THE IMPORTANCE OF TISSUE UNSATURATION IN THE CALCULATION OF SAFER DECOMPRESSION SCHEDULES

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CONTENTS

This thesis contains no material which has been accepted for the award of any other degree or diploma in any University and to the best of the author's knowledge and belief the thesis contains no material previously published or written by another person except where due reference is made in the text of the thesis.

Signed . . . . . .

DECLARATION AND ACKNOWLEDGEMENTS

I declare that this thesis is of my own composition and that it is a record of the original work conducted during the years 1970 and 1971 in the Department of Human Physiology and Pharmacology, University of Adelaide. The work described herein has not been submitted for any other degree award or diploma.

I wish to record my gratitude to the Committee of Management of the Aeromedical Research Laboratory (AMRL) for facilities offered and support received while working on this thesis. In particular I would like to thank Dr. D.H. Le Messurier, Officer-in-Charge of the Aeromedical Research Laboratory under whose guidance this work was carried out, for all the assistance he has given, his enthusiastic support of the projects undertaken and his valuable criticisms.

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INTRODUCTION

1.0 GENERAL INTRODUCTION

In his working environment, man has always been subjected to hazards which have affected his safety, health and well being and often caused suffering and economic loss. In recent times much has been done towards reducing industrial injuries and sickness, but many problems still remain. Not the least of these is the painful disabling and even fatal condition known as decompression sickness. This results from a 'rapid' reduction in ambient pressure of working environment, e.g., after working in a compressed air environment (caisson work), following diving operations, or on ascent to a rarefied atmosphere.

The research described in this report covers a study of a mathematical model of the physical and physiological factors concerned with decompression sickness. An account is given of equipment designed and developed to study one important parameter of this model, namely, the total gas tension in the tissue. In addition a series of experiments was carried out on animals and the author himself to measure changes in this parameter under environmental conditions equivalent to those met with when exposed to high altitudes.

2.0 WHAT IS DECOMPRESSION SICKNESS?

Under normal conditions man lives and works surrounded by air which at sea level exerts an average barometric pressure of 760mmHg. However, certain occupations require work to be carried out in pressures above the normal barometric pressure but on returning to normal, the reduction in pressure may cause physiological changes which give rise to a set of symptoms known as "decompression sickness."

The symptoms can vary in site and severity and include :-

- Skin itch
- Fatigue
- Swelling of lymph nodes
- "Bends" - aches and pains, usually associated with joints
- Dizziness, confusion and nausea
- Visual disturbances
- Respiratory disturbances - "Chokes"
- Motor weakness
- Parasthesia
- Paralysis
- Death

Kidd[1] quotes one simple classification of decompression sickness symptoms into two categories designated Type I and Type II.

Type I covers all symptoms involving the lymphatics or cutaneous tissue and all cases where pain is the only symptom.

Type II includes all of the more severe symptoms with central nervous system, circulatory and respiratory involvement.

Alternatively symptoms of decompression sickness may also occur at high altitudes where the barometric pressure is reduced.

The history of development of scientific and medical thought on the aetiology of decompression sickness is reviewed below. Occupations where people are subjected to changes in environmental pressure which may lead to the development of symptoms of decompression sickness are also discussed.

3.0 REVIEW OF AETIOLOGY OF DECOMPRESSION SICKNESS

Skin diving by breath holding pre-dates recorded history. In 460 B.C. Heredotus writes of a Greek diver employed to recover treasure from sunken ships, while Nukada[2] notes that the Ama (or 'sea-woman') of Japan, who dive for sea weed and shell fish, are mentioned in the Gishi-Wajin-Den which is believed to have been written in 268B.C. However, it was not until the mid-17th Century with the work of Robert Boyle[3] that scientific examination of the effects of changes in the environmental pressure on living organisms began. His observation of a bubble in the eye of a viper that he had placed in an evacuated chamber is often quoted, and he also propounded that the death of his experimental animals upon the sudden removal of the ambient pressure, was due to the blood of these animals effervescing so vehemently as to disturb the circulation. He also had thoughts on experimenting with man to observe the effects of reduced pressure on respiration.

Throughout the 150 years following Boyle's work, small numbers of people were exposed to increased pressures in the use of diving bells and early diving suits. There is little doubt that the diving bell was the first practical means whereby men engaged on engineering construction could work underwater in a compressed air environment. Haxton and Whyte[4] mention that the first recorded use of a pressurised diving bell was by Smeaton while repairing the foundations of a bridge over the Tyne in 1778. In 1819 Augustus Siebe devised the supply of pressurised air to a diving dress. Even in these early days problems were noted and Halley[5] describes the nature and mechanism of ear pain, while Liddell[6] in 1842 noticed that divers often suffered from rheumatism.

With the technical and engineering progress of the industrial revolution came a rapid development of underground mining for coal and minerals. In 1830 Admiral Sir Thomas Cochrane applied for a patent on a technique for "excavating,

sinking and mining"[7]. This was granted in 1831 and was in essence the technique of closing off mines or tunnels with an air lock and compressing the air inside to prevent seepage of ground water into the workings.

The first to use the compressed air technique was Triger in France in 1839 and he has been attributed with the first written account of its effects on workers. This technique was used intermittently from 1839 onwards but was not until 1879 with the tunnelling under the Hudson River in New York and under the Scheldt in Antwerp that it became used extensively. The first medical lock was also used in the Hudson River Tunnel.

Two French physicians, Pol and Watelle[8] in 1854, made the first serious study of the problems encountered in Triger's mines which, by that time, included fatalities. They recognised the fact that the miners got into trouble on being decompressed to leave the mine, but failed to discover the mechanisms of the syndromes they encountered. Based on autopsy observations they thought the problem was due to congestion of the lungs and brain.

The next 40 to 50 years yielded a profusion of theories. These ranged from racial factors where, in 1861, Brereton[9] suggested that Irish labourers were less tolerant of compressed air work, to Littleton's theory, in 1866, on "impediment of the vertical falling and rising of the brain with respiration"[10].

The similarity of afflictations suffered by tunnel workers and divers was pointed out by Leroy de Mericourt[11] in 1869 who believed in the importance of supersaturation of the blood in men decompressed after working in compressed air environs. He considered that under these conditions "Man is really, from the physiological point of view, in the situation of a bottle of artificial Seltz water".

At this time Paul Bert[12], working on a comprehensive study of hypoxia, asphyxia, oxygen poisoning and decompression sickness, believed that gaseous embolism following liberation of gas bubbles from the supersaturated blood was the underlying mechanism of decompression sickness and recommended

minimum times for decompression. Although physiology was developing rapidly at this time, most physicians at construction sites placed more faith in contemporary clinical practices of bleeding, blistering and purging.

Jaminet, working as medical supervisor at the construction of the St. Louis Bridge in 1869, managed to reduce markedly the mortality and morbidity by general care of the workers and the reduction of shift lengths. Others had similar successes but had rather vague ideas on the causes of decompression sickness.

In 1907, Haldane, Boycott and Damant[13] were appointed by the Lord Commissioners of the Admiralty to investigate deep diving. In their now classical report they expounded the concepts of multiple tissues, saturation and desaturation rates, and the principle that the ratio of initial to final absolute pressure was the factor which governed the presence or absence of symptoms. Although the evidence they cited to support their theories was scanty, it is on this work that the modern regulations governing compressed air and diving practice are founded and they undoubtably provided the greatest advance in terms of analysing and forecasting human limitations in this field.

More recently Hills[14] has carried out a rigorous mathematical analysis of the diffusion of gas in a model of the tissue. He emphasized the importance of energy considerations in predicting conditions under which phase separation of gas could occur and lead to the development of symptoms of decompression sickness.

4.0 PEOPLE SUBJECTED TO CHANGES IN THE ENVIRONMENTAL PRESSURE

4.1 HYPERBARIC STUDY

There are two broad categories of people who are subjected to hyperbaric pressures, viz., divers and caisson workers.

Divers are subjected to increasing pressure from the water as they descend and this external pressure is matched by an increase in air pressure within the lungs. This is achieved either by allowing the lungs to compress, as occurs when a "single breath" dive is made, or by supplying the diver with air at a pressure equal to the surrounding water pressure.

Caisson workers, on the other hand, work in a compressed air environment and breath the environmental air.

Each of these groups is discussed in more detail below.

4.1.1 Divers

Breath Hold Divers

The oldest form of diving is the breath hold dive where the lungs are filled with ambient air at the surface; a short working dive is made and the diver returns to the surface. Several groups of people have been diving in this manner for centuries with varying degrees of safety.

The diving Ama of Japan is probably the largest and oldest of these groups and has the safest diving pattern. Many ancient references indicate that the Ama have existed for at least 2,000 years[15].

In Japan today, Ama refers to male or female divers but the majority of Japanese Ama are female. These divers collect plants or animals from the sea bed and their diving pattern is highly developed. The more experienced Ama work in depths of 25 to 60 feet

making about 30 dives in an hour with each dive lasting from 40 to 60 seconds. They dive from a boat carrying one helper, wear goggles and have a ballast belt with a line from the belt back to the helper.

Prior to diving they regulate their respiration but do not hyperventilate and both descent and ascent are carried out with the minimum effort. To descend they carry a heavy weight and usually adopt a vertical posture which offers the minimum resistance. On completing the dive the tender pulls them quickly to the surface while the Ama once again uses the minimum physical effort[16].

Studies of the occupational health of the Amas were first made by G. Teruoka[17] in 1928, and since then others have made further studies of these groups. Although they do suffer from diving maladies, such as ear and upper respiratory tract infection, there is no definite description of decompression sickness in any of the Japanese references[18].

Another group of breath hold divers are the pearl divers of the Tuamotu Archipelago[19]. In the height of the pearling season these people dive repetitively to depths of 120 feet for up to 6 hours a day. There are two notable groups among these native divers; Tuamotans - from the island of Tuamota, and Mangarevans - from the island of Mangareva.

Prior to diving the Tuamotans hyperventilate for 4 to 6 minutes, descend rapidly with a weighted rope and shell basket, spend about 1½ minutes on the bottom gathering shell and then quickly haul themselves to the surface hand over hand up their weighted rope. Upon surfacing they immediately recommence hyperventilating and dive again after 4 to 6 minutes.

This group frequently suffer from diving maladies known as "Taravana" (meaning to fall crazily). The various symptoms of this syndrome are vertigo, nausea, mental anguish, paralysis, unconsciousness, and death. These are all indicative of circulatory

and cerebral disorders and represent the most severe manifestations of decompression sickness, however, no report has been published of recompression treatment for victims of Taravana to investigate whether this therapy will remove the various signs and symptoms.

Divers from the nearby island of Mangareva, however, never experience "Taravana". The only difference between the diving techniques of the Tuamotans and Mangarevans is in the spacing of the dives. The Mangareva divers make a descent every 12 to 15 minutes instead of every 4 to 6 minutes, and this increased surface time appears to be sufficient to prevent the occurrence of the dreaded "Taravana".

One other case of verified decompression sickness, following rigorous repetitive breath hold diving, has been reported. A Danish diving instructor, P. Paulev[20], who after spending about 5 hours in the water on repeated breath hold dives with rapid rates of ascent (100 ft/min) in a submarine escape training tank, suffered from progressive symptoms of nausea, dizziness, paresthesia of the limbs, abdominal pains, blurring of vision, and near shock. His symptoms and signs were removed by recompression.

Divers Supplied with Compressed Air

The development of diving equipment for the free swimming diver was pioneered during the Second World War and this led to the development of the present SCUBA (Self Contained Underwater Breathing Apparatus). Recently there has been a rapid increase in the popularity of diving for recreation and sport which has resulted in increasing numbers of divers getting into serious difficulties with circulatory and central nervous system symptoms of decompression sickness.

Naval divers and other professional divers make repeated short dives to inspect well heads of undersea drilling rigs, carry out salvage work and make under-

water geological surveys. Being professional or semi-professional however, they are easier to train and supervise than amateur civilian divers.

Abaloni divers off the coasts of Australia are free swimming divers supplied with compressed air from a vessel on the surface. They dive repeatedly to depths of about 50 feet to gather the abaloni shell and have found that the use of currently accepted repetitive dive tables leads to impractically long decompressions for their diving conditions. Many claim to have no faith in current tables or decompression meters.

Torres Strait Islanders, off northern Australia, perform long and deep dives to gather shell. Typically they spend up to one hour at 200 feet or more and may take three hours to decompress. These are hard hat divers clad in a half suit and supplied by compressed air from a compressor on board their diving lugger. They have developed their own decompression formats which differ from those of the tables currently in use by the U.S. Navy and British Navy but the incidence of decompression sickness among these Torres Strait Islanders appears to be no greater than that of other groups using the accepted tables[21].

With the expansion of oceanographic research and the desire to stay under water for longer periods to allow more useful amounts of work to be done, a new form of diving has been developed[22]. This involves underwater living - spending longer periods living and working under high pressure. Once the body tissues have become thoroughly saturated at the new pressure the decompression time required is thought to reach a maximum. An increase in the duration of the dive past the time taken for saturation does not increase the decompression time. In this way the ratio of useful working time to non useful decompression time is increased as the length of the dive is increased. This makes long periods of deep diving a practical proposition.

Decompression rates used for these dives are very conservative at present, being as slow as one foot every 15 minutes and under these rigorously controlled conditions serious decompression sickness has been avoided.

4.1.2 Caisson Workers

The basic principles for caisson work have remained unaltered since their conception by Sir Thomas Cochrane in 1830 and improvements have been confined to details in application. Some recent research has been aimed at the practicability of keeping workers in a raised environmental pressure for periods extending to days, weeks or even months[23]. This would hold men available for work at all times and gain an overall saving in decompression time. Whilst prolonged exposure to the pressures involved (15-45 psia.) have been proven possible - as with saturation diving - it is unlikely that civilian workers will readily accept conditions which deprive them of social and family contacts for long periods. At present, shifts and decompressions for caisson workers are organised around a daily regular return to atmospheric conditions and in Britain in recent years the decompression sickness rate has been about 1½ per cent to 2 per cent of man/decompressions[24].

4.2 HYPOBARIC PRESSURES

Decompression sickness suffered as a result of exposure to hypobaric pressures is commonly called Dysbarism.

With the development during World War II of aircraft capable of fast rates of ascent and high altitudes, there was a rapid increase in the number of men suffering from symptoms of decompression sickness and this led to an upsurge of interest in dysbarism in aviators. However, introduction in the 1950's of pressure suits and pressurised cabins virtually eliminated this problem and interest subsequently waned.

In the 1960's there was a revival of interest in dysbarism associated with manned space flights. The United States National Aeronautics and Space Administration (NASA), by using an oxygen enriched atmosphere (at a pressure of 5 psia.) achieved a significant saving in structural weight of their manned space craft. The use of this pressure and the even lower pressure of approximately 3.5 psia. encountered by the astronauts when outside the craft in only a space suit, has stimulated much research into the lower limits of pressure that can be safely tolerated by man for long periods of time. It has also led to the detailed investigation of the relative merit of various inert gases for use in breathing mixtures as a possible measure for the prevention of decompression sickness[25].

5.0 SCOPE OF STUDY

Any theory used for generating decompression schedules must be capable of dealing with all the forms of decompression mentioned in the previous section.

This report describes the development and analysis of a mathematical model of the gas transfer system in the body. In an attempt to cover the diversity of situations under which decompression sickness occurs the importance of both the rate of decompression and the total gas tension in the tissue, in the development of conditions liable to cause decompression sickness, have been emphasised.

Due to the importance of the total gas tension of the tissue in this analysis, practical means of measuring this parameter are also described and the results of measurements made in rat and man are given.

PART 1

THEORETICAL STUDY OF GAS TRANSFER IN THE BODY

6.0 GENERAL BACKGROUND

6.1 CURRENT APPROACH IN CALCULATING DECOMPRESSION SCHEDULES

The aetiology of decompression sickness is currently thought to be the phase separation of gas in body tissue and decompression schedules are therefore designed to prevent the occurrence of conditions liable to cause this. However, several different criteria have been postulated for achieving a so-called "safe" condition.

Haldane[13] originally proposed that providing the ratio of initial to final absolute pressure did not exceed 2:1, the decompression would be safe. More recently Van der Aue[26] advanced the concept of a series of critical pressure ratios instead of the single ratio of Haldane and this multiple ratio approach is used in calculating the current U.S. Navy decompression tables[27]. For these tables a series of tissues is considered where the time courses for filling with and emptying of gas are exponential. These exponentials have a different half time for each tissue and the pressure change each can tolerate before phase separation will occur is also assumed to be different. In general, the longer the half time of the tissue the smaller is the pressure change considered to be "safe" for that tissue.

The whole of this current approach is based on the theory first developed by Haldane and most of the modifications have been of an empirical nature where pressure ratios are changed or tissues with longer half times are invoked as the duration of dives increases.

6.2 ENERGY REQUIREMENTS FOR PHASE SEPARATION OF GAS

Hills[14], from a thermodynamic consideration of the energy requirements for phase separation of gas from solution, has emphasised that "spontaneous" phase separation cannot occur until the system becomes supersaturated and the higher the supersaturation the greater the probability of phase separation. In a heterogeneous medium like animal tissue, the energy requirements for phase separation of gas can be influenced by the surface energy associated with boundaries.

For example, membrane surfaces in joints or around tendons, and possibly even cell walls. These surfaces could act as preferential sites for the initiation of phase separation and the minimum energy configuration for the gas phase at these surfaces need not be a spherical bubble but may be a sheet or film of gas.

The spontaneous phase separation of gas becomes more probable the higher the supersaturation because there is more free energy available to form the new phase. A measure of peak supersaturations developed during a decompression should therefore give an indication of any potentially dangerous regions in a decompression format. However, should phase separation be initiated, the growth or reabsorption of these regions will depend on the energy of the gas in the supersaturated tissue and any subsequent changes in ambient pressure[14, 28].

To examine local peak supersaturations in the tissue it was necessary to determine the gas tension distribution and this in turn required modelling the entire physiological gas transfer system. Furthermore, a knowledge of how the total gas tension of the tissues varied with the environmental pressure, was required.

7.0 PHYSIOLOGICAL BACKGROUND

To develop a realistic model of the body for examining the spatial distribution of gas in tissue it was necessary to understand the way in which gas transfer from the environment to the tissue is effected. Salient feature of this gas transfer system in the body is outlined and the relation between total gas tension in the tissue and the environmental pressure are discussed in Sections 7.1 and 7.2 respectively.

7.1 GAS TRANSFER FROM EXTERNAL ENVIRONMENT TO CELLS

Most of the energy requirements of the body are met by aerobic oxidation reactions which require a continual supply of oxygen and produce carbon dioxide as one of the by-products. Adequate supply of oxygen and clearance of carbon dioxide are the major functions of the respiratory and circulatory systems.

7.1.1 Gas Exchange Mechanism

The mechanism of gas exchange from alveolar air to blood, and blood to tissue is generally considered to be one of simple diffusion from a region of high gas tension to one of lower gas tension with each gas diffusing independently along its own partial pressure gradient.

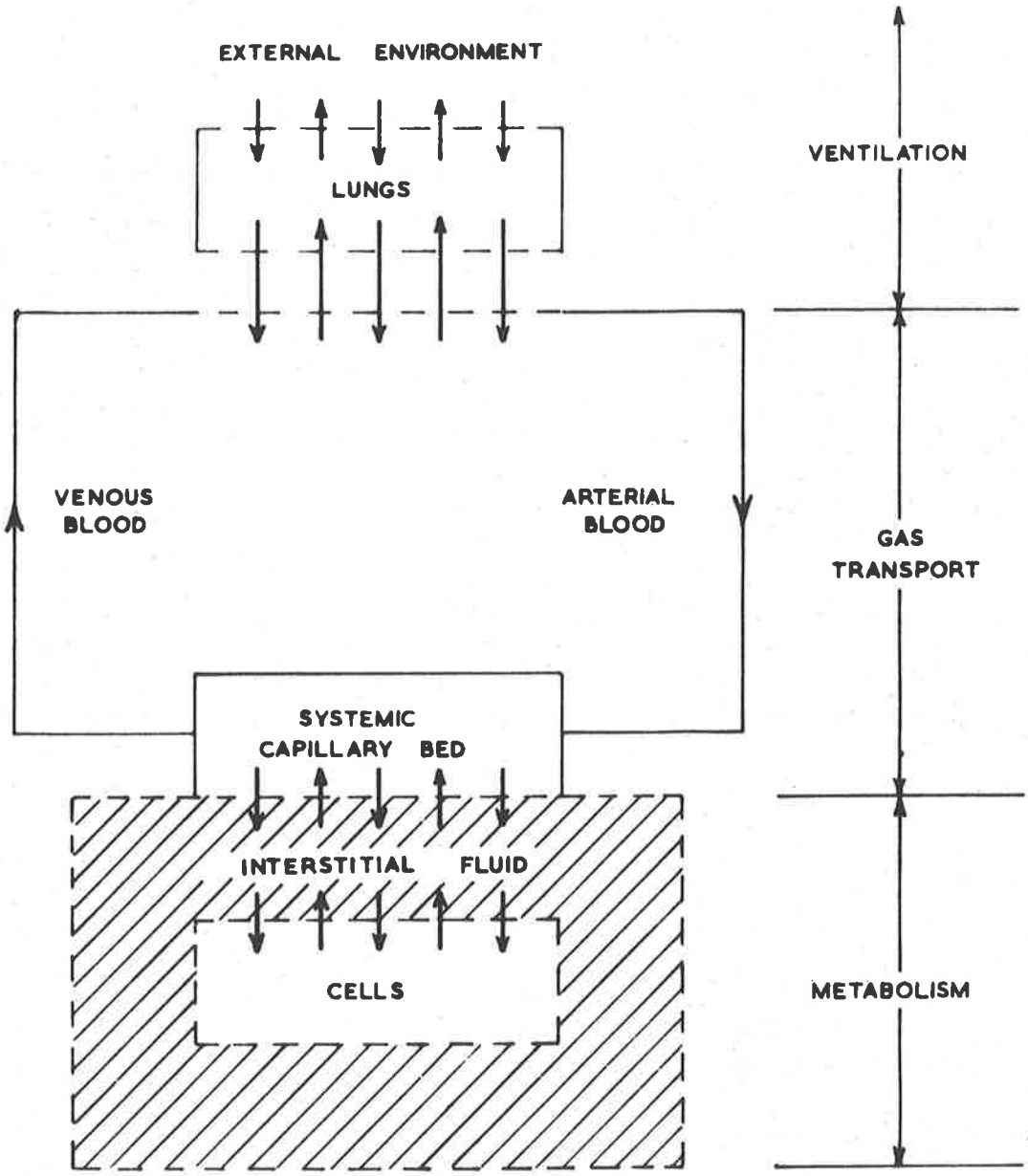
In the pulmonary capillary bed diffusion distances are very short and gas transfer is across highly permeable membranes which allow rapid equilibration of the blood with alveolar air.

In the systemic capillary bed, however, diffusion distances are generally much greater, and equilibration times for the tissues must be correspondingly longer.

7.1.2 Gas Transfer System (Figure 1)

Ventilation

As a result of the respiratory movements, ventilation leads to the exchange of alveolar gases with



GAS TRANSPORT FROM EXTERNAL ENVIRONMENT TO CELLS

Fig. 1

the external environment. Respiration is regulated to maintain the plasma partial pressures of oxygen and carbon dioxide at preset control levels commensurate with metabolic needs. The blood is found to equilibrate with alveolar air in one pass through the pulmonary capillary bed where excess carbon dioxide is eliminated and oxygen absorbed.

Transportation

From the lungs the equilibrated blood passes into the arterial system. The gas content and gas tension of arterial blood is then considered to remain unaltered until the blood reaches the systemic capillary bed where the gases diffuse between the capillaries and tissue cells down their respective tension gradients. Four gases are involved, viz :- oxygen, carbon dioxide, nitrogen, water vapour.

Oxygen - Most of the oxygen is carried in chemical combination with the haemoglobin as oxyhaemoglobin, but is transferred to the tissue through the plasma where it is in physical solution.

Its solubility is fairly low and so relatively few molecules are required in solution to saturate the plasma and produce a high tension. Unless the plasma tension falls below 100-105 mmHg oxyhaemoglobin does not release its combined oxygen.

Carbon dioxide - In arterial blood the carbon dioxide is carried in physical solution buffered as H_2CO_3 and HCO_3^- in the plasma, while in venous blood some is also carried in chemical combination with the haemoglobin as carboxyhaemoglobin.

Carbon dioxide is about 25 times more soluble than oxygen and consequently many more molecules are required to create a saturated solution. This applies also to the solution of carbon dioxide in the tissue.

Nitrogen - Nitrogen is thought to be physically inert and carried entirely in physical solution in the blood plasma. It is the least soluble of the four gases and diffuses the most slowly.

The rate of diffusion of nitrogen is therefore a rate limiting factor when considering the diffusion of these gases through the tissue.

Water vapour - Water is present in the blood plasma in the liquid phase and its vapour tension is fixed by the absolute pressure and temperature. Changes in pressure of the order of magnitude encountered in compressed air work and diving operations only have a second order effect on water vapour pressure[29].

7.1.3 Metabolism

The metabolic requirements of the cells govern the gas tensions in the venous blood and these requirements are met by alterations in the local perfusion of the tissue and more generally by changes in respiration and circulation. Carbon dioxide and unused oxygen are transported back to the lungs in the venous blood and the cycle is repeated.

The body has many of these gas transfer loops operating in parallel, with path lengths and diffusion distances ranging from the short circulation times and short diffusion distances of coronary muscle to the much longer circulation time associated with the extremities and the long diffusion distances in joints and other fibrous tissue.

The only two places in the system where gas tensions can be substantially altered are the lungs and the tissue, i.e., where gas exchange occurs. In the vessels linking these regions the gas tensions of the blood remain relatively constant. Arterial blood gas tensions are fixed by alveolar air partial pressures while venous blood gas tensions are fixed by metabolism in the tissue.

The systemic capillary beds are complex three dimensional meshes of minute blood vessels through which the velocity of blood flow is continuously changing. There is also a continuous alteration in the local perfusion of the tissue on a microscopic scale and this autoregulation of blood flow through the capillaries is governed by several factors including local tissue hypoxia[50]. The dynamics of capillary circulation has been described by Nicolls[30].

Direct control of respiration and circulation is mainly through the chemical monitoring of pCO_2 and pO_2 levels in the arterial blood. However, other factors also influence this control including psychological stress, changes in general body temperature and changes in the acid base equilibrium of the blood. All of these factors interact to effect the blood distribution in a manner commensurate with the metabolic requirements of the tissue and the maintenance of homeostasis.

7.2 TISSUE GAS TENSIONS AND THE DEVELOPMENT OF UNSATURATION

Under normal conditions the partial pressure of oxygen at sea level is about 158mmHg in inspired air. This is reduced to about 100mmHg in the alveoli by the addition of carbon dioxide and water vapour. Water vapour tension is fixed by the absolute pressure and temperature while carbon dioxide partial pressure depends upon the relationship between its production and alveolar ventilation.

In the metabolic processes oxygen is utilised by the cells and carbon dioxide produced as a waste product. As oxygen diffuses out of the blood plasma the oxygen tension in the plasma falls causing the oxyhaemoglobin to dissociate and so release more free oxygen into the plasma.

While breathing air at atmospheric pressure the haemoglobin in arterial blood is normally about 97 per cent saturated. (Figure 2). Metabolic requirements utilise a quantity ΔQ of the total oxygen content of the blood and this causes the blood oxygen tension to fall from arterial tension T_{A1} to the venous tension T_{V1} as it passes through the capillary bed. This drop, designated ΔT_1 amounts to about 60mmHg when breathing air at atmospheric pressure.

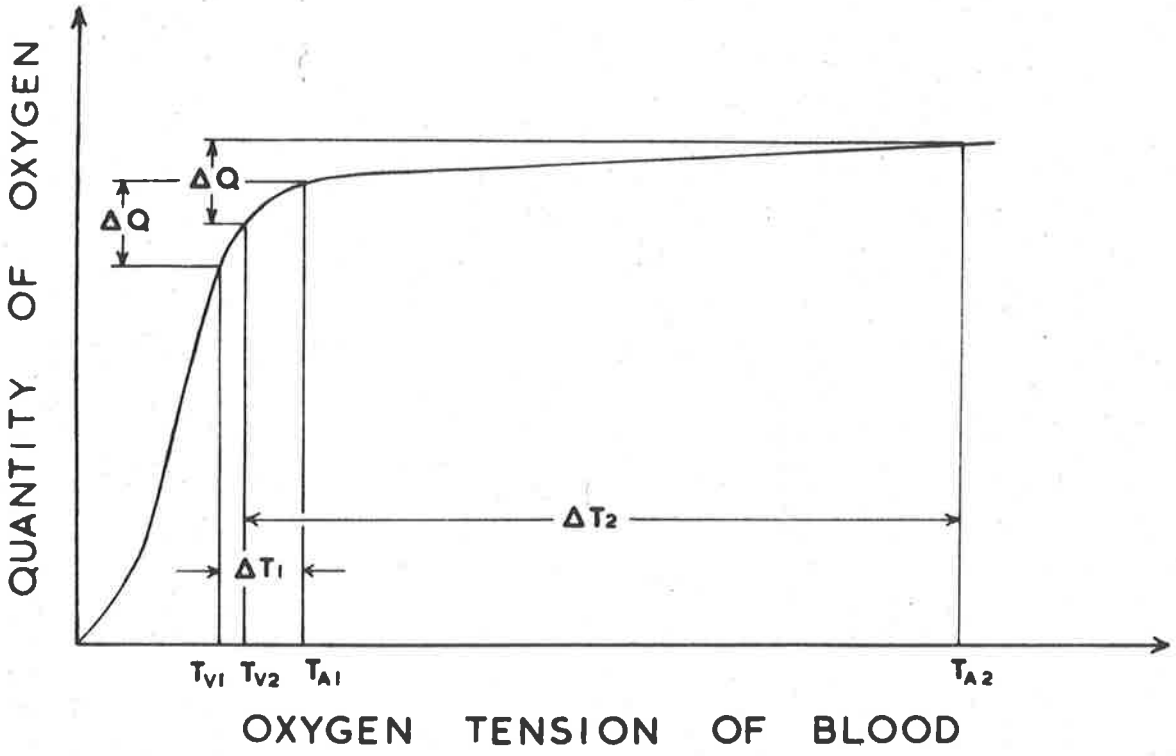

QUANTITY OF OXYGEN
ΔQ
ΔQ
ΔT2
ΔT1
TV1 TV2 TA1
TA2
OXYGEN TENSION OF BLOOD

Fig. 2

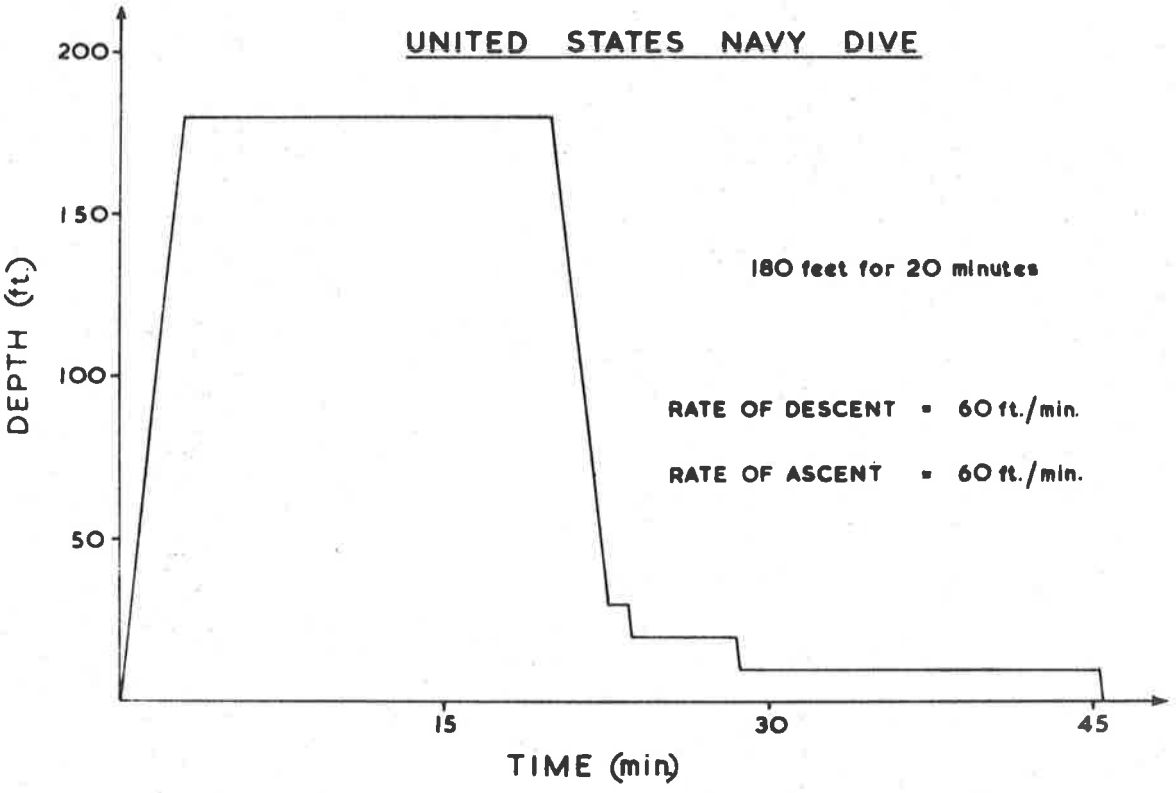

UNITED STATES NAVY DIVE
200
150
100
50
DEPTH (ft.)
180 feet for 20 minutes
RATE OF DESCENT = 60 ft./min.
RATE OF ASCENT = 60 ft./min.
15
30
45
TIME (min)

Fig. 3

At the same time the cells are producing carbon dioxide which diffuses down its partial pressure gradient into the blood plasma. However, with carbon dioxide being 25 times more soluble than oxygen and with a respiratory quotient of 0.85, the increase in pCO_2 in the blood plasma is only about 6mmHg.

The net result is a fall of about 54mmHg in the total gas tension of blood in passing from the arterial to the venous side of the capillary bed. This gas tension deficit leaves the venous blood undersaturated with respect to the arterial blood and has been referred to by Le Messurier and Hills as UNSATURATION[21]. In general the unsaturation in any tissue is :-

Unsaturation = Ambient pressure - Sum of gas tensions in the tissue.

Normal values of oxygen, carbon dioxide, nitrogen and water vapour partial pressures in inspired air, alveolar air, arterial blood, venous blood and tissue are shown in Table 1.

TABLE 1

SAMPLE / GAS	GAS PARTIAL PRESSURE (mmHg)				
	Inspired Air	Alveolar Air	Arterial Blood	Venous Blood	Tissue
O_2	158	100	100	40	< 40
CO_2	0.3	40	40	46	> 46
N_2	596	573	573	573	573
H_2O	5.7	47	47	47	47
TOTAL	760	760	760	706	≤ 706

In Table 1 tissue oxygen tensions are indicated to be less than 40 mmHg. There appears to be some controversy as to what the extra vascular oxygen tension is in human subjects and animals. Sibree[31] has found that oxygen tensions

in gas depots are often 20-30mmHg below venous oxygen tensions. This indicates that from the capillary to the tissue fluid there may be a considerable oxygen tension gradient and the cellular oxygen tensions may be expected to be even lower still. Campbell[32], however, quotes gas pocket oxygen tensions as being close to oxygen tensions in venous blood and dismisses low oxygen tension measurements as being erroneous readings.

Carbon dioxide partial pressures in gas depots in human subjects and animals are generally found to be close to those of venous blood which indicates that the tissue fluid contains only a slight gradient for this gas.

When 100 per cent oxygen is administered to a healthy individual at one atmosphere pressure the oxygen tension of arterial blood T_{A2} rises towards the new alveolar level. See Figure 2. In the absence of nitrogen, the alveolar oxygen partial pressure is equal to the barometric pressure less the partial pressure of water vapour and carbon dioxide. Under these conditions it is about 670mmHg, nearly seven times higher than when breathing air. The haemoglobin saturation increases from 97 per cent to 100 per cent and more oxygen dissolves physically in the blood plasma. However, the total oxygen content of arterial blood is only elevated by a small amount. If the metabolic requirements of the tissue remain constant, the quantity of oxygen utilised by the tissue ΔQ does not alter and blood tensions of water vapour and carbon dioxide remain fairly constant. As seen from Figure 2 there will now be a large drop in blood pO_2 (designated ΔT_2) and hence a correspondingly large increase in blood unsaturation.

Blood unsaturation will increase whenever the alveolar pO_2 increases and this occurs when the ambient pressure is increased or when breathing oxygen enriched air. Similarly the unsaturation can be reduced by decreasing pO_2 in the alveolar air as occurs when the ambient pressure is reduced.

The tolerable increase in pO_2 in man is set by the tension at which convulsions start and this is generally found to be when pO_2 in the inspired gases reach approximately two atmospheres absolute. Likewise there is a lower

limit to the pO_2 which is determined by the onset of hypoxia. Hypoxic symptoms start to occur at about 10,000 feet altitude when breathing air and this corresponds to an alveolar pO_2 of approximately 60mmHg.

With this physiological background in mind it is now possible to develop a mathematical model of gas transfer within the whole body that takes into account the difference between ambient pressures and total gas tension in the tissue (tissue unsaturation).

The development and analysis of this model is outlined in the following section.

8.0 MATHEMATICAL MODEL OF GAS TRANSFER SYSTEM

8.1 DEVELOPMENT AND NUMERICAL ANALYSIS OF MODEL

The present work involved determining the spatial distribution of gas in tissue in order that the local supersaturation could be examined. To do this it was necessary to develop a model describing gas transfer within the physiological environment. Salient physiological features of the overall gas transfer system were outlined in Section 7.1 and are summarised below.

- Immediate equilibration of the pulmonary blood with alveolar air was assumed and this fixed the gas tensions of arterial blood.
- Changes in ambient conditions can not immediately effect the gas tension of blood already in the arterial or venous system.
- Gas tensions of venous blood are fixed by metabolic requirements of tissue.
- Gas transfer between capillaries and extravascular tissue was assumed to be a diffusion process.

To develop the mathematical model, the diffusion process is considered in more detail.

Equation (1) is the general equation describing diffusion through a homogeneous medium.

$$\frac{\partial C}{\partial t} = D \nabla^2 C \qquad (1)$$

where

C = c(x,y,z,t) is the gas concentration

t = time

x,y, and z are cartesian co-ordinates

D = diffusion co-efficient

∇ = differential operator $\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial x^2} \right)$

This equation can be solved by both analytical and numberical methods and the required boundary conditions are found from the model of the tissue used.

Krogh[33] has developed the most realistic model of the systemic capillary bed. He considered each capillary to be surrounded by six others in a regular hexagonal pattern and set in a homogeneous intercapillary medium.

However, the complexity of the solution to equation (1) is substantially reduced when a one dimensional model of the tissue is used. Furthermore, the laws governing diffusion are independent of the geometry of the model. The simplest one dimensional model was used to demonstrate this approach.

With this one dimensional model, equation (1) was reduced to equation (2)

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \qquad (2)$$

where

$$C = c(x,t)$$

With gas diffusing from two parallel capillaries into the intermediate tissue symmetry considerations gave an effective back wall at half the intercapillary spacing. A homogeneous intercapillary medium was also assumed.

The analytical solution to (2) is relatively straightforward for a step change in gas concentration but becomes more complex where ramp functions are involved. An idealised dive profile, as shown in Figure 3, consists of a series of ramp functions with positive, zero and negative slopes. An actual dive profile, however, may be much more complicated than this. The principle of superposition can be used to calculate analytically the gas concentration distribution at any time after the start of the dive but this soon becomes a very complex process when a continuous record of the distribution throughout an entire dive is required. The gas concentration distributions found just prior to and just after decompression, for three different times of exposure to the same pressure, are shown schematically in Figure 4.

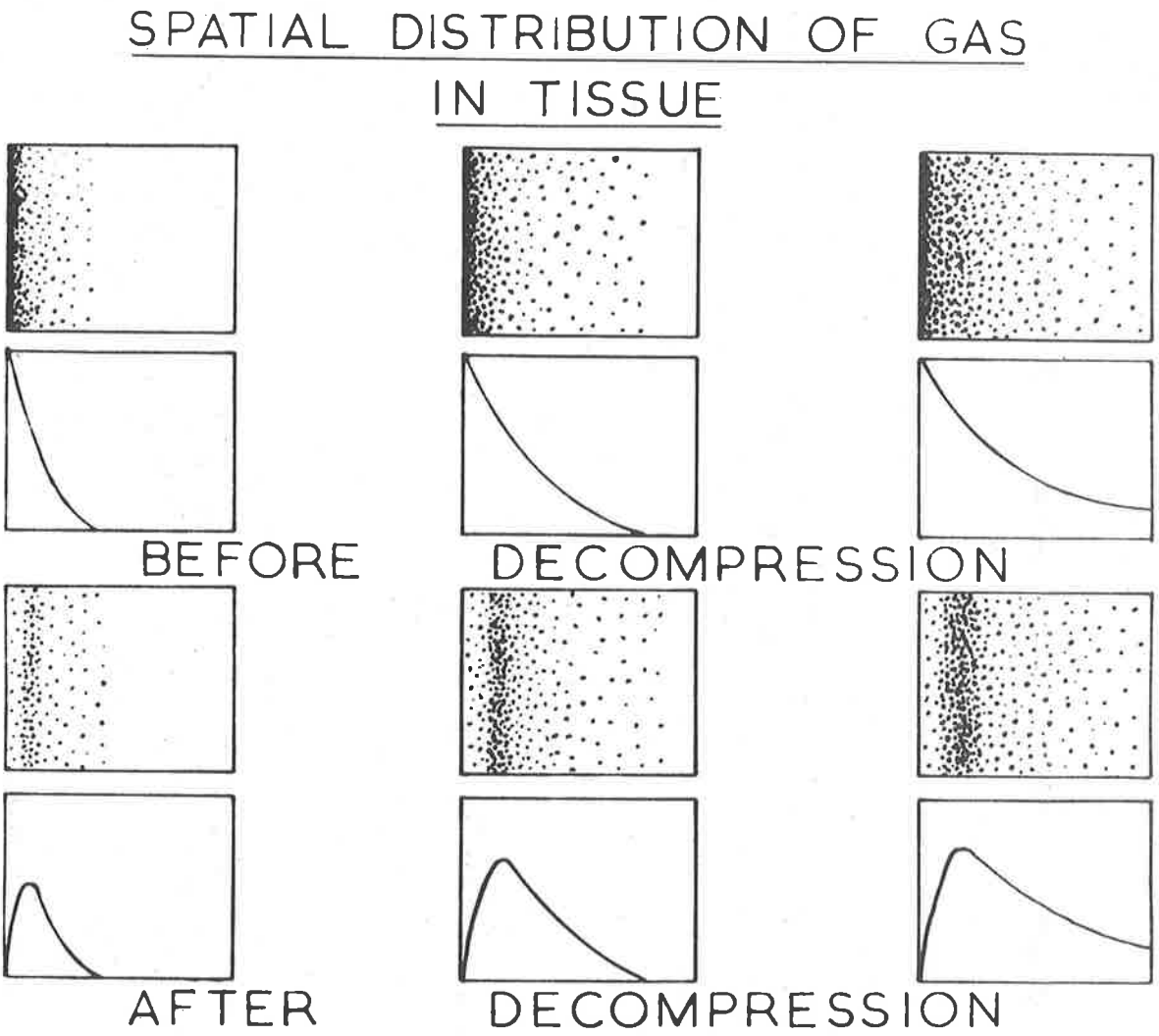


Fig. 4
Spatial Distribution of Gas Before and After Decompression for Three Different Times of Exposure to Pressure.

Problems of this type where transients are of importance, are amenable to solution using numerical techniques in which the differential equation is approximated by a finite difference equation. Furthermore, the tedious computations involved in numerical methods are readily handled by digital computing techniques and, as computing facilities were available, it was decided to adopt a numerical approach rather than an analytical approach.

A numerical process know as the finite difference method was used and involved dividing the diffusible medium between the capillary and the backwall into n equally spaced planes 1, 2, ... r .....n. The initial gas concentration at each of these points was specified to give the set of initial conditions while boundary conditions were generated by the gas concentration of the blood in the capillary. The capillary gas tension was taken to be that of venous blood and lagged behind the alveolar gas tensions by the circulation delay. A finite difference equation was then used to calculate the gas concentration distributions at later times during the course of a dive.

Equation (3) is a general finite difference equation suitable for solving the one dimensional diffusion equation.

$$C_{r,t+1} = (C_{r-1,t} + C_{r+1,t}) + (1 - 2\alpha) C_{r,t} \quad \ldots\ (3)$$

where

$C_{r,t}$ is the gas concentration at plane r and time t.

This is stable for $0 < \alpha \leq \frac{1}{2}$ with the simplest case being when $\alpha = \frac{1}{2}$. Under these conditions equation (3) then becomes the first order difference equation (4)

$$C_{r,t+1} = \frac{C_{r-1,t} + C_{r+1,t}}{2} \quad \ldots\ (4)$$

This equation was used as the basic algorithm in a Fortran program developed for a CDC 6400 computer. The program continually calculated and analysed the concentration distributions at regular time intervals throughout a whole dive or sequence of dives and the time interval of calculation was adjusted to give the required accuracy of calculations.

The peak supersaturation was determined by subtracting the ambient pressure from the peak tissue gas tension at that time and the result expressed in feet of sea water. See Figure 5. Magnitudes and rates of change of these peaks were then examined for different dive profiles.

As the programme was designed to be a research tool versatility was aimed at and on removal of the section dealing with the calculation of unsaturation and circulation delays, diffusion into any homogeneous medium could be investigated.

One medium found to be useful for examining diffusion and phase separation of gas was a gelled 12 per cent solution of gelatine in water. The coefficient of diffusion of nitrogen into this medium was assumed to be 1.7×10^{-5} cm^2/sec. (approximately 90 per cent of the diffusion coefficient for nitrogen into water). Based on this figure the backwall distance required for the medium to become 90 per cent saturated in 24 hours was calculated and found to be 1.2cm. This roughly corresponded to the U.S. Navy's four hour half time tissue and was considered to represent poorly perfused regions such as joints and fibrous tissue.

Model dimensions can be scaled for any diffusion coefficient and also scaled to allow the determination of gas concentration changes occurring in a tissue with any desired half time. This scaling is achieved by calculating the backwall distance necessary for the tissue to reach 50 per cent saturation in the required half time.

8.2 RESULTS AND DISCUSSION OF INITIAL STUDIES USING THE MODEL

Bends pains are generally thought to be associated with poorly perfused tissues where intercapillary distances are large. As pointed out above this is thought to correspond to a tissue taking 24 hours to reach 90 per cent saturation and so a tissue with these characteristics was used to examine the peak supersaturations developed when dive parameters such as depth, duration of dive, and rates of ascent were varied.

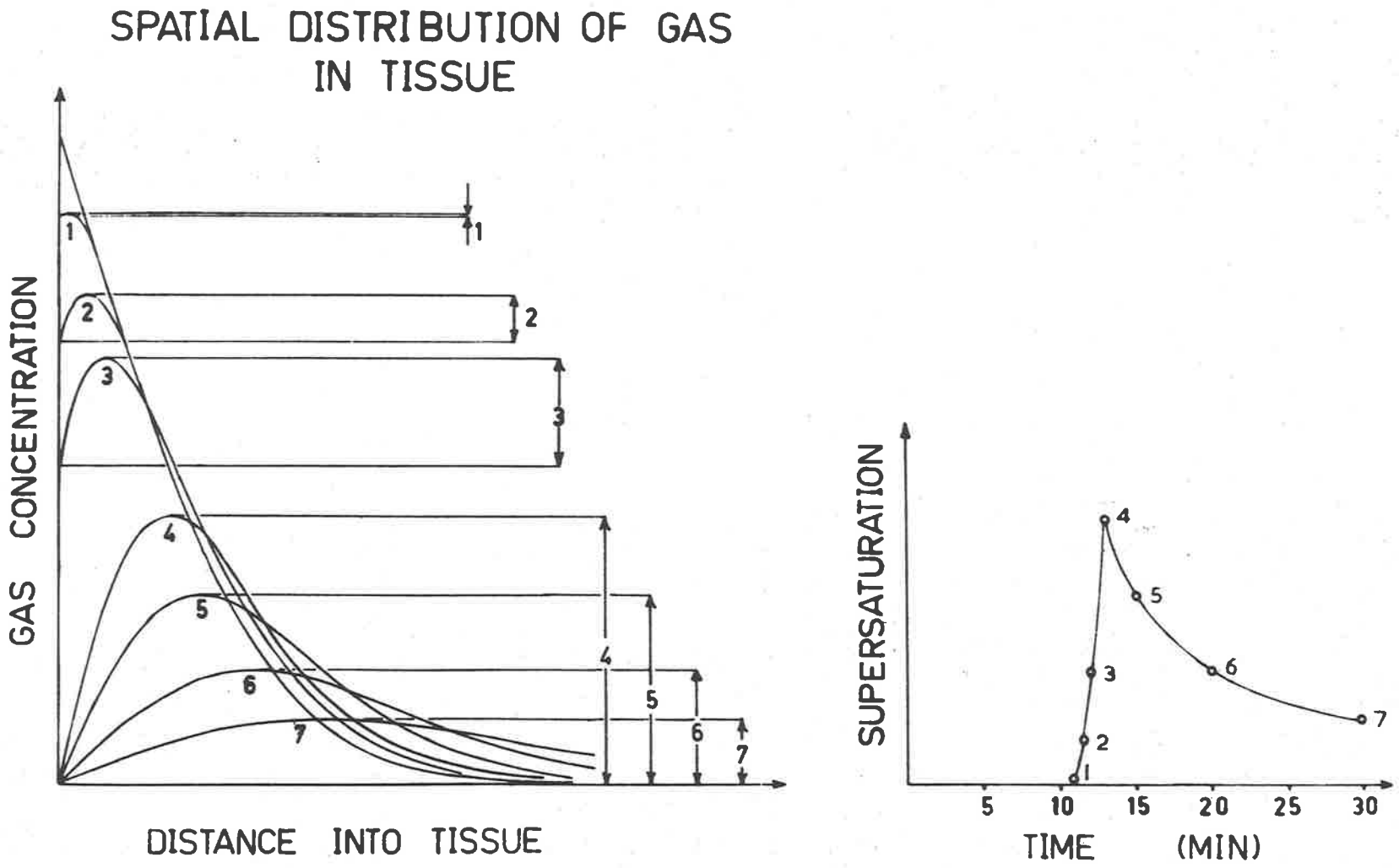


Fig. 5

Development of Peak Supersaturation
on Decompression

Figure 6 shows the development of peak supersaturation following a dive to 300 feet for 20 minutes with non stop decompressions of different rates of ascent. Peak supersaturations occur on surfacing and can be markedly reduced by decreasing the ascent rate. Furthermore, they fall off rapidly on reaching the surface or a staging point.

Figure 7 exemplifies the method of analysis described in the previous Section. A dive profile from an Okinawan Pearl Diver, as recorded by Le Messurier[21], is shown along with the peak supersaturation developed during the course of this dive. A comparable U.S. Navy dive[34] to 220 feet for 50 minutes is also analysed in exactly the same manner. All calculations presume gas phase separation has not occurred.

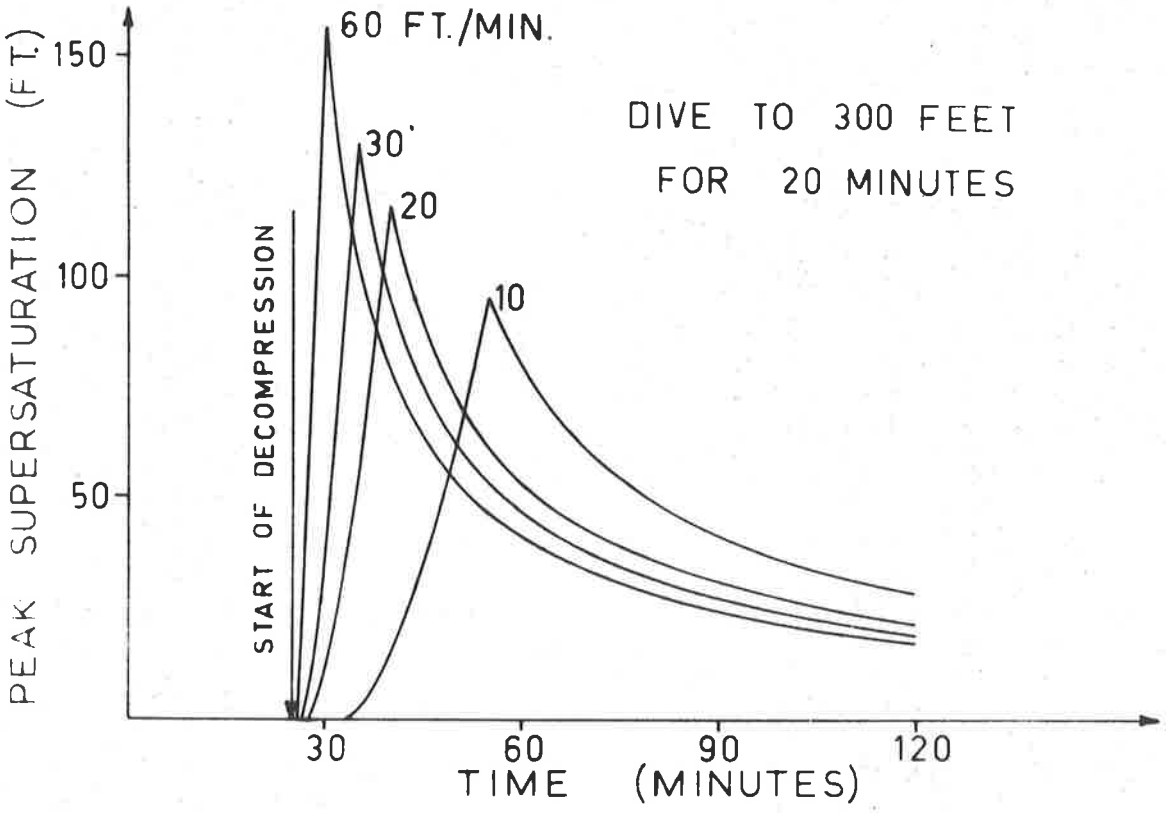
Important features of the U.S. Navy dive are :-

- very high peak supersaturations (up to 70 feet) are developed in the early stages of decompression.
- low peak supersaturations (about 15 feet) develop on surfacing.
- tissue is supersaturated throughout the entire decompression.

By contrast the Okinawan dive shows :-

- relatively low peak supersaturations developed intermittantly during the early phases of the decompression (about 25 feet).
- the diver surfaces from 40 feet and develops 29 feet of supersaturation during this last step.
- apparent "overstaging" during the latter phases of the decompression where the body's unsaturation is only driving force for the elimination of excess gas.

Initiation of phase separation of gas is a function of the excess free energy of the system[14, 35] and phase separation will not occur spontaneously unless the system becomes supersaturated. By examining the gas concentration distribution and peak supersaturations developed during a



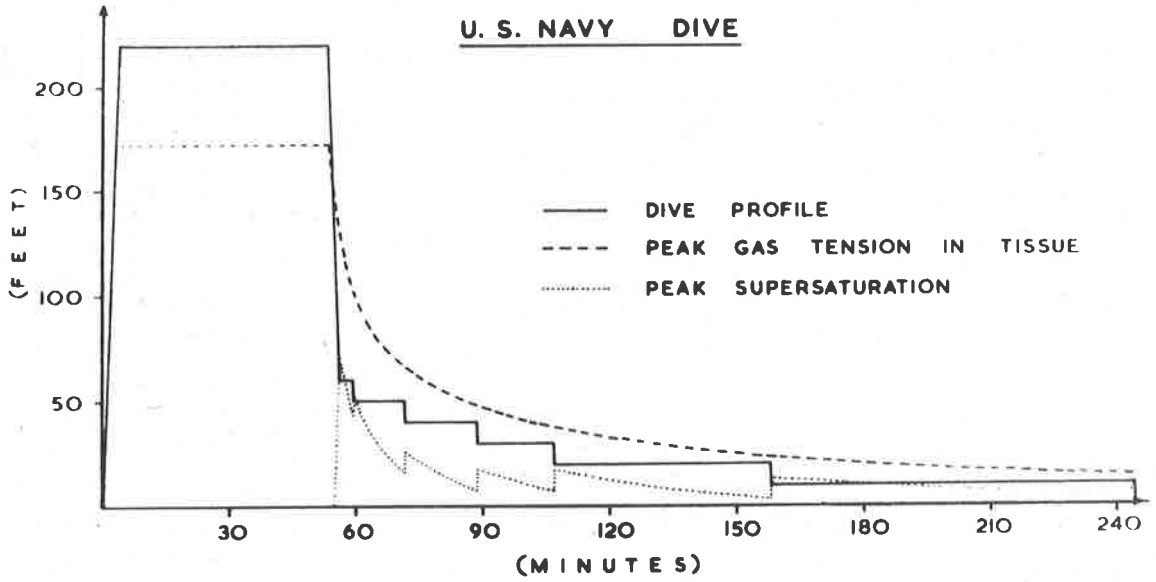
EFFECT OF RATE OF ASCENT
ON PEAK SUPERSATURATION

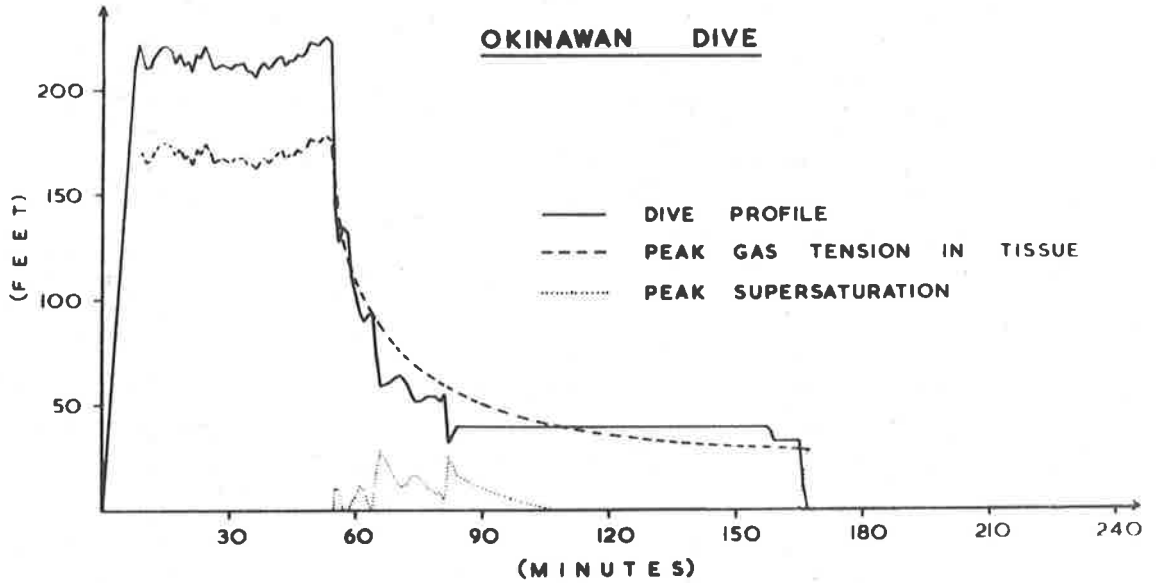
Fig. 6

FIGURE 7 : U.S. NAVY DIVE TO 220 ft. FOR 20 MINUTES WITH PEAK SUPERSATURATIONS DEVELOPED DURING THE DECOMPRESSION.

OKINAWAN DIVE TO 220 ft. FOR 20 MINUTES WITH PEAK SUPERSATURATIONS DEVELOPED DURING THE DECOMPRESSION.

DIVE TO 220 ft. FOR 50 MINUTES WITH DECOMPRESSION PROFILE THAT LIMITS THE PEAK SUPERSATURATION TO A MAXIMUM OF 20 ft.


U. S. NAVY DIVE
200
150
100
50
(FEET)
DIVE PROFILE
PEAK GAS TENSION IN TISSUE
PEAK SUPERSATURATION
30
60
90
120
150
180
210
240
(MINUTES)


OKINAWAN DIVE
200
150
100
50
(FEET)
DIVE PROFILE
PEAK GAS TENSION IN TISSUE
PEAK SUPERSATURATION
30
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(MINUTES)

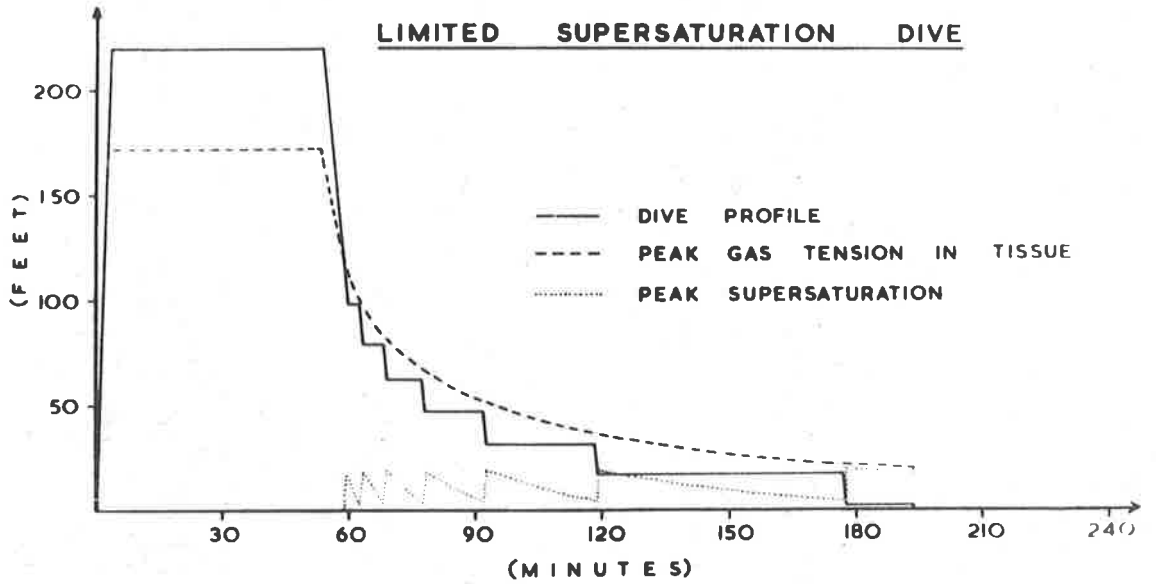

LIMITED SUPERSATURATION DIVE
200
150
100
50
(FEET)
DIVE PROFILE
PEAK GAS TENSION IN TISSUE
PEAK SUPERSATURATION
30
60
90
120
150
180
210
240
(MINUTES)

Fig. 7

dive, in the manner described above, potentially dangerous points in a decompression schedule become evident.

With the profiles illustrated the most dangerous regions of the U.S. Navy table appear to occur early during the decompression where the long first pull with a rate of ascent of 60 feet per minute created high supersaturations. In the latter stages, however, the supersaturations generated are much lower as the long staging times allow the peak gas tensions to approach the ambient conditions.

The Okinawan dive shown here avoids high supersaturations during the early phases of decompression by having a generally slower rate of ascent and introducing short, deep stages. The latter parts of this dive overstage the diver and a high supersaturation was generated on surfacing directly from a depth of 40 feet.

Crocker[36] has shown that some men develop symptoms of decompression sickness on surfacing directly from depths as shallow as 31 feet after dives of 6 to 12 hours duration, while others have no symptoms after 12 hours at 41 feet. At a depth of 30 feet the total gas tension in the venous blood is equivalent to approximately 24 feet. The tissue tension will be less than this, probably nearer 20 feet, so on surfacing after an extended dive to a depth of 30 feet the peak supersaturation developed in the tissue will be close to 20 feet. It would thus appear that the Okinawan diver created potentially dangerous conditions on surfacing with a peak supersaturation in the tissue of about 30 feet and, in fact, this particular dive resulted in the diver developing bends symptoms.

If there is a maximum level of supersaturation a given tissue can tolerate before phase separation of gas is initiated, and this level can be determined, then, decompression profiles where the supersaturations generated do not exceed this limit can be calculated for any dive or sequence of dives. If such a limit exists it will probably be a function of several parameters including absolute pressure, tissue properties, physiological condition

of diver or caisson worker, solubility and diffusion coefficients of the gases used in the breathing mixture.

An example of how a limit can be imposed on the peak supersaturation is shown in Figure 7. An idealised dive to 220 feet for 50 minutes was programmed with an ascent rate of 20 feet per minute and the maximum tolerable peak supersaturation set to 20 feet. The program then calculated the depths at which stages must be introduced in order that this supersaturation limit was not exceeded. The duration of each stage was set by time taken for the peak supersaturation to decay to 5 feet. The resultant decompression profile and supersaturations generated are also shown in Figure 7.

Most theories concerning the development of decompression tables place importance on avoiding excessive supersaturation of the tissue. With the current approach of the U.S. Navy, the total gas content of the tissue containing the most gas is noted and using this quantity of gas the permissible pressure drop for that tissue is applied to determine the position of the next stage. The supersaturation generated is thus effectively based on the quantity of gas in the tissue. However, the approach proposed here highlights the importance of the distribution of gas in the tissue when determining supersaturation.

If supersaturation is taken as a necessary prerequisite for initiation of phase separation then a "perfectly safe" dive, based on the model outlined in this study, can be readily calculated. On such a decompression the body's unsaturation would be used to prevent the occurrence of supersaturated conditions. Such decompression schemes were first suggested by Le Messurier and Hills[21] in 1965.

Buckles[28] in observations on the dynamics of capillary beds in hamster cheek pouch experiments has noted that capillary blood flow is arrested for up to one to two minutes at a time. The effect of such a cessation of flow on the development of supersaturation can be simulated by

increasing the circulation delay. When considering a diver ascending at a rate of 60 feet per minute the supersaturation developed, if capillary flow is arrested for two minutes, could be as high as 120 feet. Localised peaks of this type may well initiate phase separation and could lead to the development of the so called "silent bubble". This highlights the importance even on very short dives of slow rates of ascent and short pauses to allow localised peaks of this type to clear.

The total gas tension in the tissue is an important parameter in the calculation of supersaturation. Hills[14] developed equation (5) that relates the total gas tension in the tissue to the absolute pressure when the inert gas fraction in the breathing mix is known.

$$xP - 46x + 92 \leq P_{tissue} \leq xP - 46x + 132 \quad .... \quad (5)$$

where

x is the inert gas fraction

P ambient pressure (absolute)

P_{tissue} total gas tension in tissue.

The limits are imposed by the metabolic requirements of the tissue. The minimum tissue tension occurs when all the oxygen is utilised and pO_2 falls to zero, while the maximum would correspond to conditions of minimum metabolism of oxygen. The latter case gives tissue gas tensions equal to those of venous blood. Examination of equation (5) shows that the total gas tension in the tissue is kept to a minimum by having the maximum amount of oxygen in the breathing mix. However, there are physiological limits to the tolerable partial pressure of oxygen and these are set by the level at which oxygen toxicity occurs.

The advantage of adjusting the partial pressure of oxygen to maintain the maximum level of unsaturation can be seen from the above analysis. Controlling the oxygen partial pressure is quite feasible in chamber decompressions and is used with the oxygen tables in the therapeutic treatment of decompression sickness.

Pellegrini[37] has demonstrated the protection afforded divers by breathing oxygen enriched breathing mixtures. He reported the successful surfacing of divers from a depth of 82 feet with no decompression after seven hours breathing approximately 50 per cent oxygen. In this case the inert gas fraction is 0.5 and substitution into equation (5) gives a tissue gas tension of 60 feet (absolute). This would generate approximately 27 feet of supersaturation on returning to the surface. The same supersaturation would be generated on surfacing directly from 37 feet after seven hours breathing air (i.e, 20 per cent O_2) and Crocker[36] has shown that some men can tolerate surfacing directly from a depth of 37 feet after exposures of up to 12 hours duration without any symptoms of decompression sickness.

In the model described above it is possible to optimise any decompression profile to limit the peak supersaturation developed and minimise the time spent in decompression. This would obviously lead to a continuous decompression with a continuously varying rate of ascent where the maximum permissible driving force for the elimination of gas was maintained. Such decompressions would be feasible where there is a high degree of control on the pressure, as in caisson work and experimental or medical pressure chambers, but would not be practical for divers working under water. During practical dives, environmental conditions must be considered. For example, when working from a pitching or rolling boat on a rough day, it may be difficult to maintain a 10 feet or even a 20 feet stage and under conditions such as this the importance of having a large margin of safety in practical decompression tables becomes apparent.

9.0 SUMMARY OF THEORETICAL STUDY

The general principles involved in the determination of supersaturation from the spatial distribution of gas in the tissue have been demonstrated on a simplified model of the body. These same principles will also apply to more complex models such as the tissue model proposed by Krogh[33] and the more complex heterogeneous model put forward by Hills[38].

A digital computer program was developed to generate and examine the spatial distributions of gas occurring during a dive or dive sequence. With this program, the effects of varying parameters such as intercapillary spacing, circulation delays, diffusion coefficients of different gases, and unsaturation levels encountered when breathing enriched oxygen mixtures, can all be examined.

Removal of the strictly physiological sections such as circulation delay and unsaturation leave the program suitable to analyse diffusion or heat conduction in any homogeneous medium.

The importance of unsaturation, or the total gas tension in the tissue, in the development of supersaturation during a decompression has also been outlined. As unsaturation is such an important factor in developing decompression schedules in the manner described above, the second part of this study deals with the measurement of the total gas tension of tissue in rat and man.

PART 2

EXPERIMENTAL STUDY OF GAS TENSIONS IN SUBCUTANEOUS TISSUE

10.0 WAYS OF DETERMINING TISSUE GAS TENSIONS

The total gas tension of tissue can be determined either by measuring the gas tension of each of the component gases and summing or by direct measurement of the total gas tension. Both of these approaches are reviewed below.

10.1 DETERMINING GAS TENSION OF EACH COMPONENT GAS

J. Argyll Campbell, in a comprehensive review article[32], gives a historical survey and discussion of several methods that have been used to investigate the gas tensions of the component gases in tissue. The most successful of these are -

- Quantitative Gas Analysis of Body Fluids
- Analysis of Gas from Gas Pockets.

10.1.1 Quantitative Gas Analysis of Body Fluids

Estimation of gas tensions are made from the quantities of gas in solution in body fluids. These fluids are usually removed from the body for analysis either by tonometric gas extraction[39] or by using gas pumps. Previous workers have found gas pumps difficult to keep air tight and because such small quantities of gas are involved, even small leaks will invalidate the results. Furthermore, during the time taken to manipulate and analyse these fluids the gas tensions may change if active reactions are still occurring.

10.1.2 Analysis of Gas from Gas Pockets

A quantity of gas is injected into tissue and allowed to equilibrate. Samples of gas are then removed and analysed and the partial pressures of the gases in the pocket give an indication of the gas tensions in the tissue[31, 32, 40, 41, 42, 43, 44, 45, 46].

This technique appears to have been more successful than analysing the gases extracted from body fluids and is referred to as the "Gas Depot" or "Gas Pocket" method.

10.2. DETERMINING TOTAL GAS TENSION OF TISSUE

Two techniques are considered here and both were used in this study.

- Constant Pressure System
- Constant Volume System.

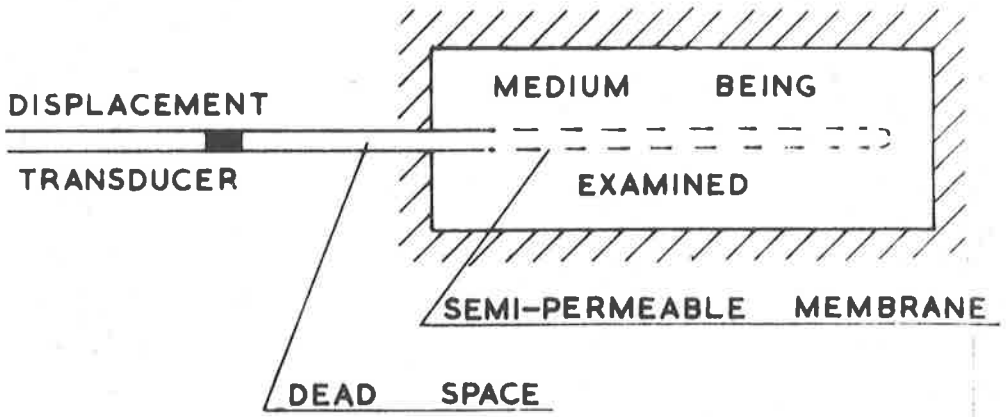
Both of these rely on the production of an artificial gas pocket of fixed volume which is joined to a transducer by impermeable connections. In the constant pressure system rate of gas absorption is measured, while in the constant volume system pressure is measured.

10.2.1 Constant Pressure System

The constant pressure system uses a displacement transducer to monitor the rate at which gas is absorbed. This transducer is essentially a frictionless piston sliding in a calibrated tube. (See Figure 8). If at equilibrium the ambient pressure within the system is higher than the total gas tension in the medium surrounding the membrane then a driving force for the absorption of gas exists. Under conditions of equilibrium the volumetric rate of absorption of gas will be proportional to the pressure gradient providing the area of the gas transfer surface remains constant. The pressure required to prevent gas exchange across the membrane will be equal to the total gas tension in the surrounding medium.

The advantage of this system becomes apparent when studying the response of a tissue to a change in the ambient conditions. Once equilibrium conditions have been established changes in the tissue gas tension will be reflected immediately by a change in the rate of gas absorption and once a new equili-

CONSTANT PRESSURE SYSTEM



RESPONSE TO A STEP CHANGE IN GAS TENSION OF MEDIUM BEING EXAMINED

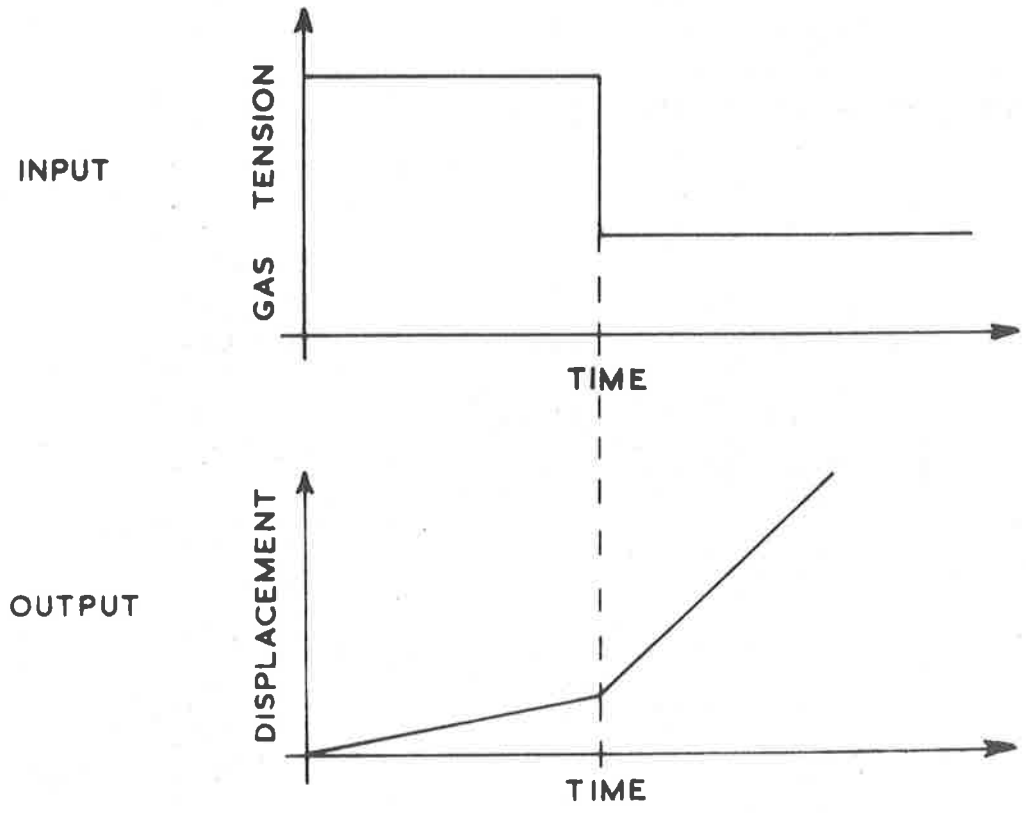


Fig. 8

brium has been reached the rate of gas absorption will settle down at a new constant level.

10.2.2 Constant Volume System

A schematic representation of a constant volume system is shown in Figure 9.

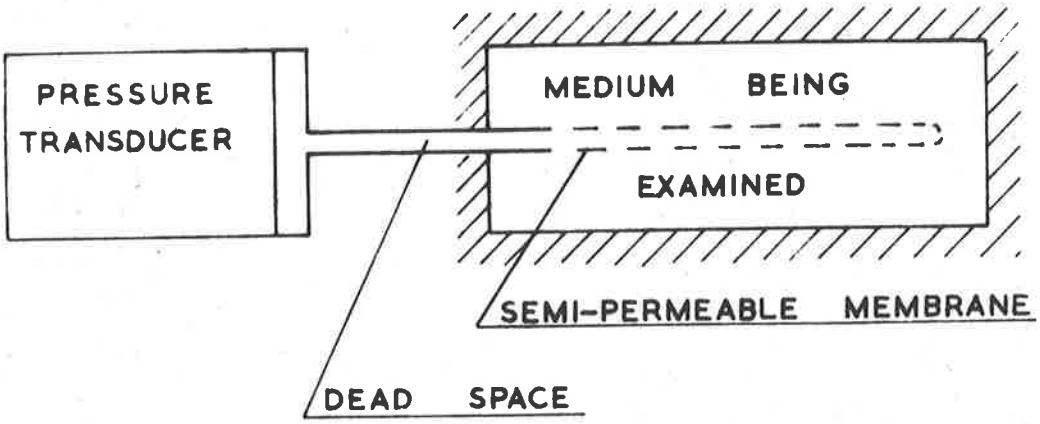
A pressure transducer is connected to the gas pocket and as the gas within the system equilibrates with the medium surrounding the membrane the transducer registers the total pressure developed.

Lategola[47] and Hills and Le Messurier[48] have both used this system. Lategola had a large dead space volume that required about two days to equilibrate while Hills and Le Messurier's transducer had a very much smaller dead space but the diffusing membrane was polyvinyl chloride tubing and passed the gases relatively slowly. The pressure in this latter transducer took about 12 hours to attain 95 per cent of its asymptotic value[48].

By monitoring the total gas tension within a gas pocket using either of these systems there is no need to withdraw gas samples for analysis and the size of the gas pocket can be kept to a minimum. This will create the minimum tissue trauma and leave the tissue in a state approximating its normal physiological condition.

As both these methods were used in this study to determine the total gas tension in subcutaneous tissue and they both involve the use of artificial gas pockets, gas pockets in general are reviewed below.

CONSTANT VOLUME SYSTEM



RESPONSE TO A STEP CHANGE IN GAS TENSION OF MEDIUM BEING EXAMINED

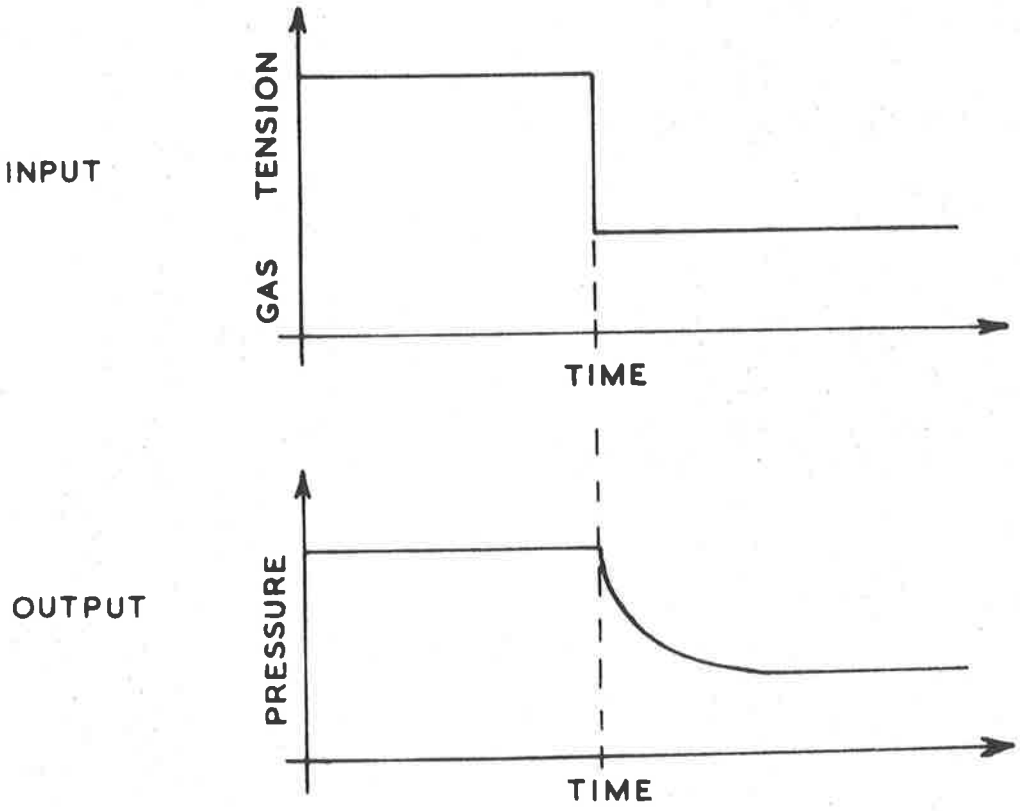


Fig. 9

11.0 REVIEW OF GAS POCKETS

Abernethy[49] quotes that as early as 1781 Astley Cooper showed that the injection of air and other gases under the skin and into the pleural and abdominal cavities was harmless. He found that the gas was absorbed and disappeared completely with no inflamation resulting but more recently it has been found that gas pockets do cause some very slight reaction[45]. Injections of air, nitrogen and sulfahexafluoride into the pleural cavity cause the lung to collapse and creates an artificial pneumothorax. As this was used clinically in the treatment of some tuberculosis cases much work has been done on the absorption of gas from such gas pockets.

11.1 RELATION BETWEEN GAS POCKET PARTIAL PRESSURE AND INTERCELLULAR GAS TENSIONS

If a gas depot is created in subcutaneous tissue by injecting a quantity of gaseous dry nitrogen a non-equilibrium condition will initially be created with a gradient for diffusion of oxygen, carbon dioxide and water vapour into the pocket and a gradient for diffusion of nitrogen out of the pocket. The total pressure within the gas depot will be slightly higher than ambient pressure due to the distension of the tissue but if the tissue is loose the pocket pressure closely approaches the environmental pressure. Oxygen, carbon dioxide and water vapour, being the faster diffusing gases, rapidly equilibrate with the gas pocket so that the partial pressure of these gases within the gas depot are equal to their gas tensions in the surrounding tissue. Nitrogen, being the only remaining gas, must supply the partial pressure necessary to keep the total pocket pressure equal to the ambient pressure. However, as described in Section 7.2, the total gas tension in the tissue is less than the ambient pressure by the tissue unsaturation. The partial pressure of nitrogen in the gas pocket will therefore be higher than its gas tension in the surrounding tissue and there will be a

driving force for the absorption of nitrogen from the pocket. As nitrogen is absorbed oxygen and carbon dioxide partial pressures will increase which in turn creates a driving force for their absorption. In this manner the gas pocket is eventually totally absorbed. The same mechanism is applicable if an air filled gas pocket is created in tissue except there will initially be an eflux of oxygen and an influx of carbon dioxide and water vapour until these gases equilibrate with the surrounding tissue.

This gas absorption mechanism is applicable to any gas depot in tissue and is the mechanism postulated for the re-absorption of phase separated gas following an "unsafe" decompression.

11.2 REACTION OF TISSUE TO A GAS POCKET

Following the initial injection of gas into the tissues there is a sterile hyperaemic reaction that lasts for several days. This is similar to the "foreign body reaction" and while it is difficult to determine the exact nature of the phenomenon it has been found to be independent of the type of gas injected, its volume, temperature and water vapour content[31]. It appears as though the molecular nature of the free gas, as opposed to gas in solution, exerts some stimulating effect either directly on the tissue or on the capillaries.

During the hyperaemic reaction the partial pressure of oxygen in a gas pocket approaches that found in venous blood then gradually drops to a fairly constant level. During the quiescent period following the hyperaemic stage Sibree[31] found "occasional observations in rabbits and in many human subjects give oxygen tension figures under 10mmHg."

Campbell[32] has noted that the tissue around gas pockets becomes thickened with a fibrous deposit and has demonstrated this thickening with histological sections of tissue from gas pockets in the rabbit. Tobin[45] also found fibrous thickening in the walls of gas pockets

in subcutaneous tissue of rats. Sibree found that in human subcutaneous gas pockets the skin and subcutaneous tissue thickening is more pronounced than in the rabbit. "Thickening commences at once, but is usually only slight during the first seven to ten days. Thereafter the thickening increases rapidly until at the end of fourteen to twenty days the depot must be abandoned".[31] This thickening gradually disappears but the skin remains slightly thickened and tough for many months.

As the deposit of fibrous tissue builds up, a diminished circulation in the region of the gas pocket could be expected, leading to an increase in diffusion distances and hence a delay in the response of a gas pocket to changes in blood gas tension. However, such changes if they occur do not seem to cause significant changes in the response of gas pockets and Sibree found gas pockets in man to be remarkably sensitive. "Changes in respiration, for instance, sometimes cause appreciable changes in gas tension in a subcutaneous depot at the end of one minute."[31]

The rapidity with which changes in the tissue tension will be reflected by the gas pocket is related to both the surface area and volume of the pocket. With rabbits, where large pockets are used (often 50cc), the volume is large compared with the surface area while in man, gas pockets usually form a thin loculated layer with a large surface area. This leads to a rapid response by these latter gas pockets to changes in tissue gas tensions. Due to the different diffusion rates the delay in oxygen response will be longer than that for carbon dioxide.

The evidence cited above indicates that the tissues are not in a perfectly normal state when gas is present and this abnormality is one of the shortcomings of the gas depot method. However, the effect of this abnormality on the normal tissue gas tensions are not known.

12.0 MEASUREMENT OF TOTAL GAS TENSION IN SUBCUTANEOUS TISSUE USING BOTH CONSTANT PRESSURE AND CONSTANT VOLUME SYSTEMS

The general principles of both the constant pressure and the constant volume systems for measuring total gas tensions in any medium were discussed in Section 10.2. The equipment and techniques developed for making these measurements in vivo in subcutaneous tissue are discussed below.

Preliminary investigations were carried out, using rats as the experimental animals, to develop satisfactory surgical techniques for implanting and securing the artificial gas pockets and to uncover problems associated with using the micro quantities of gas involved in these systems.

12.1 EQUIPMENT

12.1.1 Artificial Gas Pocket

The disadvantages normally encountered with gas pockets in the subcutaneous tissue and described previously were overcome in this study by creating a gas pocket within a non-reactive membrane.

The gas transfer membrane used to form the gas pocket had to be :-

- Freely permeable to the gases found in subcutaneous tissue (i.e., O_2, CO_2, N_2, H_2O).
- Biocompatible, non-irritating, and non-degradable in a physiological in vivo environment.
- Sufficiently pliable to allow normal movement of the tissue being studied.
- Capable of withstanding about -700mmHg pressure internally without collapsing.

Three materials, P.V.C., Teflon, and Silicone Rubber, known to be physiologically suitable, were tested for their relative permeability to the gases mentioned above and the results are given in Appendix 1.

Silicone rubber was found to be the most permeable and also the most pliable. It was readily available as tubing with 0.5mm I.D. and 1.00mm O.D., and in these dimensions held vacuums down to 10^{-2}mmHg without collapsing. Suitable lengths of tubing were determined experimentally where factors such as size of the animal, volume of dead space in transducers, and useful rate of movement of the water bead in the displacement transducer were all taken into account. This resulted in pockets about 3.5cm long in the rats while 6cm lengths were used in man. One end of this tubing was sleeved for 5mm over a 25mm length of 20 gauge hypodermic needle while the other end was sealed with a glass plug.

When embedded in the tissue this silicone tubing formed a non-reactive membrane, highly permeable to gas but impermeable to body fluids, enclosing a small cylindrical gas cavity of fixed dimensions.

As there was no reaction to the implanted membrane the useful life of the gas pocket was not limited by thickening of the surrounding tissue, gas transfer conditions at the start of any series of tests were the same as those at the end and these conditions were easily reproduced. Furthermore, the tissue surrounding the implant was thought to closely approximate normal conditions.

12.1.2 Displacement Transducer (Constant Pressure System)

The displacement transducer consisted of a uniform bore, glass capillary tube (12.4cm long; 0.64mm I.D.) containing a bead of water about 1cm in length. When the capillary is properly cleaned with fresh chromic acid and rinsed with distilled water, a bead of water, which retains a concave miniscus at each end, will run freely along the tube under a pressure head of less than 1mm H_2O. This can be demonstrated by placing a 1cm bead of

water near the centre of a clean capillary then tilting the tube through an angle of 5^{o}. The water will move freely along the capillary and a simple trigonometric calculation gives the effective hydrostatic pressure head acting on the water.

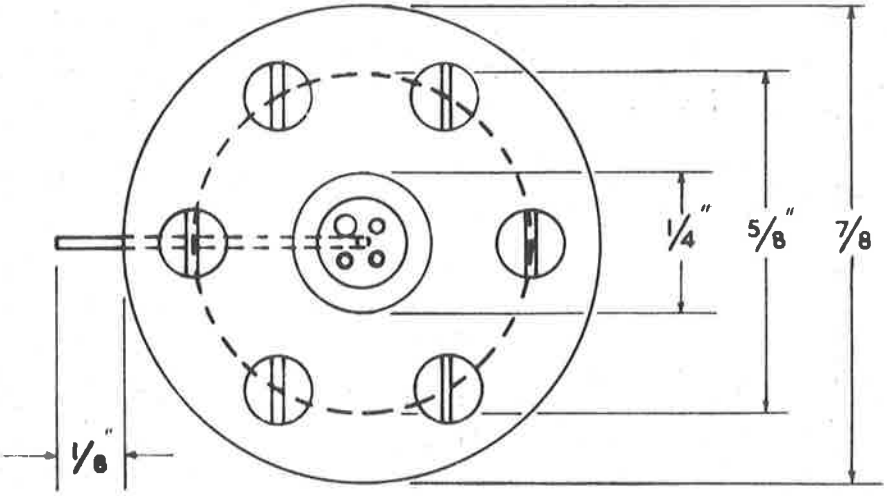
The result is a very sensitive displacement transducer with the water effectively forming an air tight plunger which moves under differential pressures of less than 0.1mmHg.

12.1.3 Pressure Transducer (Constant Volume System)

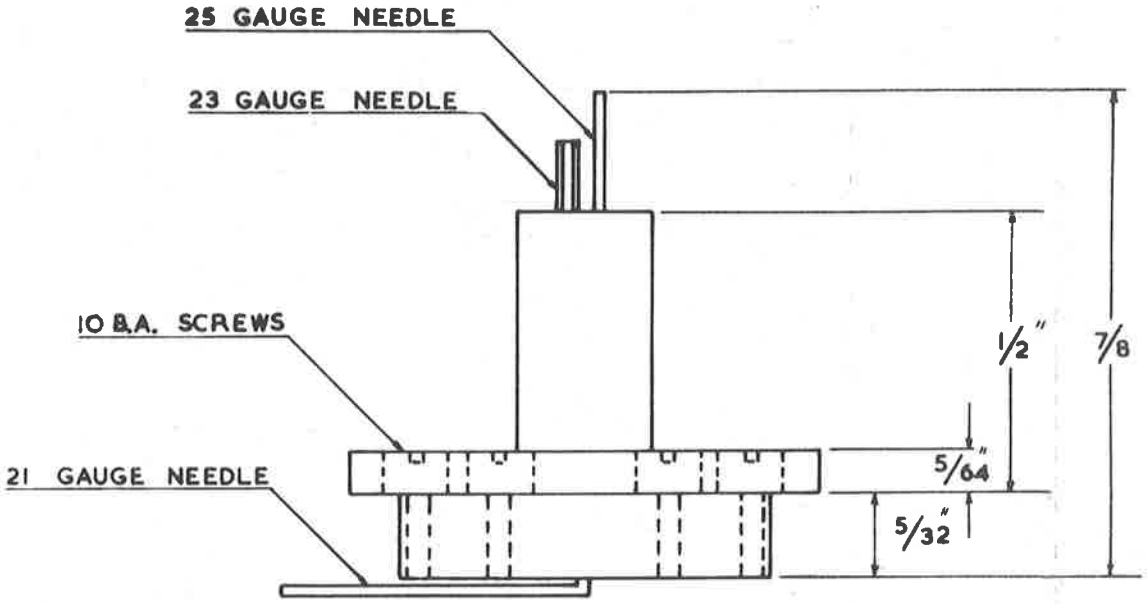
The pressure transducer was designed to be implanted under the skin of an experimental animal the size of a cat or rabbit. This imposed several design criteria which influenced the design and construction of the transducer. These criteria are outlined in Appendix 2. During the series of tests covered by this study, however, the transducer was used only externally and not implanted.

Plan, elevation, cross-section and materials used in the construction of the pressure transducer are shown in Figures 10 and 11. The membrane and its mounting ring were machined from the one piece of metal and sandwiched between the upper and lower halves of the casing to form two cavities. The upper chamber was vented to atmospheric pressure and the lower one connected via a 21 gauge needle to a blind length of silicone rubber tubing which acted as a semi-permeable membrane. The tubing, being permeable to gases and water vapour, allowed rapid equilibration of the dead space in the lower chamber with gases in the surrounding medium.

The membrane separating the two chambers deflected when there was a pressure differential across it and this deflection was monitored using a matched set of four semi-conductor strain gauges arranged in a Wheatstone bridge. Two active gauges were on the membrane; one in compression and one in



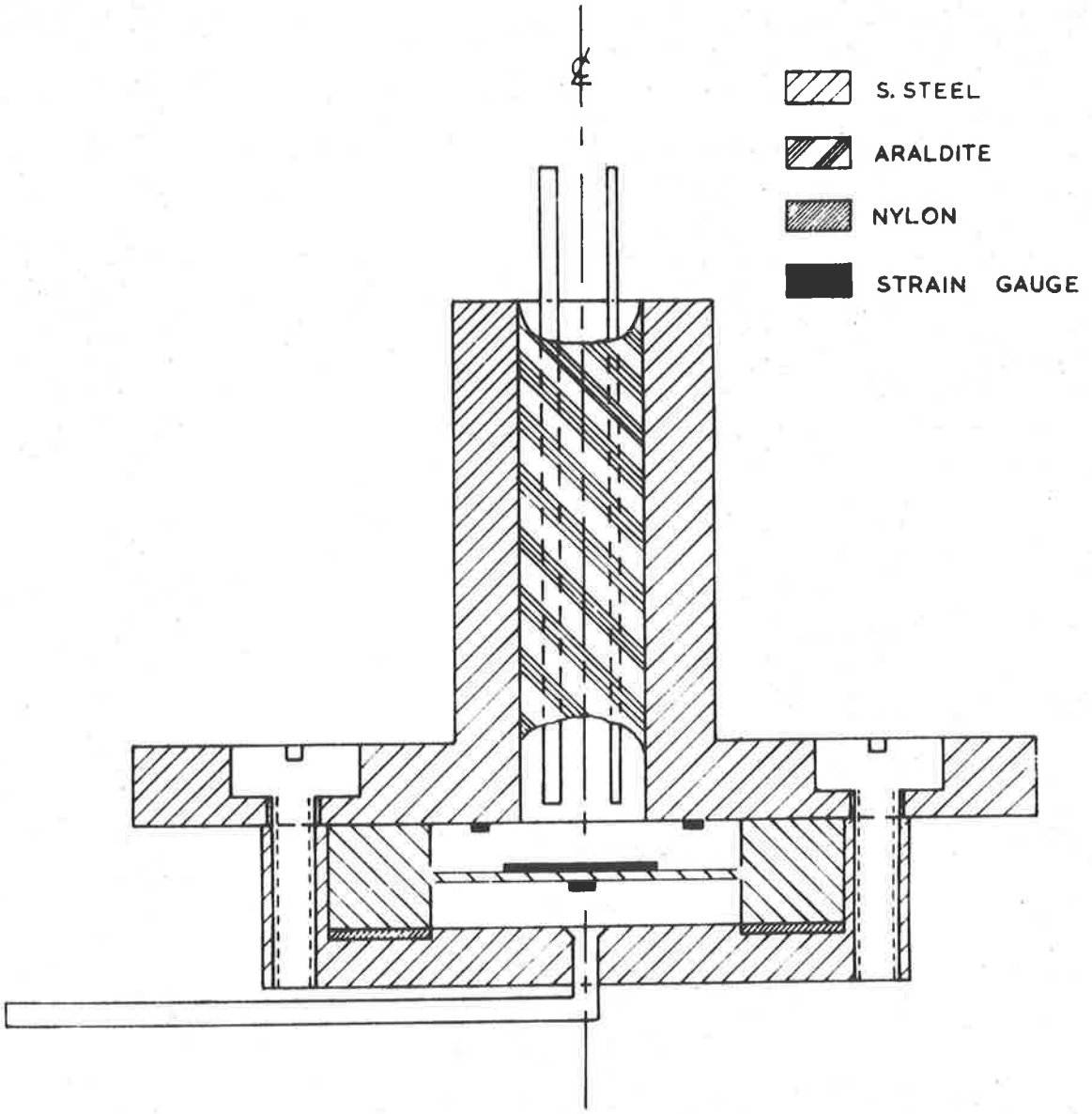
PLAN



ELEVATION

PRESSURE TRANSDUCER

Fig. 10



X – SECTION

OF

PRESSURE TRANSDUCER

Fig. 11

tension; and two dummy gauges on the inside wall of the casing as shown in Figure 11. Details of the membrane design are given in Appendix 2. The upper chamber was vented to ambient pressure through one of the needles set into the lid. This vent needle acted as the common node for the two dummy gauges while enamelled copper wires, soldered to the active gauge leads, passed up the centres of the remaining three needles and were soldered at the top. These four needles then acted as electrical pins with one at each node of the bridge. Figure 12 shows the wiring diagram of the pressure transducer.

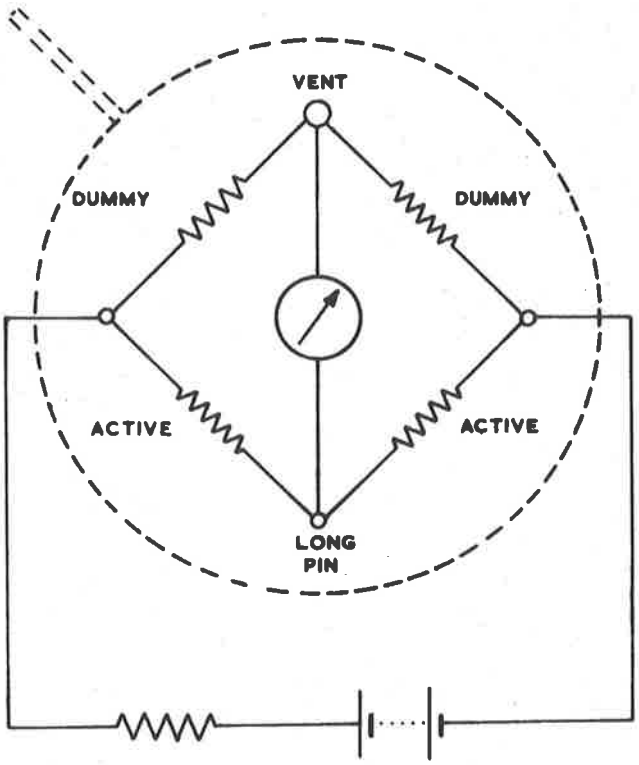
The casing was screwed together allowing easy access to the lower cavity for the purpose of cleaning. However, to completely dismantle the unit and separate the membrane from the upper part of the casing, the soldered tops of the needles would need to be cut off to free the copper leads. This would allow the membrane to be removed without damaging the strain gauges or their bonded fine leads. The internal construction of the pressure transducer is shown in Figure 13.

12.2 OPERATIONAL TECHNIQUES

12.2.1 Inserting Gas Pocket into Rats

The plugged end of the silicone rubber tubing was glued to one end of a length of flexible 20 gauge nichrome plated copper wire. This wire was used as a probe for inserting the tubing by blunt dissection into the subcutaneous tissue.

The rats were anaesthetised with an intraperitoneal injection of Nembutal (0.1cc/100g body weight) and an incision made in the skin at the nape of the neck. The free end of the wire probe passed subcutaneously from this incision to a point proximal to the root of the tail where it emerged through a second small cut in the skin. On withdrawing the wire through the lower opening the tubing was drawn into the subcutaneous tract made by the wire. The



WIRING DIAGRAM
OF
PRESSURE TRANSDUCER

Fig. 12

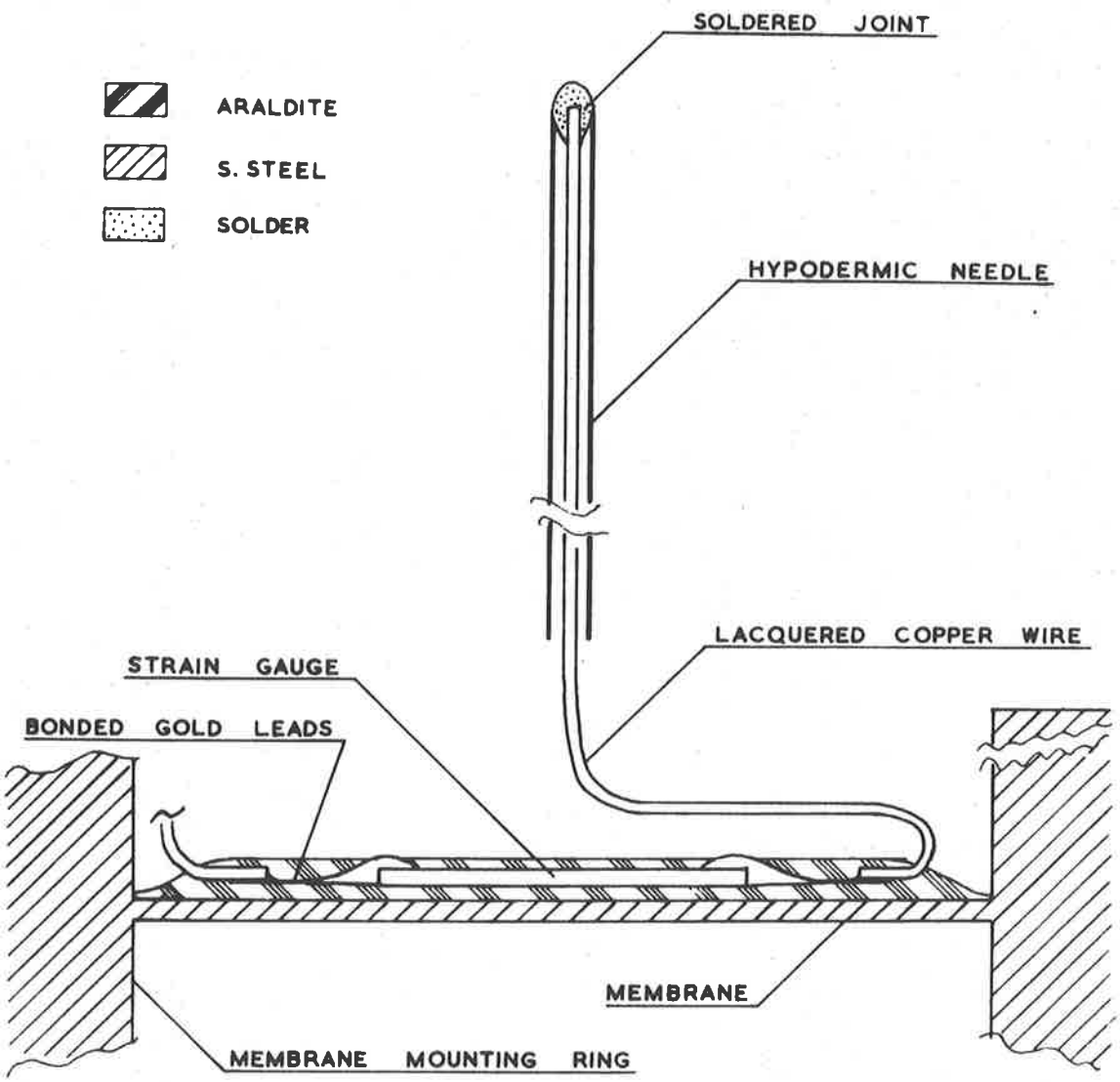


Fig. 13

Internal Construction of
Pressure Transducer

needle was left protruding through the skin at the neck and the silicone tube severed between the end of the wire and the glass bead. The exit hole in the skin was closed with one suture and another was inserted at the neck to anchor the needle and prevent displacement of the implant during animal activity.

The rats were allowed one or two days to recover from the effects of the anaesthetic and operation before any measurements were undertaken.

By using blunt dissection all the artificial gas pockets were introduced with the minimum trauma to the tissue being examined.

12.2.2 Inserting Gas Pocket into Man

The author acted as the experimental subject and in three series of trials a piece of silicone rubber tubing, exactly the same as that described above, was implanted in the subcutaneous tissue on the extensor surface of the left forearm. The tubing ran subcutaneously from a point approximately two inches distal to the elbow to a point about four inches proximal to the wrist.

Exactly the same surgical technique of blunt dissection was used to insert the gas pockets but the operations were performed under a local anaesthetic and sterile conditions. The first and second implants lasted two weeks each and the third four weeks.

The second implant was removed after two weeks when X-rays revealed that fluid was leaking into the tube. Results obtained in this series were discounted as the gas transfer area decreased markedly as the tube filled. Chromatographic analysis of the fluid showed it to have a 2 per cent protein content suggesting an extracellular fluid contamination. Examination of the implant after removal revealed longitudinal score marks on the needle and by testing the system with both ends blocked and the tubing and needle immersed in a syringe of degassed water, it

was found that water leaked into the tubing along the score marks down the side of the needle. A closer examination of several other needles revealed similar score marks and these were thought to be extrusion scores. To prevent similar leaks with the third implant the silicone rubber was glued to the needle using "Aron alpha" glue.

12.2.3 Restraining the Rats

Following the recovery period the experimental animal was placed in a cage specially designed to restrict its movements. This cage had a flat floor of steel rods that the animal could grip with its claws. The ends were made of clear perspex with a hole for the rat's tail and a hole for its snout. Eighth inch diameter steel rods spaced about ¼" apart formed the sides and top. The dimensions of the cage could be adjusted to suit the size of the animal. The needle was readily accessible between the bars, and the capillary tube was connected to the needle with a short piece of thick-walled gum rubber joined to a short piece of "mylar" tubing. These joining pieces were found to be essentially gas tight over several hours of test.

By wrapping a piece of paper towelling around the cage the animals were kept warm. As the towelling also cut down their field of view they were less restless and tended to doze most of the day. If an animal became too restless it became difficult to take accurate readings. Increased activity also increased the metabolic rate giving spurious results under these conditions. When this occurred measurements for that day were discontinued.

After completing a day's measurements the joining tubes and capillary were removed. If the needle was capped to prevent gas from being absorbed during the night the animals scratched and chewed at the cap, usually dislodging the entire implant. As a result the tube was not plugged overnight and air

was continuously absorbed into the subcutaneous tissue. However, there was no reason to believe that this caused significant changes in the tissue surrounding the tubing even over a period of four to five weeks. The gas absorption characteristics of a pocket remained constant throughout any series of tests and a macro examination of the tissue surrounding these gas pockets in rats revealed no tissue reaction.

12.2.4 Constraining the Man

For the human experiments the subject was in a sitting position with the arm containing the implant couched in a half plaster cast. The transducers were attached in a similar manner to that described above.

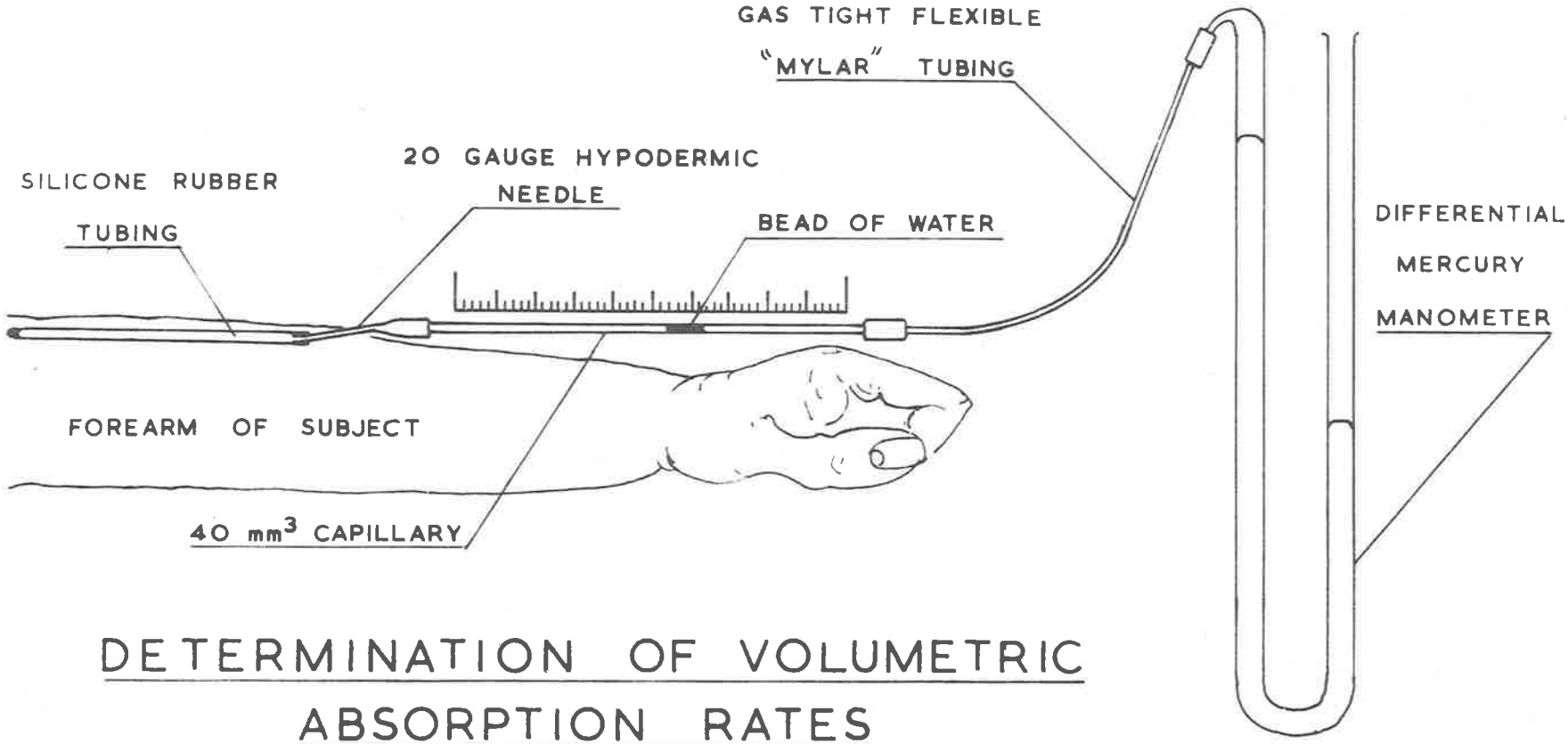
12.3 EXPERIMENTAL TECHNIQUES

12.3.1 Constant Pressure System

Figure 14 is a schematic diagram of the constant pressure system in use.

By connecting a capillary displacement transducer to the gas pocket and recording the movement of the bead of water, a displacement-time curve was obtained as the gas in the system is absorbed. From this curve, and knowing the cross-sectional area of the capillary, the volume of gas absorbed per unit time was calculated.

With the artificial gas pocket there was a constant gas transfer area and at equilibrium the driving force for gas absorption was constant. This resulted in a constant rate of absorption of gas once equilibrium conditions were reached within the system. As the rate of absorption of gas was a function of the gas transfer area as well as the driving force, the volumetric absorption rate per unit length of buried tube was calculated and corrected to standard temperature and pressure. The volumetric absorption rate (V.A.R.) calculated in this manner was designated $\dot{V}_{760}$



DETERMINATION OF VOLUMETRIC ABSORPTION RATES

Fig. 14

Constant Pressure System
For Determining Subcutaneous Gas Tensions

and had units of $mm^3/hr/cm$ tubing. This allowed the direct comparison of all results regardless of the length of tubing used.

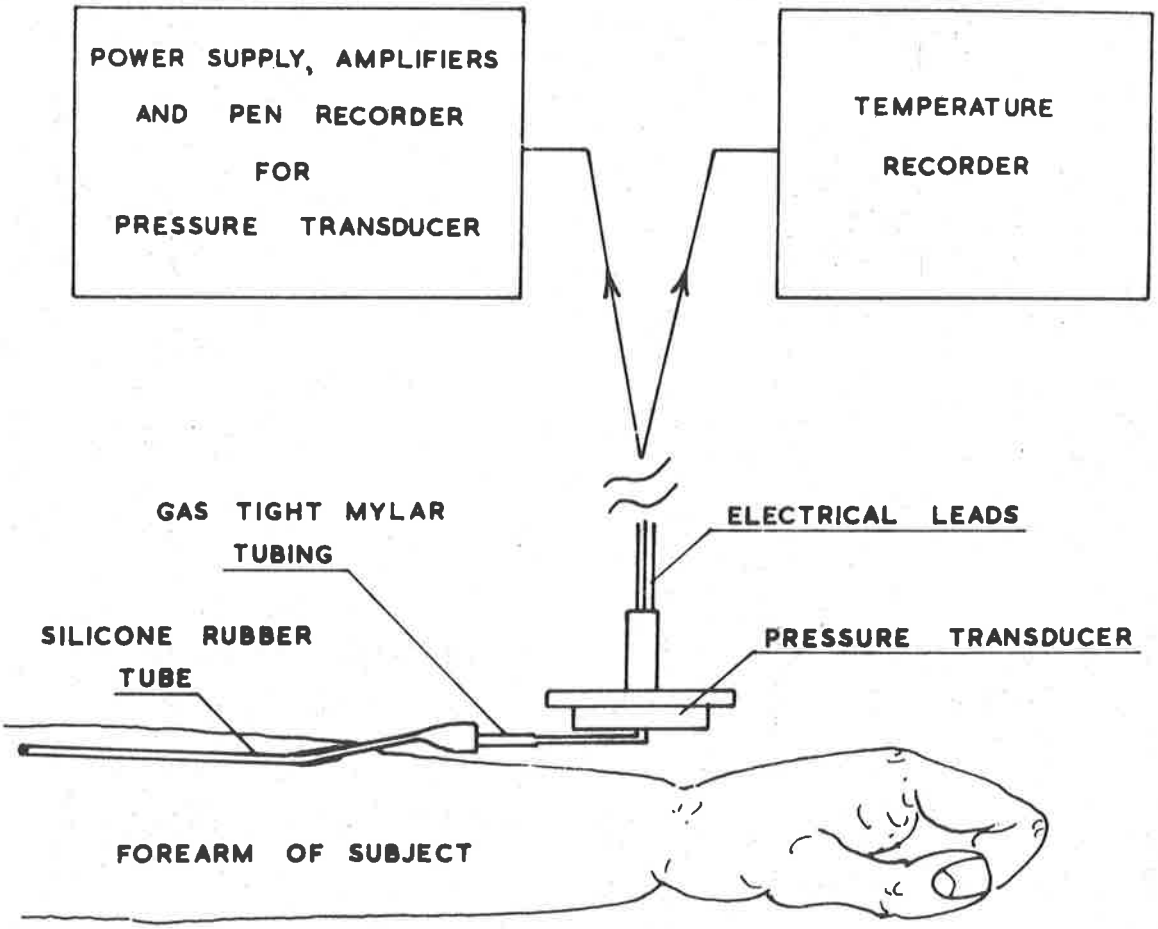
Once the gases in the system had equilibrated with the tissue gas tensions a differential mercury manometer was connected to the open end of the capillary tube and by reducing the pressure in the system (applying a back pressure to the bead of water) the driving force for the absorption of gas was reduced. For each of these negative pressures the V.A.R. can be determined. At equilibrium when the total pressure within the gas pocket is equal to the total gas tension in the surrounding tissue there will be no driving force for the absorption of gas and hence V.A.R. will be zero. If the pressure in the pocket is less than the tissue gas tension there will be an efflux of gas and V.A.R. will be negative. The negative pressure required to produce no net gas exchange, or a V.A.R. of zero, was thus a measure of the tissue unsaturation.

Experimental results obtained in this manner were corrected for the effect of thermal depression of water vapour pressure within the transducer and the corrected values gave the tissue unsaturation at $37^{o}C$. (See Appendix 3 for details of temperature corrections). The total gas tension in the tissue is simply the ambient pressure less the tissue unsaturation. This technique for measuring tissue gas tensions is applicable to a gas pocket of fixed dimensions in any tissue.

12.3.2 Constant Volume System

Figure 15 is a schematic diagram of the constant volume system in use.

As shown in Figure 9 the constant pressure system can only respond slowly to a step change in gas tension of the medium surrounding the gas pocket. This slow response is due to the time taken for gas to diffuse out of the transducer dead space and is a rate



DETERMINATION OF UNSATURATION USING PRESSURE TRANSDUCER

Fig. 15

Constant Volume System
For Determining Subcutaneous Gas Tensions

limited process governed by the mass transfer coefficients of the gases involved. These coefficients depend upon the membrane permeability and diffusion characteristics of the medium surrounding the membrane.

Due to the thermal drift in the transducer and recording equipment it was not possible to determine exactly the system transient. However, as the transducer was coupled externally to both the rats and the man the "mylar" tubing used to couple the transducer to the gas pocket was severed after varying periods of time. The resultant step change in output gave a direct measure of the negative pressure that had developed in the transducer while it was connected.

When in use in the human tests, the transducer was separated from the skin of the forearm by a gauze pad, covered lightly with another piece of gauze and then taped to the forearm to prevent movement and to take all the strain off the sutures holding the implanted tubing in place. To check on the transducer temperature under these conditions a thermocouple was embedded into the lower chamber of the transducer. With the room temperature at 20°C the dead space in the transducer was found to reach 26°C. Room temperature changes did cause fluctuations in the transducer temperature but these fluctuations were damped by the transducer's thermal inertia and the light gauze bandage.

13.0 RESULTS OF MEASUREMENTS

All the results obtained for both the rats and man using both the constant pressure and the constant volume systems are tabulated in Appendix 4.

13.1 RATS

Equipment and techniques used in this study were developed using rats as the experimental animals and the tissue unsaturation was examined for the following conditions :-

- Atmospheric pressure breathing air
- Reduced pressure breathing air
- Atmospheric pressure breathing oxygen enriched air.

13.1.1 Atmospheric Pressure Breathing Air

The tissue unsaturation was determined using both the constant pressure and the constant volume systems.

Constant Pressure System

Eighteen rats were studied, twelve females and six males. Preliminary investigations showed a greater variability in the values of V.A.R. obtained for female rats. These values also showed a cyclic variation over five-day periods and these cyclic changes were thought to be related to metabolic changes during the oestrous cycle. A detailed study was therefore carried out on five of the male animals.

A sample displacement vs. time curve showing the movement of the water miniscus is shown in Figure 16 while the cumulative V.A.R. results obtained from the detailed study of the five male rats are shown in Figure 17.

As the V.A.R. appeared to decrease linearly with decreasing pressure in the system, a line of best fit, using the least square regression method, was

FIGURE 16 : SAMPLE DISPLACEMENT - TIME CURVES FOR CONSTANT PRESSURE SYSTEM SHOWING HOW $\dot{V}_{760}$ VARIES WITH ALVEOLAR pO_2.

RATS

(a) Breathing air at atmospheric pressure

(b) Breathing air at reduced pressure

pO_2 decreased

$\dot{V}_{760}$ decreased

(c) Breathing oxygen enriched air

pO_2 increased

$\dot{V}_{760}$ increased.

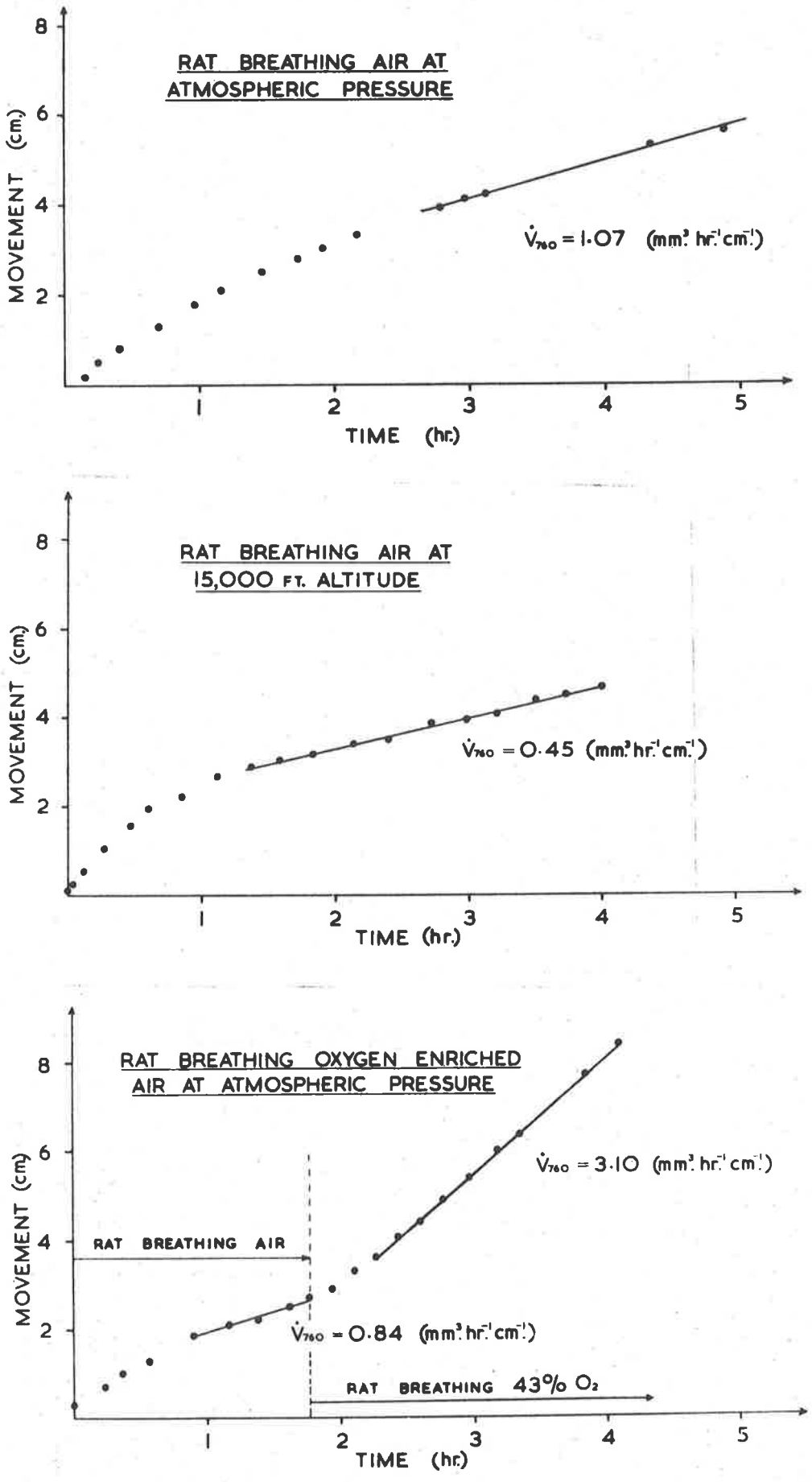

RAT BREATHING AIR AT
ATMOSPHERIC PRESSURE
MOVEMENT (cm.)
TIME (hr.)
$\dot{V}_{760}$ = 1·07 (mm.³ hr.⁻¹ cm.⁻¹)
RAT BREATHING AIR AT
15,000 FT. ALTITUDE
$\dot{V}_{760}$ = 0·45 (mm.³ hr.⁻¹ cm.⁻¹)
RAT BREATHING OXYGEN ENRICHED
AIR AT ATMOSPHERIC PRESSURE
$\dot{V}_{760}$ = 3·10 (mm.³ hr.⁻¹ cm.⁻¹)
RAT BREATHING AIR
$\dot{V}_{760}$ = 0·84 (mm.³ hr.⁻¹ cm.⁻¹)
RAT BREATHING 43% O₂

Fig. 16

FIGURE 17 (a) RATS

CUMULATIVE V.A.R. VALUES FOR RATS SHOWING THE DECREASE IN $\dot{V}_{760}$ AS THE PRESSURE IN THE SYSTEM IS REDUCED. ANIMALS BREATHING AIR AT ATMOSPHERIC PRESSURE.

(b) MAN

CUMULATIVE V.A.R. VALUES FOR MAN SHOWING THE DECREASE IN $\dot{V}_{760}$ AS THE PRESSURE IN THE SYSTEM IS REDUCED. ANIMALS BREATHING AIR AT ATMOSPHERIC PRESSURE.

N.B. Negative Pressures are not corrected for water vapour depression.

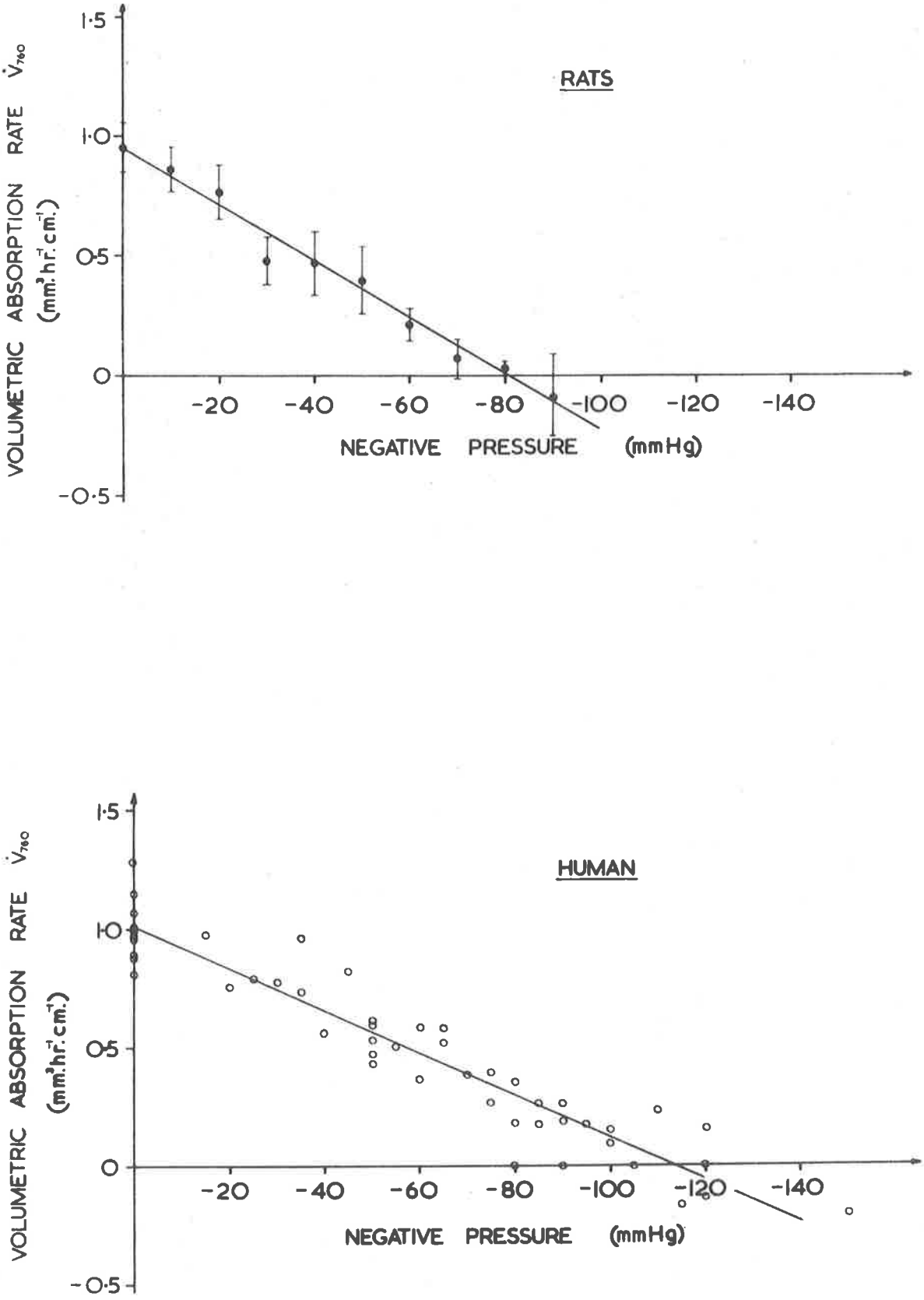

RATS
VOLUMETRIC ABSORPTION RATE $\dot{V}_{H_2O}$ (mm³.hr⁻¹.cm⁻¹)
1·5
1·0
0·5
0
-0·5
-20
-40
-60
-80
-100
-120
-140
NEGATIVE PRESSURE (mmHg)
HUMAN
VOLUMETRIC ABSORPTION RATE $\dot{V}_{H_2O}$ (mm³.hr⁻¹.cm⁻¹)
1·5
1·0
0·5
0
-0·5
-20
-40
-60
-80
-100
-120
-140
NEGATIVE PRESSURE (mmHg)

Fig. 17

fitted to the data and is also plotted in Figure 17. This gave a reading of -81mmHg which corresponded to an unsaturation of 67mmHg when the temperature correction for the partial pressure of water vapour was applied. An explanation of the temperature correction is given in Appendix 3.

Constant Volume System

The results obtained using this system are shown graphically in Figure 18.

From the graph it can be seen that the transient period, while the gas pocket and transducer dead space are equilibrating with the surrounding tissue, lasts approximately one and a half hours. The mean pressure developed at equilibruim is -73mmHg and when temperature corrections are applied this results in a tissue unsaturation of 67mmHg.

13.1.2 Reduced Pressure Breathing Air

Detailed investigations were not carried out for this condition but preliminary results using the constant pressure system showed that there was a marked drop in V.A.R. when the ambient pressure was reduced. Figure 16 shows the results of one such test. This condition is equivalent to reducing the partial pressure of oxygen in the breathing mix.

13.1.3 Atmospheric Pressure Breathing Oxygen Enriched Air

Once again only preliminary investigations using the constant pressure system were carried out under these conditions. Figure 16 shows the way in which V.A.R. increased when the animal was breathing 43 per cent O_2.

13.2 MAN

The subcutaneous tissue unsaturation was examined in one man for conditions similar to those investigated in the rat.

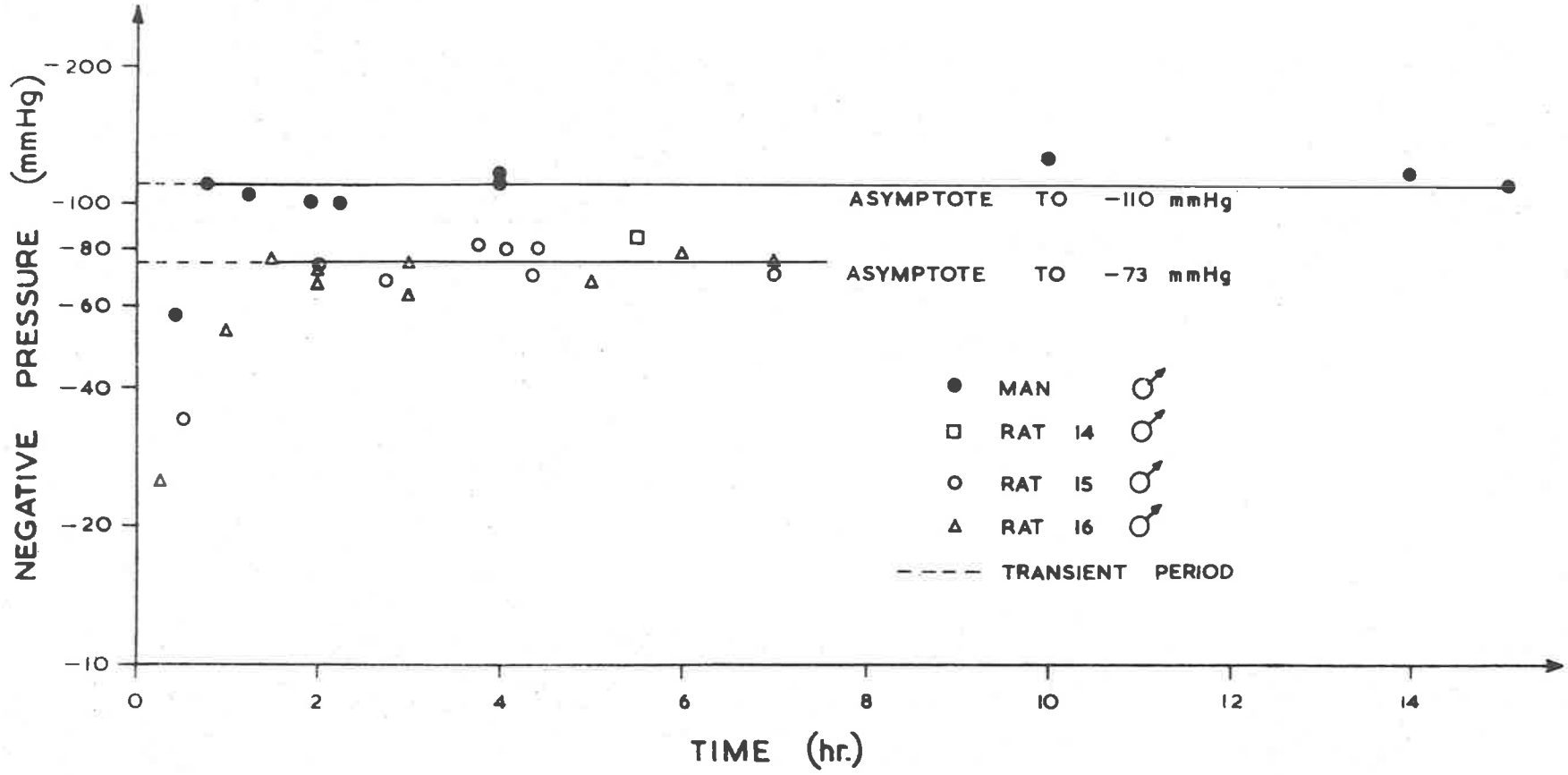


FIGURE 18 : UNSATURATIONS IN SUBCUTANEOUS TISSUE OF BOTH RAT AND MAN MEASURED WITH THE CONSTANT VOLUME SYSTEM

N.B. Pressures are not corrected for water vapour depression.

Three series of tests were carried out, the first and third series were successful while the results from the second series were invalid because fluid leaked into the silicone tubing.

13.2.1 Atmospheric Pressure Breathing Air

As with the rat a thorough examination of the tissue unsaturation was carried out using both the constant pressure and the constant volume system.

Constant Pressure System

A sample displacement vs. time curve showing the movement of the bead of water in the displacement transducer is shown in Figure 19, while Figure 17 shows the cumulative V.A.R. readings obtained from the successful trials.

The least squares regression line of best fit to this data gave a negative pressure of 115mmHg at equilibrium. This corresponded to a tissue unsaturation of 97mmHg when water vapour is corrected for temperature.

Constant Volume System

Figure 18 shows the results obtained using this system.

In these experiments the transient period for the pressure transducer was approximately three quarters of an hour and a mean asymptotic pressure of -110mmHg was developed. This corresponded to a tissue unsaturation of 92mmHg when temperature corrections for water vapour were applied.

13.2.2 Reduced Pressure Breathing Air

Three series of experiments were carried out at reduced pressures with the subject being decompressed to altitudes of 4,000, 6,000 and 10,000 feet.

The constant pressure system was used and Figure 19 shows a displacement vs. time curve obtained on one of the 10,000 feet runs.

FIGURE 19 : SAMPLE DISPLACEMENT TIME CURVES FOR CONSTANT PRESSURE SYSTEM.

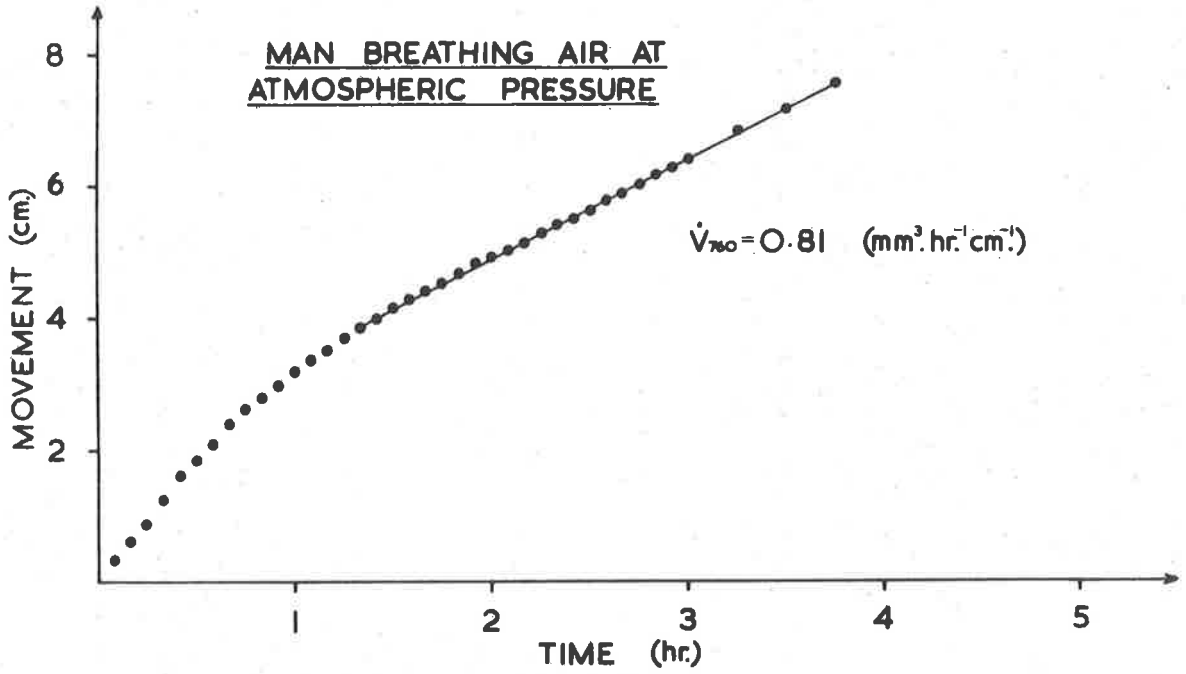
MAN

(a) Breathing air at atmospheric pressure

(b) Breathing air at reduced pressure

pO_2 decreased

$\dot{V}_{760}$ decreased


MAN BREATHING AIR AT
ATMOSPHERIC PRESSURE
$\dot{V}_{760} = 0.81$ (mm³. hr.⁻¹ cm⁻¹)
MOVEMENT (cm.)
8
6
4
2
1
2
3
4
5
TIME (hr.)

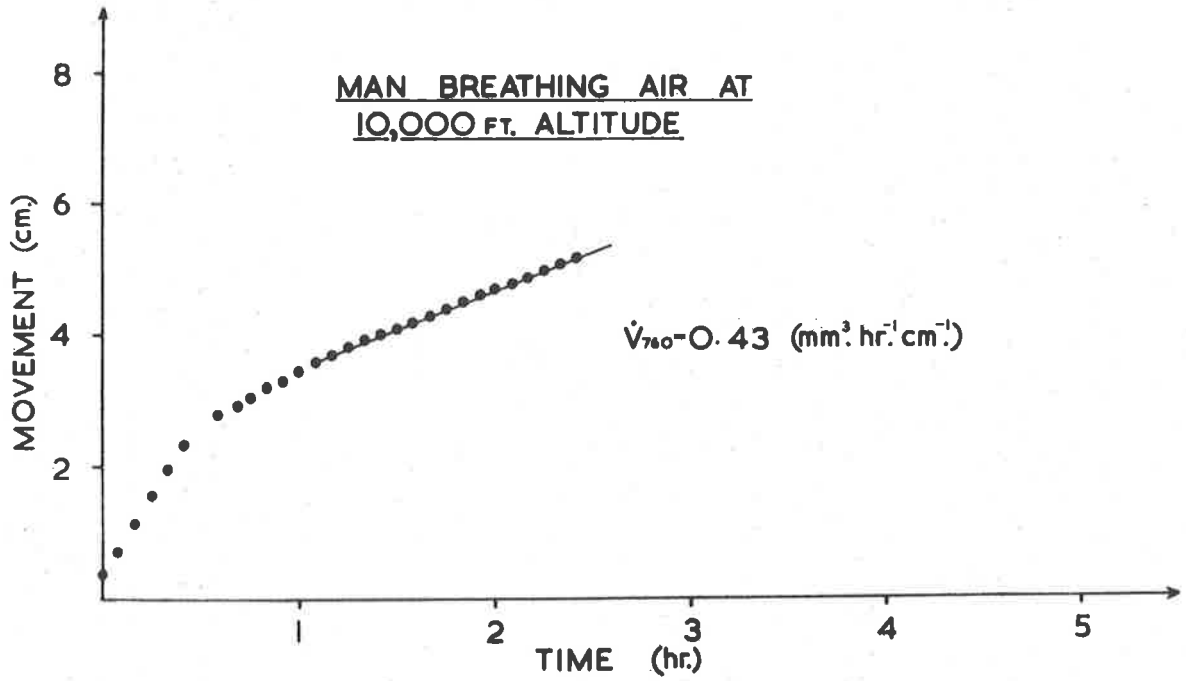

MAN BREATHING AIR AT
10,000 FT. ALTITUDE
$\dot{V}_{760} = 0.43$ (mm³. hr.⁻¹ cm⁻¹)
MOVEMENT (cm.)
8
6
4
2
1
2
3
4
5
TIME (hr.)

Fig. 19

Volumetric absorption rates were noted at equilibrium for each altitude and V.A.R. values were also determined for several back pressures. These results did show that V.A.R. decreased significantly as the ambient pressure was reduced (Figure 20). Furthermore, as shown by the V.A.R. readings at 10,000 feet (Figure 21) the tissue unsaturation decreased as the altitude increased. However, insufficient data was obtained to determine accurately the unsaturations developed at these reduced environmental pressures.

All results obtained are tabulated in Appendix 4.

13.2.3 Atmospheric Pressure Breathing Oxygen Enriched Air

Three exploratory tests under these conditions were made using the constant pressure system.

In the first the transducer was attached and one and a half hours allowed for equilibration. A mixture of 60 per cent oxygen, 40 per cent nitrogen was then breathed for two hours and 40 minutes from a face mask and for a further one and a half hours through a mouth piece supplied by a scuba demand valve. This was a total of four hours and 10 minutes on 60 per cent oxygen, and resulted in the development of 262mmHg unsaturation (corrected value).

The second test entailed an equilibration period of three hours 20 minutes with the subject breathing air and then one hour 40 minutes on 100 per cent oxygen from a face mask and a further one and a half hours on 100 per cent oxygen from a mouthpiece. This was a total of three hours 10 minutes and the unsaturation developed was 310mmHg (corrected value).

The third test entailed breathing 100 per cent oxygen for nine hours. This was supplied by placing a large plastic bag over the subject's torso and flushing 100 per cent oxygen through at a flow rate of 10 litres per minute. On disconnecting the trans-

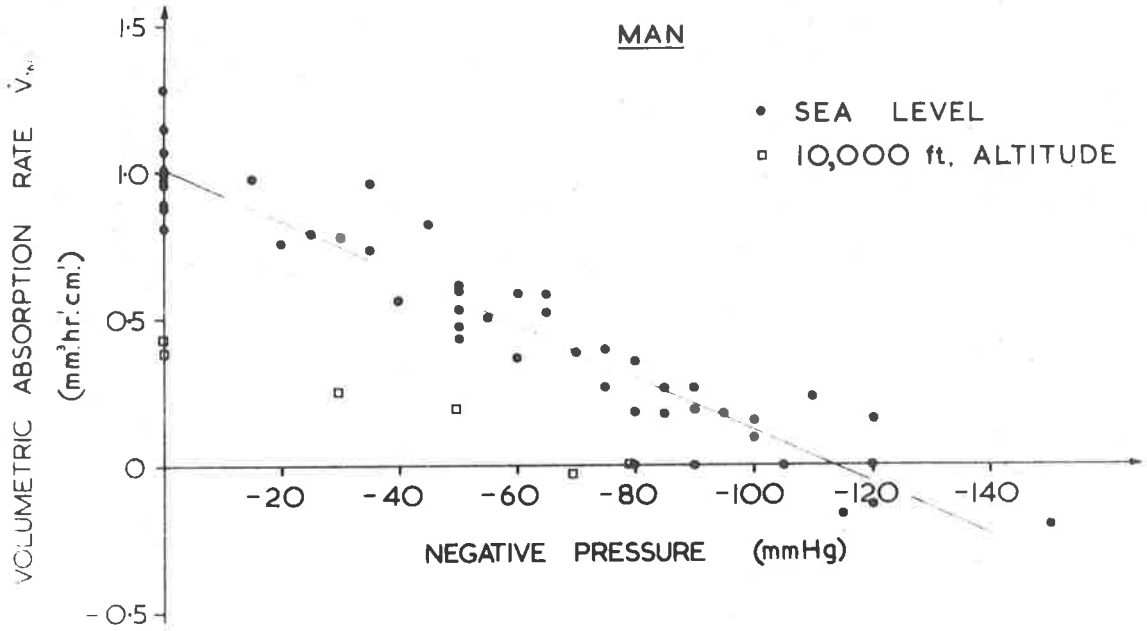

MAN
SEA LEVEL
10,000 ft. ALTITUDE
VOLUMETRIC ABSORPTION RATE $\dot{V}_{N_2}$
(mm³.hr⁻¹.cm⁻¹)
1·5
1·0
0·5
0
-0·5
-20
-40
-60
-80
-100
-120
-140
NEGATIVE PRESSURE (mmHg)

Fig. 20

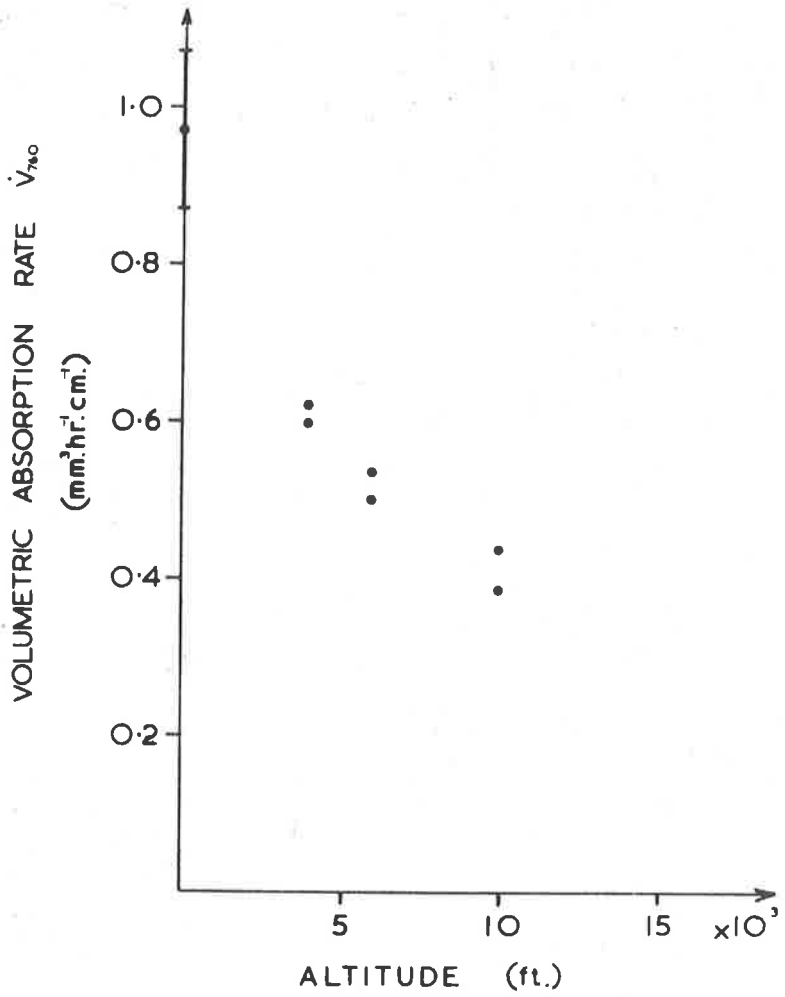

VOLUMETRIC ABSORPTION RATE $\dot{V}_{760}$
(mm³.hr⁻¹.cm⁻¹)
1·0
0·8
0·6
0·4
0·2
5
10
15
x10³
ALTITUDE (ft.)

Fig. 21

ducer, the recorder exceeded the full scale deflection at that particular amplification and it is only possible to say that an unsaturation of more than 560mmHg had been developed over the nine hour period. The tube became dislodged from the arm following this test and thus terminated this final series of tests.

The results of all these tests on both rats and man are summarised in Table 2.

TABLE 2 - SUMMARY OF MEASUREMENTS OF GAS TENSIONS IN SUBCUTANEOUS TISSUE MADE ON 18 RODENTS AND 1 HUMAN SUBJECT

	Unsaturation Developed in Subcutaneous Tissue		Test Conditions
	Constant Pressure System	Constant Pressure System	
	ATMOSPHERIC PRESSURE BREATHING AIR		
Rat	67mmHg	57mmHg	
Man	95mmHg	92mmHg	
	ATMOSPHERIC PRESSURE BREATHING OXYGEN ENRICHED AIR		
Rat	$\dot{V}_{760}$	-	43% O_2 for 2hrs. 40 mins.
Man	-	262mmHg	60% O_2 for 4hrs. 10 mins.
Man	-	310mmHg	100% O_2 for 3hrs. 10 mins.
Man	-	>560mmHg	100% O_2 for 9hrs.
	REDUCED PRESSURE BREATHING AIR		
Rat	$\dot{V}_{760\downarrow}$	-	15,000 ft. Altitude (429mmHg)
Man	$\dot{V}_{760\downarrow}$	-	4,000 ft. Altitude (656mmHg)
Man	$\dot{V}_{760\downarrow}$	-	6,000 ft. Altitude (609mmHg)
Man	$\dot{V}_{760\downarrow}$	-	10,000 ft. Altitude (523mmHg)

GENERAL DISCUSSION

GENERAL DISCUSSION

The approach toward development of decompression schedules outlined in this study is based on a simplified model of gas transfer in the body where diffusion is assumed to be the mechanism for transferring gas between the capillaries and the tissue. By using numerical methods to determine gas tension distributions in the tissue model and employing digital computing techniques, the effects of circulation time, tissue unsaturation and intercapillary distance were readily simulated for even the most complicated dive profiles. The programme developed was used in two ways :-

- to analyse a given dive profile in terms of the spatial distribution of total gas tension in the tissue
- to generate decompression profiles based on predetermined criteria of safety (viz. limited peak supersaturations).

Two examples of dive analyses and one example of how a limited supersaturation profile can be generated are shown in Figure 7. These computations highlighted the necessity for careful structuring of the depth and duration of stages and the significance of short deep stages and slow rates of ascent in preventing the development of supersaturation was also demonstrated. The whole approach is aimed at preventing the occurrence of conditions liable to cause phase separation of gas. As supersaturation of the system is a necessary prerequisite for phase separation then by preventing supersaturation at any point in the tissue throughout an entire decompression a perfectly safe decompression can be generated.

This technique can be readily extended to generate profiles where no supersaturation is created or even where a level of unsaturation is maintained. It can also be used to examine the effect, on gas concentration distribution and development of supersaturation, of increasing

the oxygen content of the breathing mixture; furthermore, other parameters such as quantity of gas or energy density of the gas can be determined as functions of the gas concentration distribution.

Throughout this analysis the total gas tension in the tissue is the important factor to be followed because at equilibrium it is lower than the ambient pressure. This gas tension discrepancy arises through the "mechanism of unsaturation" and means that the ambient pressure can be lowered until it is equal to the total gas tension of the tissue without creating supersaturated conditions.

All the calculations and examples given in this study assume that phase separation of gas has not been initiated. If phase separation did occur the model used would not predict the correct concentration distribution around the phase separated region.

In developing the model of the overall gas transfer system in the body, the importance of knowing accurately the total gas tension in the tissue became apparent. The second part of this study was therefore concerned with the measurement of this parameter in rat and man.

Tissue tensions measured with both the constant pressure and constant volume techniques were in close agreement. In man the mean values of tissue unsaturation (ambient pressure minus total gas tension in tissue), 95 and 92 mmHg using the constant pressure and constant volume techniques respectively, were about 40mmHg greater than the accepted venous blood unsaturation. As all the gases involved were found to pass freely through the silicone rubber tubing the only explanation that can be offered is that the oxygen tension in the tissue is indeed very low, even lower than previous workers have shown[31,32]. From Table 1, if the tissue oxygen tension is zero and all other values remain constant, the total gas tension becomes 656mmHg. Therefore, unsaturation becomes 760 - 656 = 94mmHg which is close to the measured values.

The tissue unsaturations obtained for the rats with the constant pressure and constant volume systems were 57mmHg and 67mmHg respectively. These values are approximately 30mmHg less than the values obtained for man.

Hills and Le Messurier[48], using a constant volume system, measured 79mmHg in the subcutaneous tissue of a rabbit. These figures for man, rat and rabbit indicate that there is a species difference in tissue unsaturation.

If the blood gas tensions in rat and rabbit are similar to those found in man, then the oxygen tensions in subcutaneous tissue of both these animals is closer to the venous blood oxygen tension than is the tissue oxygen tension in man. As all measurements on the rats were taken during the day and these animals are normally nocturnal they dozed most of the time. This would have resulted in lower metabolic requirements than when they were active and may account for the low unsaturation.

From time to time some of the animals became restless during the course of a day's readings and when this occurred it was difficult to continue the readings using the constant pressure system. However, it was noticed that this increased level of activity increased the volumetric absorption rate (V.A.R.), although it usually led to the termination of the test. As a result it was not possible to accurately correlate V.A.R. with animal activity level. The subcutaneous tissue gas tensions measured in man showed less variation than those in rats. This could have been due to better control of the level of activity of the human subject.

Attempts were made to obtain micro quantities of equilibrated gas from the artificial gas pockets for analysis by gas chromatographic methods. These attempts were unsuccessful due to poisoning of the chromatograph columns with volatile components from the sealant used in the sampling syringes. As a result it is not possible to state the gas tensions of the individual gases in the tissue. However, it is the TOTAL gas tension in tissue that is the important factor in determining supersaturation

and hence the likelihood of phase separation of gas in tissue.

The constant pressure system proved to be a very sensitive method of determining tissue gas tensions and was employed in the tests done at reduced pressure. The initial tests at 10,000 feet altitude showed that there was still a significant unsaturation at this altitude and, as predicted from equation (5), the unsaturation decreased as pO_2 was reduced. This is demonstrated by the V.A.R. results shown in Figure 20 but there are insufficient points to determine accurately the new unsaturation. Figure 21 shows that there is a definite relation between ambient V.A.R. values and the alveolar pO_2.

All the tests at reduced pressure were conducted without the use of oxygen and each was of about six hours duration. While this period of time was probably insufficient for complete equilibration of all the body tissues with the new pressure, the constant rate of absorption of gas at equilibrium indicated that the subcutaneous tissue being examined had equilibrated with the new conditions.

The unsaturation developed in the subcutaneous tissue of man at sea level pressure when breathing 100 per cent oxygen for nine hours was found to be in excess of 560mmHg. This is approaching the range 628 to 668mmHg predicted by equation (5), and 600 mmHg predicted by Rahn[40]. Furthermore, Hills and Le Messurier[48] measured 628 mmHg of unsaturation in the subcutaneous tissue of a rabbit after 24 hours on 100 per cent oxygen.

The importance of maintaining the maximum unsaturation (or minimum tissue gas tension) has been emphasised throughout this study and the "denitrogenation" or "washing out" process undertaken by air crews and astronauts where they breathe 100 per cent oxygen for several hours prior to take off is in fact decreasing the total gas tension in their tissue. This greatly increases the drop in ambient pressure that can be tolerated by these personnel before their tissues become supersaturated and phase separation

of gas can occur. Breathing oxygen therefore offers increased protection against development of decompression sickness. Where practical, oxygen breathing between dives of a repetitive nature should be encouraged to help lower the residual gas tensions from previous dives and thus afford increased protection on subsequent dives. If the technical expertise, necessary to supply a diver with a continuously variable gas mixture, was combined with a thorough knowledge of the toxic limits of oxygen partial pressures, it should be possible to continuously generate a breathing mixture that would keep the tissue gas tensions to a minimum and thus afford maximum protection against development of decompression sickness due to the phase separation of gas.

GENERAL SUMMARY

This study highlights the importance of considering both the spatial distribution of gas in tissue and the tissue unsaturation when developing decompression schedules based on a diffusion model.

Part I of this study deals with the theoretical analysis of a simplified model of the gas transfer system in the body to determine gas concentration distributions and peak supersaturations in tissue during decompression.

Part II deals with the experimental determination of total gas tensions in the subcutaneous tissue of rat and man. The effects, on tissue gas tension, of changes in the environmental pressure and pO_2 in the breathing mixture were also examined.

The unsaturation in subcutaneous tissue in a sedentary man, breathing air, was found to be 95mmHg and 92mmHg measured with a constant pressure and constant volume technique respectively while 67mmHg and 57mmHg were measured in rat subcutaneous tissue for the same conditions.

APPENDICES

APPENDIX NO. 1

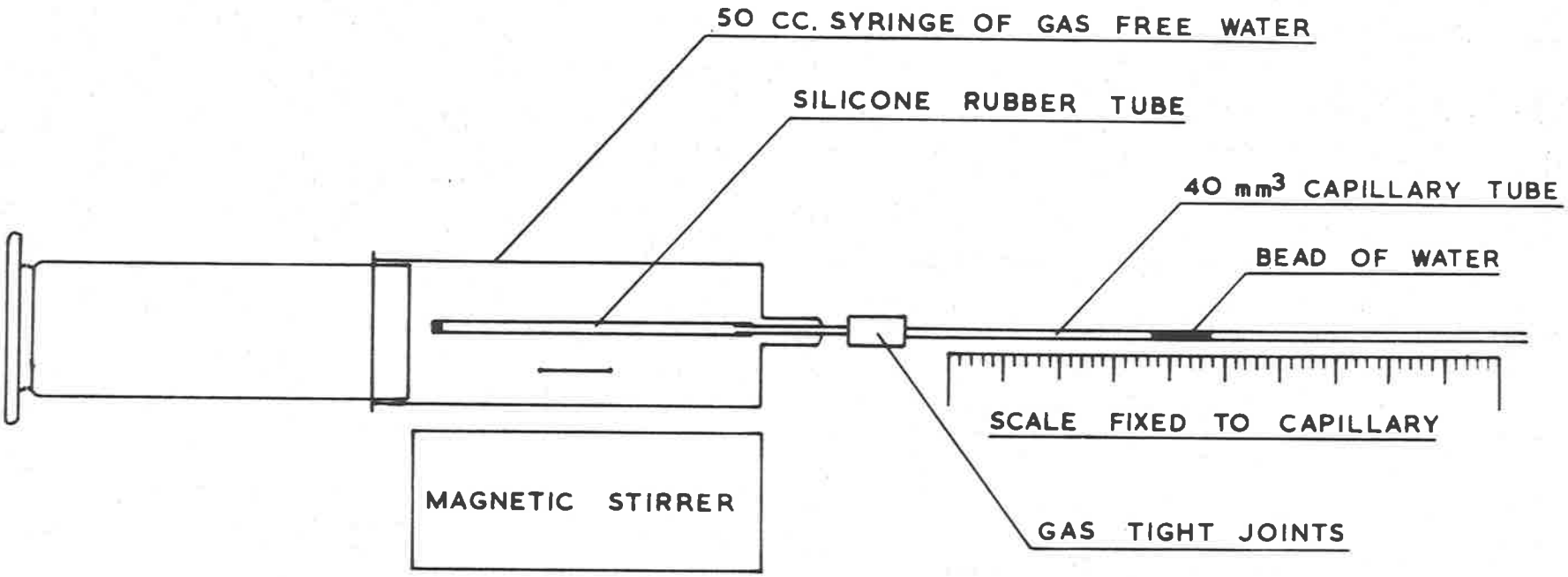
RELATIVE DIFFUSION RATES OF O_2, CO_2, N_2, AND H_2O THROUGH SILICONE RUBBER TUBING

Initially the relative permeability of air through P.V.C., teflon and silicone rubber tubing was investigated, then with the silicone tubing proving the most permeable and having the best biocompatibility properties the relative permeability of this tubing to each of the gases found in the physiological environment (O_2, CO_2, N_2, and H_2O) was investigated.

TECHNIQUE

A 50cc syringe was filled with degassed water and cooled to 20°C. The degassed water was obtained by drawing the water anaerobically from the bottom of a 250cc conical flask in which water was boiled vigorously for several minutes prior to taking sample and kept boiling while the sample was extracted. A 3cm length of the tubing being studied was then introduced through the tip of the syringe with the inserted end sealed and the other end attached via a 20 gauge needle to a displacement transducer (as described in section 12). With the tubing and transducer filled with the gas being examined at atmospheric pressure and the tubing surrounded by water with a very low gas tension there was a driving force for the absorption of gas of about 760mmHg. The water was kept well mixed throughout each test by using a magnetic stirrer. This test system is shown schematically in Figure 22.

During each test about $20mm^3$ of gas is absorbed from the capillary tube into the 50cc's of water. With N_2, the least soluble of the gases examined, this leads to a rise of about 2.5mmHg in the gas tension of the water if there is perfect mixing. Allowing for incomplete stirring of the water, there may be a rise of say 5mmHg in the gas tension of the water near the tubing. This would result



DETERMINATION OF RELATIVE DIFFUSION RATES OF OXYGEN NITROGEN AND CARBON DIOXIDE THROUGH SILICONE RUBBER TUBING

Fig. 22

in less than 1 per cent drop in the driving force for the absorption of gas. Furthermore, it is doubtful that a significant boundary layer containing high gas concentrations would develop around the tube as continuous buffeting by the stirrer would break it up. The error introduced by assuming the driving force for the absorption of gas to be equal to the barometric pressure, was therefore less than 1 per cent.

By plotting the movement of the bead of water in the transducer over a suitable period of time the volumetric rate of absorption of gas for the tube was determined in terms of the volume of gas absorbed (mm^3/hour/cm tubing) at 20^oC and with a driving force for the absorption of gas of 760 mmHg. This was satisfactory for O_2, N_2, CO_2 and air but for water vapour a different technique was used.

A length of tubing was filled with water, the ends blocked off and then the tube was placed into a dessicator over calcuim chloride. The tubing was weighed at regular intervals and by converting the weight loss per hour into an equivalent volume of water vapour at S.T.P. a volumetric absorption rate for water was calculated. While the different conditions for gas transfer of water vapour precluded the direct comparison of V.A.R. values for water vapour with the values obtained for the other gases, the test was satisfactory for showing that water vapour would pass freely through the tubing.

RESULTS

The results obtained showing the relative permeability of P.V.C., teflon and silicone rubber tubing to air are given below in Table 1. From this it can be seen that the silicone is about 80 times more permeable than P.V.C.

Results of the more detailed analysis of the permeability of silicone tubing to CO_2, O_2, N_2 and H_2O are shown in Table 2 which indicates that these gases will all pass freely through this tubing.

Tests in vivo and tests with a length of tube blocked at each end and immersed in a container of degassed water showed that neither body fluids nor liquid water would pass through the tubing.

CONCLUSIONS

These tests showed that of the materials examined the silicone rubber tubing was the most suitable. It was impervious to water and other body fluids, freely permeable to O_2, N_2, CO_2 and water vapour, and non-reactive in a physiological environment.

TABLE 1

RELATIVE PERMEABILITY OF AIR THROUGH P.V.C., TEFLON and SILICONE RUBBER TUBING

Tubing	Volumetric Absorption Rate $\dot{V}_{760}$ (mm^3/hr/cm)	
Polyvinyl Chloride (P.V.C.)	0.3	
Teflon (P.T.F.E.)	1.2	
Silicone Rubber	MEAN 24.8	S.D. 3.5

TABLE 2

PERMEABILITY OF CO_2, O_2, N_2 AND WATER VAPOUR THROUGH SILICONE RUBBER TUBING

Volumetric Absorption Rate
($mm^3/hr/cm$)

CO_2	O_2	N_2	H_2O
443	62.7	28.2	131
443	53.5	26.1	175
473	49.9	25.2	169
443	52.1		
Ave 450	Ave 54.5	Ave 26.3	Ave 159

APPENDIX NO. 2

DESIGN OF PRESSURE TRANSDUCER FOR CONSTANT VOLUME SYSTEM

DESIGN CRITERIA

The pressure transducer was designed to be implanted under the skin of an experimental animal and this requirement imposed the following set of design criteria.

Materials

Materials used must be corrosion resistant and compatible with the physiological environment as minimum tissue reaction to a foreign body is necessary when trying to make in vivo measurements in physiologically normal tissue.

Size

The transducer was to be small enough to be implanted under the skin of an animal the size of a rabbit or cat, and to be capable of being used externally on man and smaller animals such as rats.

Inconvenience to Animal

The inconvenience and irritation to the animal were to be kept to a minimum. This meant harnesses and permanently attached leads that would necessitate restraining the animal for long periods were to be avoided.

Pressure Range and Sensitivity

The transducer was to be capable of monitoring gas tensions of the tissue ranging from 60 to 760 mmHg Abs. and with a sensitivity of about $\pm$ 1 mmHg.

Response Rate

To achieve rapid equilibration between gas in the transducer dead space and the tissue, the dead space volume was to be kept to a minimum.

To satisfy these criteria 18/8 Mo stainless steel was chosen for the casing and membrane. This particular steel has good corrosion resistant properties and promotes minimal tissue reaction in experimental animals. A disc shape with an overall O.D. of approximately 1 inch had been used successfully by Hills[48] and similar dimensions and shape were considered to be satisfactory for the present purposes. To obtain a linear response over a pressure range of 0 to -700 mmHg a stiff membrane was designed so that membrane stresses were well within the elastic limits of the material and membrane deflection and hence displacement volume were small. High sensitivity with low strains was achieved by bonding semi-conductor resistance strain guages with a gauge factor of K=110 to the membrane. Finally, by suturing the transducer under the skin at the back of the neck and having removable electrical leads the animal need only be restrained in a sitting or standing posture while readings are actually being taken.

MEMBRANE DESIGN

The pressure transducer membrane was made of stainless steel with the membrane and its mounting ring being machined from the one piece of metal. This is the most successful method of producing a thin membrane that is built-in around the rim.

Membrane dimensions were chosen to satisfy the size requirements of the transducer, and have a maximum deflection of 0.0005" under a pressure differential of one atmosphere. Two semiconductor strain gauges were bonded to the membrane, one in compression and one in tension, and formed two arms of a Wheatstone bridge. The other two arms were formed with dummy gauges bonded to the inside of the transducer casing.

The membrane was considered to be a disc clamped at the rim and subjected to a uniformly distributed load and under these conditions a stress analysis gives :-

$$\frac{a^4 p}{d^4 E} = \frac{16}{3} \cdot \frac{1}{1-G^2} \cdot \frac{b}{d} + \frac{6}{7} \cdot \frac{b^3}{d^3} \quad \ldots\ldots (1)$$

and

$$\frac{a^2 S}{d^2 E} = \frac{2}{1-G} \cdot \frac{b}{d} + \frac{1}{2} \cdot \frac{b^2}{d^2} \quad \ldots\ldots (2)$$

where

a	=	radius of disc
d	=	thickness of disc
b	=	maximum deflection
p	=	pressure loading on disc
S	=	stress at centre of disc
G	=	Poisson's ratio
E	=	Young's modulus of elastity

Now for this membrane,

a	=	0.15"
d	=	0.005"
p	=	14.7 psia.
E	=	28×10^6 psia.
G	=	0.278

Solving (1) for b we find that the maximum deflection under a pressure differential of one atmosphere is $\doteq 0.35 \times 10^{-3}$. This is less than the maximum permissible deflection. Solving (2) for S, the stress at the centre of the disc, we find that under these conditions :

$$S = \frac{Ed^2}{a^2} \left(\frac{2}{1-G} \cdot \frac{b}{d} + \frac{1}{2} \cdot \frac{b^2}{d^2} \right) \quad \ldots\ldots (3)$$

but $S = eE$ where e = strain at centre.

Therefore

$$e = \frac{d^2}{a^2} \left(\frac{2}{1-G} \cdot \frac{b}{d} + \frac{1}{2} \cdot \frac{b^2}{d^2} \right)$$

Using the figures from above we find that the strain at the centre is approximately 200×10^{-6} inches/inch. This strain was sufficient to give more than 100mV change in bridge voltage at maximum sensitivity.

APPENDIX NO. 3

TEMPERATURE CORRECTIONS FOR MEASURED VALUES OF TISSUE GAS TENSIONS

INTRODUCTION

The measurements of unsaturation described above were carried out at temperatures less than 37°C and so the partial pressure of water vapour in these measurements was not 47mmHg but something less. The vapour pressure depression was calculated from the mean temperature of the gas cavity and dead space and by subtracting this depression from the measured unsaturation the effective unsaturation at 37°C was obtained.

The method of determining the vapour pressure in the constant pressure system for man is described below, and as the calculations for the constant volume system and for the rat experiments are similar to this the corrected values of unsaturation are only quoted for these other cases.

DETERMINATION OF WATER VAPOUR PRESSURE WITH CONSTANT PRESSURE SYSTEM

When the system, described in section 10.2.1, was in equilibrium, with no net flux of gas across the membrane, the water bead of the displacement transducer was usually about half way along the capillary. This resulted in a capillary dead space volume of about $20mm^3$. The volume of the silicone rubber tube and connector was measured and found to be $20mm^3$ also. Gas within the silicone tube and connector was assumed to be at the temperature of the subcutaneous tissue while the capillary, which was not in contact with the skin, was assumed to be at room temperature. The mean temperature was then expressed as :-

$$Tmean = \frac{VsTs + VcTc}{Vtotal}$$

where Tmean is the mean temperature

Ts is the temperature of the subcutaneous tissue

Tc is the temperature of the capillary

Vs is the volume of gas at the temperature of subcutaneous tissue

Vc is the volume of gas at the temperature of the capillary

Vtotal is the total volume of the system.

The only parameter on the R.H.S. of equation(6) that was not measured was the temperature of the subcutaneous tissue in man. The subcutaneous temperature was measured in the rat using a thermocouple probe and it was found to be about 36°C. For man, however, there are many references to measurements of temperatures of skin and other tissues. Hardy and Du Bois[52] found that with room temperatures of 22-25°C the mean skin temperature on exposed regions was 30-31°C. Abramson quotes Mayerson and Tooth[53] who found that "There is usually a gradient from skin to subcutaneous tissue with the temperature of the deeper structures being 0.2 to 0.7°C higher than that at the surface." In the region of the forearm used in this study they found skin temperatures of about 30°C under conditions where the limb was exposed, the subject sedentary and comfortable and the room temperature was 22°C. Bazett[54] has also found that in the limbs "temperatures of the muscles of the forearm at rest rarely exceeded that of the surface by more than 2° to 3°C".

On the basis of this evidence the temperature of the subcutaneous tissue was taken to be 32°C.

We now have

$$Vs = 20mm^3$$
$$Vc = 20mm^3$$
$$Ts = 32^\circ C$$
$$Tc = 22^\circ C$$
$$Vtotal = 40mm^3$$

and substitution into (6) gives -

$$Tmean = \frac{33 + 22}{2}$$
$$= 27^\circ C$$
$$= 80.6^\circ F$$

From the thermodynamic properties of water at saturation[51] the vapour pressure of water at 80.6°F is 0.517 psia.

$$\therefore \quad pH_2O = \frac{0.517}{14.7} \times 760 \text{ mmHg}$$

$$\therefore \quad pH_2O = 26.8 \text{mmHg}$$

This gives a vapour pressure depression of approximately 20mmHg and the unsaturation at 37°C becomes the measured value less the vapour pressure depression.

For this case we have unsaturation at 37°C is :-

$$115 - 20 = 95 \text{mmHg}$$

SUMMARY OF RESULTS

The vapour pressure depressions for both the constant pressure and constant volume systems used on both the rat and man were calculated in a manner similar to that described above. These results are given in Table 1 below while the corrected values of unsaturation are given in Table 2.

TABLE 1

VAPOUR PRESSURE DEPRESSION (mmHg)

	Constant Pressure System	Constant Volume System
Rat	14	16
Man	20	18

TABLE 2

UNSATURATION CORRECTED TO 37°C (mmHg)

	Constant Pressure System	Constant Volume System
Rat	67	57
Man	95	92

APPENDIX NO. 4

RESULTS

TABLE 1

VOLUMETRIC RATE OF ABSORPTION OF GAS INTO SUBCUTANEOUS TISSUE OF RAT

ATMOSPHERIC PRESSURE BREATHING AIR

CONSTANT PRESSURE SYSTEM (DISPLACEMENT TRANSDUCER)

Rat No. & Sex	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{760}$ (mm^3/hr/cm)
1	27.4.70	0	0.805
MALE	28.4.70	0	0.92
	29.4.70	0	0.83
2	29.4.70	0	0.845
FEMALE	30.4.70	0	1.23
	4.5.70	0	1.48
	5.5.70	0	1.08
3	4.5.70	0	1.38
FEMALE	5.5.70	0	1.47
	6.5.70	0	1.08
4	7.5.70	0	0.78
FEMALE	8.5.70	0	0.85
	11.5.70	0	1.26
	12.5.70	0	1.00
5	8.5.70	0	0.78
FEMALE	11.5.70	0	0.965
	12.5.70	0	1.1
	14.5.70	0	0.875
	15.5.70	0	1.1
	18.5.70	0	0.77
	19.5.70	0	0.965
	21.5.70	0	1.01
	22.5.70	0	0.965
	25.5.70	0	1.08
	26.5.70	0	0.92
	27.5.70	0	0.965
	28.5.70	0	0.92
	29.5.70	0	0.99
	1.6.70	0	0.97
	1.6.70	0	0.70

Rat No. & Sex	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{760}$ (mm^3/hr/cm)
6	15.5.70	0	0.775
FEMALE	18.5.70	0	1.07
	19.5.70	0	1.13
	20.5.70	0	1.25
	21.5.70	0	1.37
	25.5.70	0	1.25
	26.5.70	0	0.835
	27.5.70	0	1.07
	28.5.70	0	1.13
	29.5.70	0	1.13
	1.6.70	0	0.955
	2.6.70	0	1.10
	5.6.70	0	1.25
	8.6.70	0	1.13
	12.6.70	0	1.34
NUMBERS 7 to 10 IMPLANTS DID NOT LAST			
11	19.6.70	0	0.97
FEMALE	22.6.70	0	0.86
	23.6.70	0	1.23
	24.6.70	0	1.3
	25.6.70	0	1.3
12	22.6.70	0	0.80
FEMALE	23.6.70	0	0.96
	24.6.70	0	1.20
	25.6.70	0	0.94
	26.6.70	0	1.17
	29.6.70	0	0.92
	30.6.70	0	1.02
	1.7.70	0	1.01
	2.7.70	0	1.16
	3.7.70	0	1.27
13	29.6.70	0	1.08
FEMALE	30.6.70	0	1.40
	1.7.70	0	1.35
	2.7.70	0	1.6
14	10.7.70	0	0.93
MALE	13.7.70	0	1.10
	15.7.70	0	0.99
		0	1.0
		-35	0.466
		-50	0.294
	16.7.70	0	0.95
		-20	0.78
		-40	0.507
		-60	0.18

Rat No. & Sex	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{760}$ (mm^3/hr/cm)
14 (Cont.)	17.7.70	0	0.995
		-40	0.508
		-60	0.131
	18.7.70	0	1.05
		-60	0.095
	20.7.70	0	0.95
		-20	0.675
		-30	0.59
		-45	0.33
		-55	0.36
		-80	0
	21.7.70	0	1.04
		-11	0.78
		-31	0.518
		-56	0.255
		-86	-0.192
	22.7.70	0	0.785
		0	0.925
	23.7.70	0	0.743
		0	0.832
15 MALE	29.7.70	0	0.95
		0	0.974
		0	0.967
	30.7.70	0	0.952
		0	0.89
		-10	0.73
		-20	0.73
		-30	0.485
		-40	0.381
		-50	0.153
	31.7.70	0	1.02
		-20	0.722
		-40	0.615
		-50	0.505
		-60	0.263
		-80	0.032
		0	0.835
		-20	0.675
		-40	0.653
		-50	0.55
		-60	0.326
		-70	0.157
		-90	0
		-110	-0.222
	3.8.70	0	1.14
		-20	0.70
		-30	0.572
		-50	0.52
		-60	0.256

Rat No. & Sex	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{760}$ (mm^3/hr/cm)
15 (Cont.)		0	0.950
		-10	0.910
		-25	0.692
		-46	0.468
		-56	0.387
		-66	0.318
		-75	0.345
		-85	0.130
	6.8.70	-60	0.202
		-75	0.175
16	4.8.70	0	0.905
MALE		-50	0.364
		-50	0.363
		-61	0.292
		-71	0.128
		-81	0.069
		-90	-0.027
	5.8.70	0	1.15
		-20	0.788
		-40	0.564
		-60	0.232
		-81	0.043
		-100	-0.219
17	12.3.71	0	1.08
MALE		-15	0.752
		-30	0.396
	15.3.71	0	0.75
		0	1.11
		-30	0.309
		-45	0.238
		-60	0.162
		-70	0
		-90	-0.394
	16.3.71	0	0.875
		-35	0.523
		-40	0.323
		-70	0
	18.3.71	0	0.755
		-40	0.321
		-55	0.294
		-60	0.243
18	12.3.71	-10	0.938
MALE		-40	0.325
		-55	0.292
		-60	0.145
		-90	0

TABLE 2

SUBCUTANEOUS GAS TENSIONS IN RAT

ATMOSPHERIC PRESSURE BREATHING AIR

CONSTANT VOLUME SYSTEM
(PRESSURE TRANSDUCER)

Time (hr)	Negative Pressure (mmHg)	Rat No. & Sex	Date
5.5	-85	No. 14 - Male	24.7.70
2.0	-73	No. 15 - Male	27.7.70
4.33	-70		
7.0	-70		28.7.70
0.5	-34		4.8.70
2.75	-68		
4.1	-80		
3.75	-82		5.8.70
0.25	-25	No. 16 - Male	29.7.70
3.0	-63		
1.0	-53		30.7.70
2.0	-67.5		
5.0	-67.5		
3.0	-74		31.7.70
6.0	-78		
2.0	-72		1.8.70
1.5	-76		3.8.70
7.0	-76		

TABLE 3

VOLUMETRIC RATE OF ABSORPTION OF GAS INTO SUBCUTANEOUS TISSUE OF MAN

ATMOSPHERIC PRESSURE BREATHING AIR
and
REDUCED PRESSURE BREATHING AIR

CONSTANT PRESSURE SYSTEM
(DISPLACEMENT TRANSDUCER)

Test No.	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{760}$ ($mm^3/hr/cm$)	Environmental Pressure (mmHg)
1.1	13.4.71	0	1.28	764
		-20	0.757	
		-40	0.56	Sea Level
		-60	0.368	
		-80	0	
1.2	14.4.71	0	1.07	
		-30	0.778	
		-50	0.595	
		-60	0.587	Sea Level
		-70	0.385	
		-80	0.181	
		-90	0	
		-65	0.525	
		-110	0.236	
1.3	15.4.71	-35	0.965	759
		-45	0.820	
		-65	0.582	
		-75	0.395	Sea Level
		-85	0.263	
		-95	0.173	
		-105	0	
		-115	-0.167	
1.4	16.4.71	0	1.15	758
		-15	0.978	
		-25	0.79	
		-35	0.735	Sea Level
		-55	0.505	
		-75	0.266	
		-85	0.176	
3.1	14.7.71	0	1.01	759 Sea Level
3.2	15.7.71	0	0.81	758
		-50	0.439	
		-100	0.093	Sea Level

Test No.	Date	Pressure Relative to Environment (mmHg)	Volumetric Absorption Rate $\dot{V}_{3760}$ ($mm^3/hr/cm$)	Environmental Pressure (mmHg)
3.3	16.7.71	0	0.89	761
		-50	0.534	
		-90	0.188	Sea Level
		-120	-0.134	
		0	0.96	
3.4	17.7.71	0	0.973	761
		-50	0.472	
		-80	0.356	Sea Level
		-100	0.15	
		-120	0	
		0	0.99	
3.5	18.8.71	0	0.885	760
		-50	0.614	
		-90	0.265	Sea Level
		-120	0.158	
		-150	-0.301	
		TESTS AT REDUCED PRESSURE		
3.6	19.7.71	0	0.598	656
				4,000 ft. altitude
3.7	20.7.71	0	0.614	656
		-50	0.538	
		-90	0.197	4,000 ft.
		-120	-0.186	altitude
3.8	21.7.71	0	0.502	609
		-50	0.392	
		-90	0	6,000 ft. altitude
3.9	23.7.71	0	0.538	609
		-30	0.507	
		-70	0	6,000 ft. altitude
3.10	22.7.71	0	0.385	523
		-50	0.192	
		-80	0	10,000 ft. altitude
3.11	26.7.71	0	0.431	523
		-30	0.248	10,000 ft.
		-70	-0.032	altitude

TABLE 4

SUBCUTANEOUS GAS TENSIONS IN MAN

ATMOSPHERIC PRESSURE BREATHING AIR

CONSTANT VOLUME SYSTEM
(PRESSURE TRANSDUCER)

Time (hr)	Negative Pressure (mmHg)	Room Temp. (^{o}C)	Barometric Pressure (mmHg)
0.42	- 57.5	21.0	762
0.78	-110.0	26.5	762
1.25	-104.0	23.0	760
1.92	-101.5	25.0	762
2.25	-100.0	21.5	767
4.0	-115.0	22.0	767
4.0	-110.0	26.0	762
10.0	-126.0	25.0	
14.0	-117.0	24.0	762
15.25	-111.0	26.0	762
18.0	-142.5	22.0	767

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