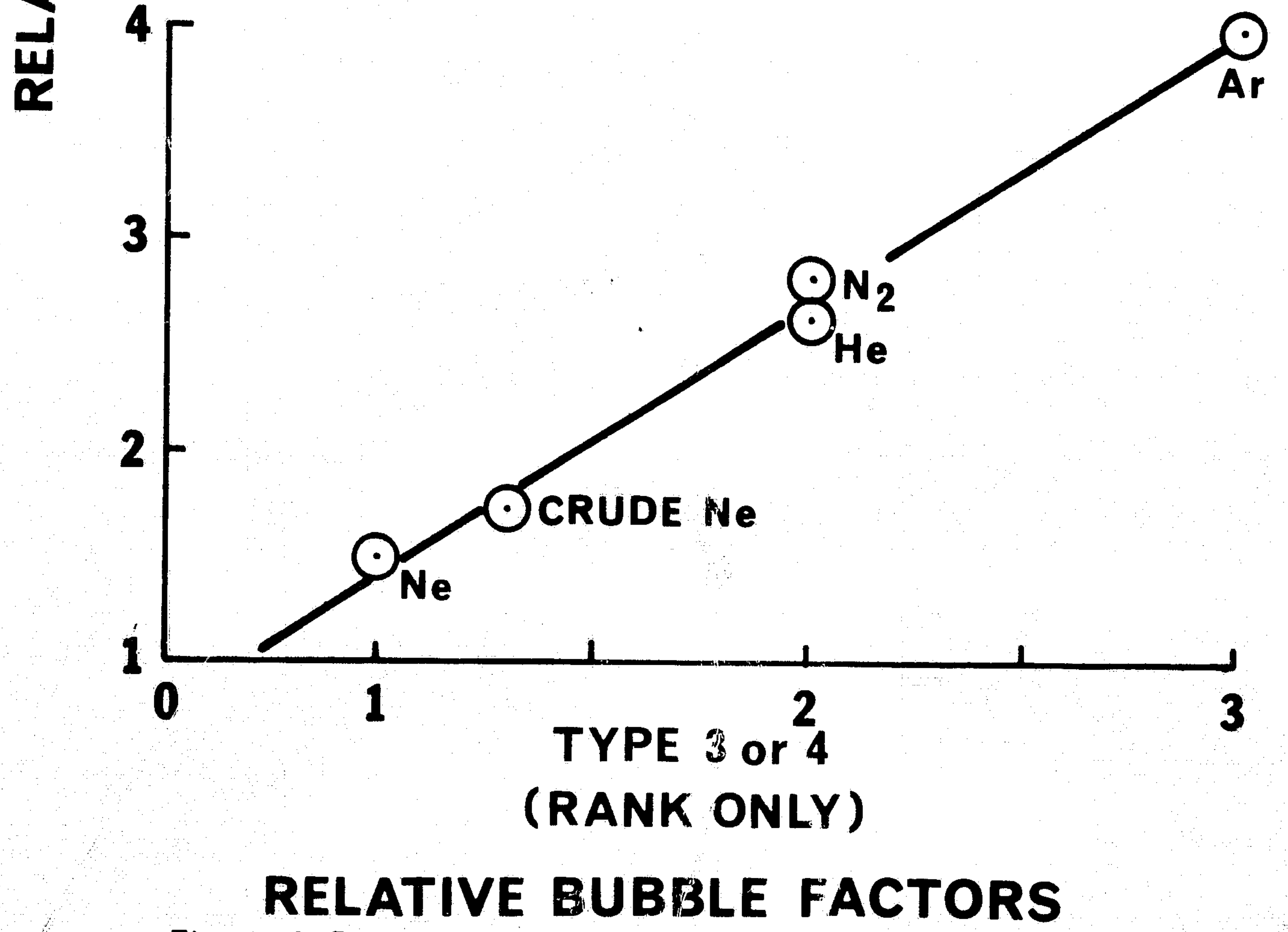


Figure 13B. Relation Between Decompression Hazard and Bubble Factors (Types 3 or 4)

V. DISCUSSION

The miniature pig appears to be a useful model for the study of altitude decompression sickness. While we agree with Gillis (22) that the pig is more resistant to decompression sickness than man, we would disagree that ear trouble is related only to pressure decrease; it appears to be related only to rapid pressure change. Pigs appear quite susceptible to hypoxia and attention to its avoidance especially in altitude decompressions is essential. Confounding factors in interpreting decompression sickness are bloating, vertigo, and hypoxia. Overall, however, it appears that the pig is a consistent and relatively sensitive model. Repeating a nitrogen flight after completing the several gases in order gave almost exactly the response shown by the particular pig some six weeks before. The pigs do appear to differ somewhat in variability of response to a given gas and in susceptibility to different inert gas exposures.

Comparison of five inert gas mixtures on the basis of overall decompression sickness responses and for individual animals on the basis of repeated decompressions in each gas clearly established the relative order of decompression risk and reasonably well afforded a quantitative basis for the ranking of relative risk. Crude neon was substantially less likely to cause decompression sickness signs, and pure neon seems perhaps even better - none of the animals developed serious decompression sickness symptoms using either of these gases. Argon caused rapid and serious symptoms on the profile used. Neon and helium were clearly separated, in response, in contrast to results obtained previously by us and by other investigators in which decompression from depth could not clearly separate these gases in response. We could not, however, clearly separate nitrogen and helium. A series of different decompression profiles will probably be necessary to accomplish this.

We initially hoped to separate the gases on the basis of safe-unsafe profiles without regard to grading symptoms. In practice this did not turn out to be a practical approach. On the profile used, however, the overall well being of the pigs in neon and crude neon was obviously better than nitrogen or helium. Argon, similarly, was obviously more hazardous.

Our data clearly suggest the ranking of the gases studied in the order of increasing decompression hazard as:

$$\text{Ne} < \text{Crude Neon} < \text{He} < N_2 < \text{Ar}$$

We are not able to explain the relative ranking or the quantitative scores on the basis of analysis of the profile in terms of computed inert gas loadings or Haldane ratios for any selected compartments - either maximum ratios upon arrival at altitude or ratios at the time of appearance of first symptoms.

In earlier studies of manned altitude decompressions Schreiner (27) was able to make accurate predictions of the relative decompression hazard associated with various flight profiles based on a consideration of compartment 15 gas loading, especially maximum Haldane ratios, when only nitrogen was present. No predictions of risk of decompression could be developed however on this basis when both nitrogen and helium were present in the tissues. He concluded also that given a particular target pressure and a computed maximum value of π_{N_2} for the No.15 compartment at that pressure, the risk of decompression sickness, all other factors being equal, would depend upon the duration of residence at the target pressure. This conclusion did not appear to be supported in the pig in which for a given gas and profile no prediction of risk could be made from computed Haldane ratios. It should be noted, however, that the profile used gave extremely high Haldane ratios for especially the slower gas exchange compartments.

For different gases, i.e. nitrogen compared to helium, tolerated degrees of relative supersaturation with widely differing risks of decompression sickness appeared to exist.

Roth (4) first suggested on theoretical grounds that neon should have a decompression advantage over helium. The data of this report appear to bear out these predictions. We found reasonably good correlation between Roth's bubble factors for type 2 - phase 2 bubbles and types 3 or 4 bubbles and overall quantitative scores for the decompression symptoms found with the five gas mixtures tested. These bubble factors are based on the product of solubility and diffusivity and hence the correlations observed suggest a distinction among the gases on the basis of how fast and to what extent bubbles grow rather than the probability of initial formation.

Neon appears to be an advantageous inert gas for both diving and spacecraft application from the standpoint of decompression risk. Data now available on rodents, pigs, and limited exposure of man in concert with a reasonable theoretical basis would suggest strongly that neon and neon mixtures should be further explored in human experimentation.

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APPENDIX A

Mathematical Analysis of Inert Gas Exchange

A simple mathematical model of inert gas transport has been used extensively in our Laboratory for the computation of partial pressures of inert gases dissolved in various body compartments as a function of total pressure, time, and composition of the breathing mixture. This model, designated "Tonawanda II" has been discussed by Schreiner (27) in a previous NASA contract report (NAS 9-6978). It considers inert gas transport as being limited by tissue perfusion. It also assumes that the probability of an inert gas remaining in supersaturated solution in tissues is dependent on the magnitude of this supersaturation relative to the prevailing ambient pressure. We assume complete equilibration of inert gas partial pressure between blood and alveoli and between capillary blood and tissues.

The alveolar partial pressure of inert gas is calculated from the alveolar nitrogen equation of Rahn and Fenn assuming a respiratory quotient of 0.8 and alveolar P_{CO_2} = 40 mm Hg. This gives the alveolar partial pressure:

$$P_{A_{IG}} = F_{I_{IG}} (B - 37)$$

B = barometric pressure

$F_{I_{IG}}$ = fraction of inert gas in dry inspired gas

Using the basic gas transport equation:

$$\frac{d\pi}{dt} = k\,(P - \pi)$$

any inert gas partial pressure, π, can be calculated for any time at a fixed pressure, P. In the calculations discussed in this report we chose to use a simple step-wise approximation of the actual decompression profile used.

The specific time constants for the several inert gases were calculated using the half time values shown in Table VIII.

$$t_{\frac{1}{2}} = \frac{\ln 2}{k}$$

In our model the $t_{\frac{1}{2}}$ values are actually determined by the gas solubilities, fat contents and blood flows of the compartments.

$$k = \dot{Q}\,\frac{\alpha\,\text{blood}}{\alpha\,\text{tissue}}$$

where $\alpha_{\text{tissue}} = (1 - X)\,\alpha_{\text{water}} + X \cdot \alpha_{\text{fat}}$

$\alpha_{\text{blood}} = \alpha_{\text{water}}$

X = fat fraction

The entire profile, including equilibration with inert gas for 20-24 hours, was divided into approximate step changes and computations suitably performed by computer. The compartments used and their definition as well as corresponding half-times for the various gases for each compartment are summarized in Table VIII.

TABLE VIII

Description of Inert Gas Exchange Compartments Employed in Computer Analysis of Decompression Profiles

Compartment No.	1	5	7	11	15
$\dot{Q}$, min.$^{-1}$	0.3	0.1	0.1	0.03	0.0085
Fat-like Fraction	0.3	0.3	1.0	1.0	1.0
$t_{\frac{1}{2}}$ He, min.	3	8	12	39	139
$t_{\frac{1}{2}}$ Ne, min.	3	9	15	49	171
$t_{\frac{1}{2}}$ N_2, min.	5	15	35	118	416
$t_{\frac{1}{2}}$ Ar, min.	5	16	37	122	432

See NASA CR-1694 (1970) for a more complete listing of compartments in the 15 compartment model.

APPENDIX B

TABLE IX

Some Properties of Inert Gases Relevant to Decompression

	Helium	Neon	Argon	Nitrogen
Solubility, water, 38°, α	0.0086	0.0097	0.026	0.013
Solubility, fat, 38°, α	0.015	0.019	0.14	0.061
Oil/water Sol.Ratio	1.7	2.1	5.3	5.1
Diffusivity in Oil, 37° cm^2/sec	18.6	8.34	5.92	7.04
Diffusivity in Water, 37°, cm^2/sec	79.2	34.80	25.20	30.10
Relative Bubble Factors: $N_2 = 1$				
Type 1	0.24	0.17	2.2	1.0
Type 2-1	1.80	0.88	1.7	1.0
Type 2-2	0.64	0.34	1.9	2.0
Type 3 (Rank)	2.00	1.00	3.0	2.0
Type 4 (Rank)	2.00	1.00	3.0	2.0

Reference: Roth (1967), reference 4 of this report.