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WADC Technical Report 53-255

THE OXYGEN-CARBON DIOXIDE DIAGRAM

Hermann Rahn

Wallace O. Fenn

The University of Rochester

August 1953

WRIGHT AIR DEVELOPMENT CENTER

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WADC TECHNICAL REPORT 53-255

THE OXYGEN-CARBON DIOXIDE DIAGRAM

Hermann Rahn
Wallace O. Fenn

University of Rochester

August 1953

Aero Medical Laboratory
Contract No. AF 18(600)-17
RDO No. 696-61

Wright Air Development Center
Air Research and Development Command
United States Air Force
Wright-Patterson Air Force Base, Ohio

FOREWORD

This summary of experimental investigations and theoretical development in respiratory physiology presented in this report were carried out over a period of many years in the Department of Physiology, School of Medicine and Dentistry, University of Rochester, New York, and were conducted under the provision of various Air Force contracts. This present summary was written under the provision of Contract AF 18 (600)-17 with Dr. J.W.Wilson and Dr. W.Hull of the Physiology Branch, Aero Medical Laboratory acting as project monitors. Work was performed under RDO No. 696-61, "High Altitude Physiology."

ABSTRACT

This report presents the O_2-CO_2 diagram which is useful in charting and predicting O_2 and CO_2 tension, blood gas content, blood pH, respiratory exchange ratios and alveolar ventilation as a function of changes of one or more parameters which may be encountered under various physiological stresses such as high altitude. The applications of this diagram are illustrated.

PUBLICATION REVIEW

This report has been reviewed and is approved.

FOR THE COMMANDER:

ROBERT H. BLOUNT
Colonel, USAF (MC)
Chief, Aero Medical Laboratory
Directorate of Research

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LIST OF DIAGRAMS AND FIGURES

LIST OF DIAGRAMS AND FIGURES (Cont'd.)

PREFACE

It is our purpose to present the oxygen-carbon dioxide diagram and some of its many applications in convenient form for study and consultation. We have found this diagram so helpful in the solution of our own daily problems that we believe it can be made equally useful to others. With oxygen plotted as abscissae and carbon dioxide as ordinates, it can be used to represent the simultaneous quantities of these two gases found in tissues, blood or lungs in any respiratory maneuver. In L. H. Henderson's classical monograph on Blood seven respiratory variables were considered and to represent the interrelations of these variables 105 different charts were presented as theoretically necessary for completeness. While all of these presented essentially the same basic facts, not all were equally useful. Similarly the O_2-CO_2 diagram is only one of many useful schemes for presenting the complicated processes involved in respiration. This particular diagram is unique, however, in its versatility and convenience and perhaps particularly its ready applicability to tissues, blood and pulmonary gases. The whole oxygen transport system can therefore be represented on a single diagram from the point of inspiration to the point of combustion in the tissues.

Like any other chart this one is highly forbidding at first acquaintance and even the most mathematically-minded physiologists are inclined to resent this particular type of symbolism as an unnecessary complication -- and they therefore put it aside in expectation of the day when the necessary facts can be stated in a few words with such simplicity that the atrocities of our diagrams can be neglected. This, unhappily, is a false hope for the only alternative is merely a rather complicated equation which to most people is still less meaningful. In fact, the two most awkward equations, those for alveolar air and alveolar ventilation, are fortunately plotted as families of straight lines on this diagram. When these lines are drawn as a transparent chart appropriately superimposed on the CO_2-O_2 diagram, the desired parameters can be read off graphically and therefore do not require special calculations. Indeed we have found increasing numbers of physiologists making consistent use of this device for straight thinking and some have copied our transparent charts to save the labor of lengthy calculations. We are encouraged to believe, therefore, that with the aids provided here anyone can master its various intricacies even though he is allergic to equations. Once mastered it provides a precise and comprehensive framework into which all the various pieces of the respiratory jig-saw puzzle can be fitted so that the interrelations stand out clearly.

In the Diagrams I - X we have built up the main outlines of the subject. With the legends it is hoped that they are self-explanatory. These diagrams include some familiar nomograms such as Diagrams VI and VII from Dill and his associates, which are so useful that they could not well be omitted from any set of working charts. These are printed large enough, however, so that they can really be used to obtain reliable figures for practical problems.

Unlike these Diagrams the various text figures included in the remainder of the book are intended chiefly to aid the reader in understanding some of the many possible applications of the O_2-CO_2 diagram. Our selection of these applications has been quite arbitrary and could be extended almost indefinitely to include such subjects as breath holding, drowning, explosive decompression, diving operations, and oxygen poisoning. Perhaps the most important omission, however, is the very fundamental problem of "distribution" and "diffusion" in the lung which has been so superbly presented by Riley and Cournand (14) using the O_2-CO_2 diagram. Our consideration will be given to the inclusion of these subjects if we ever have an opportunity in a second edition to correct the many errors (minor ones only, we hope) which must inevitably have escaped our notice in this volume. Meanwhile, we hope that our indulgent readers will be kind enough to call our attention to any such inaccuracies which may come to their attention.

Almost all the work represented herein has been generously supported by the Aero Medical Laboratory, Wright Air Development Center over the last ten years and we take pleasure at this time in expressing our gratitude and appreciation to the officers at that institution.

We are particularly indebted also to our many colleagues, past and present. Among the former, special mention should be made of Dr. Arthur B. Otis and, at an earlier date, Dr. Leigh E. Chadwick, both of whom made important contributions.

Hermann Rahn
Wallace O. Fenn
Department of Physiology
School of Medicine and Dentistry
University of Rochester

August 21, 1953
Rochester, New York

INTRODUCTION TO DIAGRAMS

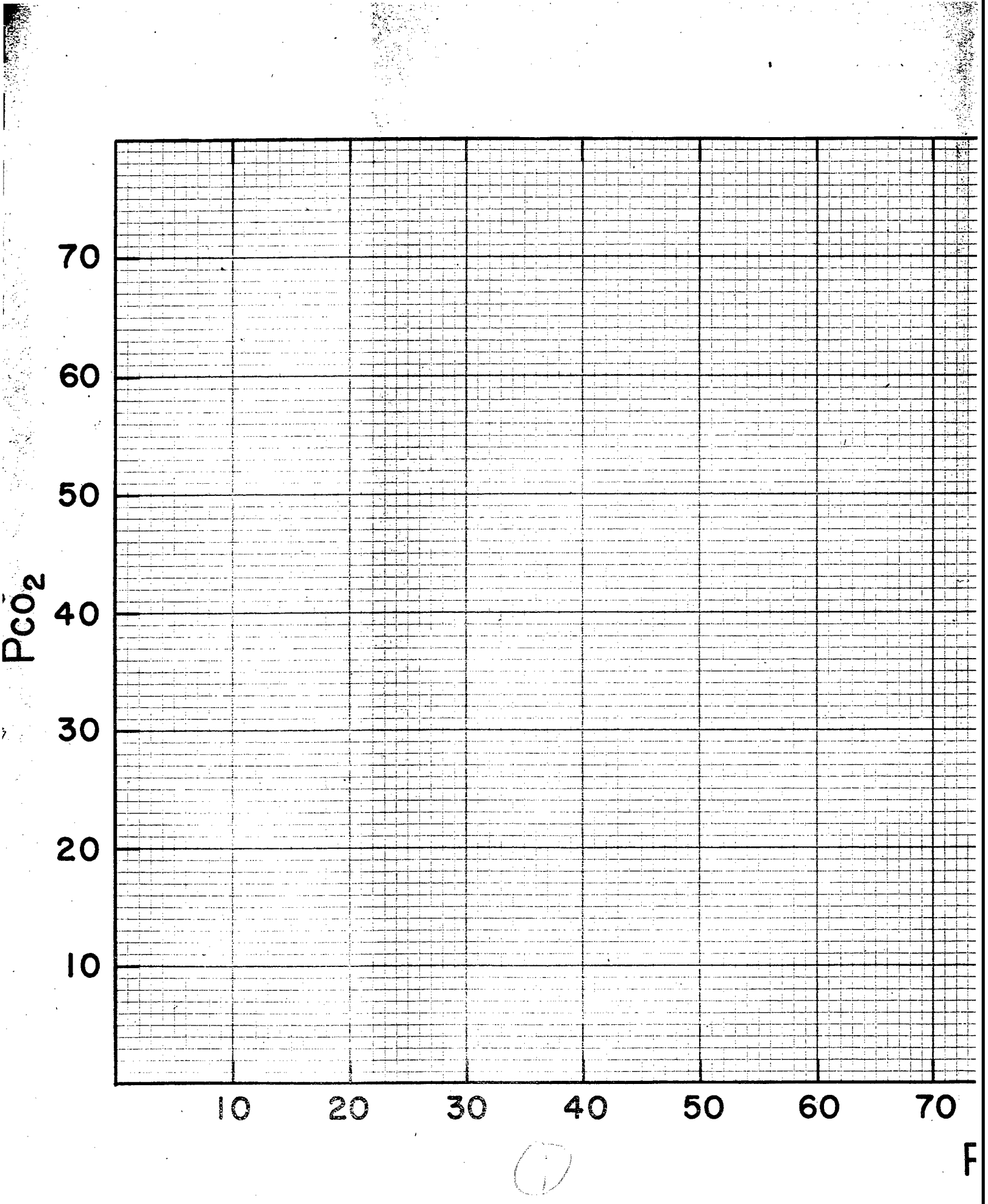
The ten diagrams which follow are designed to contain much of the data necessary for the solution of problems in respiratory gas exchange and gas transport. These diagrams themselves will suffice for many of the common problems which are frequently encountered, particularly those concerned with subjects breathing air or pure oxygen either at ground level or altitude. When other gas mixtures are involved, it will be necessary to replace Diagrams VIII and IX and to construct special diagrams. A work sheet is provided for that purpose. The methods of making these constructions are described in a special section at the end of the diagrams and the necessary equations are provided in the Equations section. Two of the diagrams are reproduced on transparent charts so that they can be superimposed on other diagrams at the proper position depending upon the value of the inspired oxygen pressure. For convenience we have provided a table of the barometric pressures at different altitudes (see special section) as well as the familiar nomograms of Dill and his associates. The latter are slightly simplified and are printed large enough for easy reading.

The physiological principles exemplified by these diagrams can easily be expressed in simple words but it is not possible in words to convey an accurate quantitative picture of the changes involved. It is in this way that the diagrams will be able to make their greatest contribution if one masters the habit of making frequent use of them. There is no respiratory maneuver involving changes in tensions of the respiratory gases in any part of the body which cannot be studied in terms of this diagram and the attempt to do so can hardly fail to prove profitable.

Of particular significance for the usefulness of these diagrams is the fact that within the limitations described they are applicable to any animal or person, the equations being independent of the size of the person, his metabolic rate, or the volume of his lungs.

Diagram I

Work Sheet. Abscissa, pO_2 - mm Hg. Ordinate, PCO_2 - mm Hg.


70
60
50
40
30
20
10
P_{CO_2}
10
20
30
40
50
60
70
F

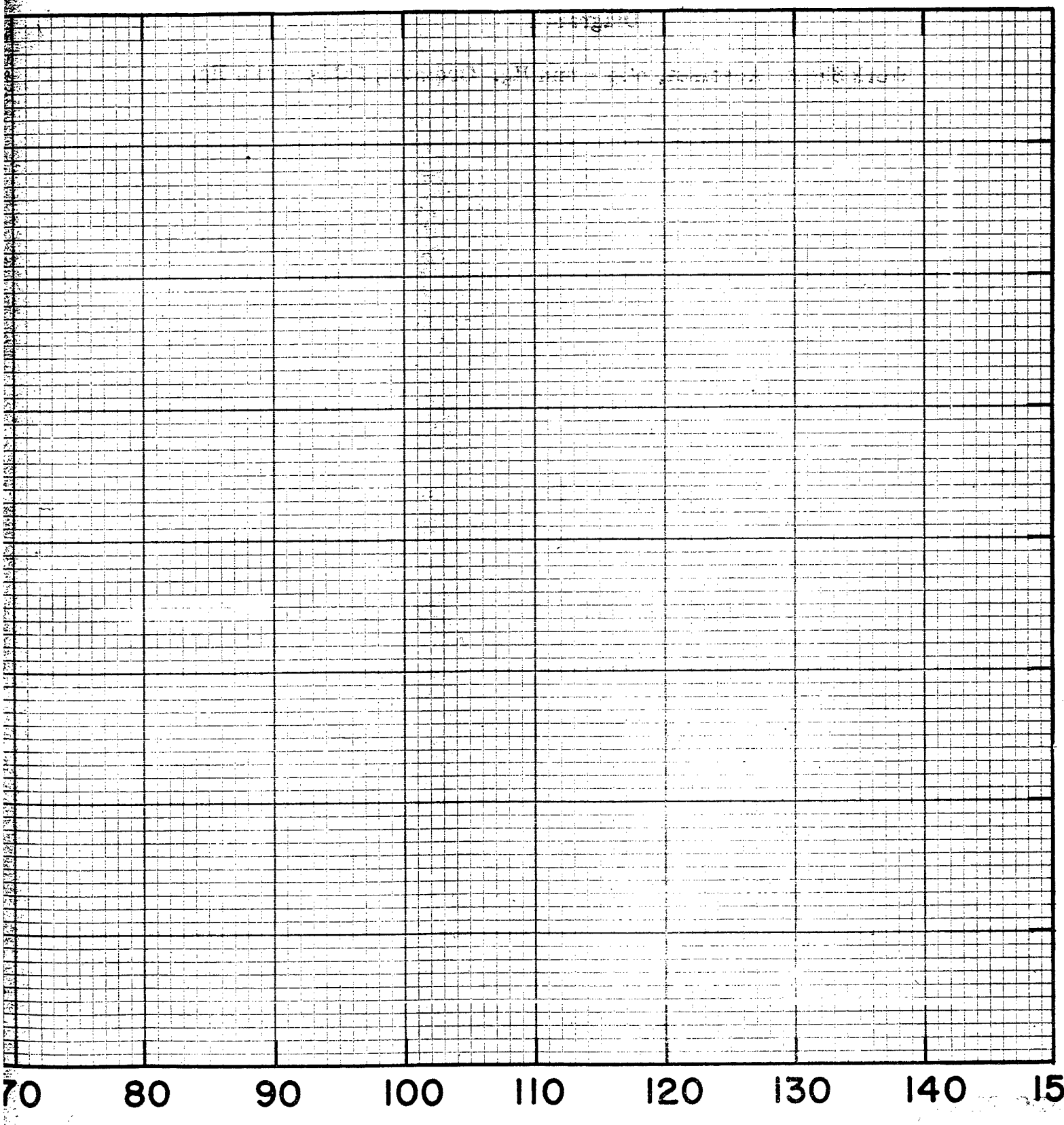

70
80
90
100
110
120
130
140
150
Po_2

Diagram II

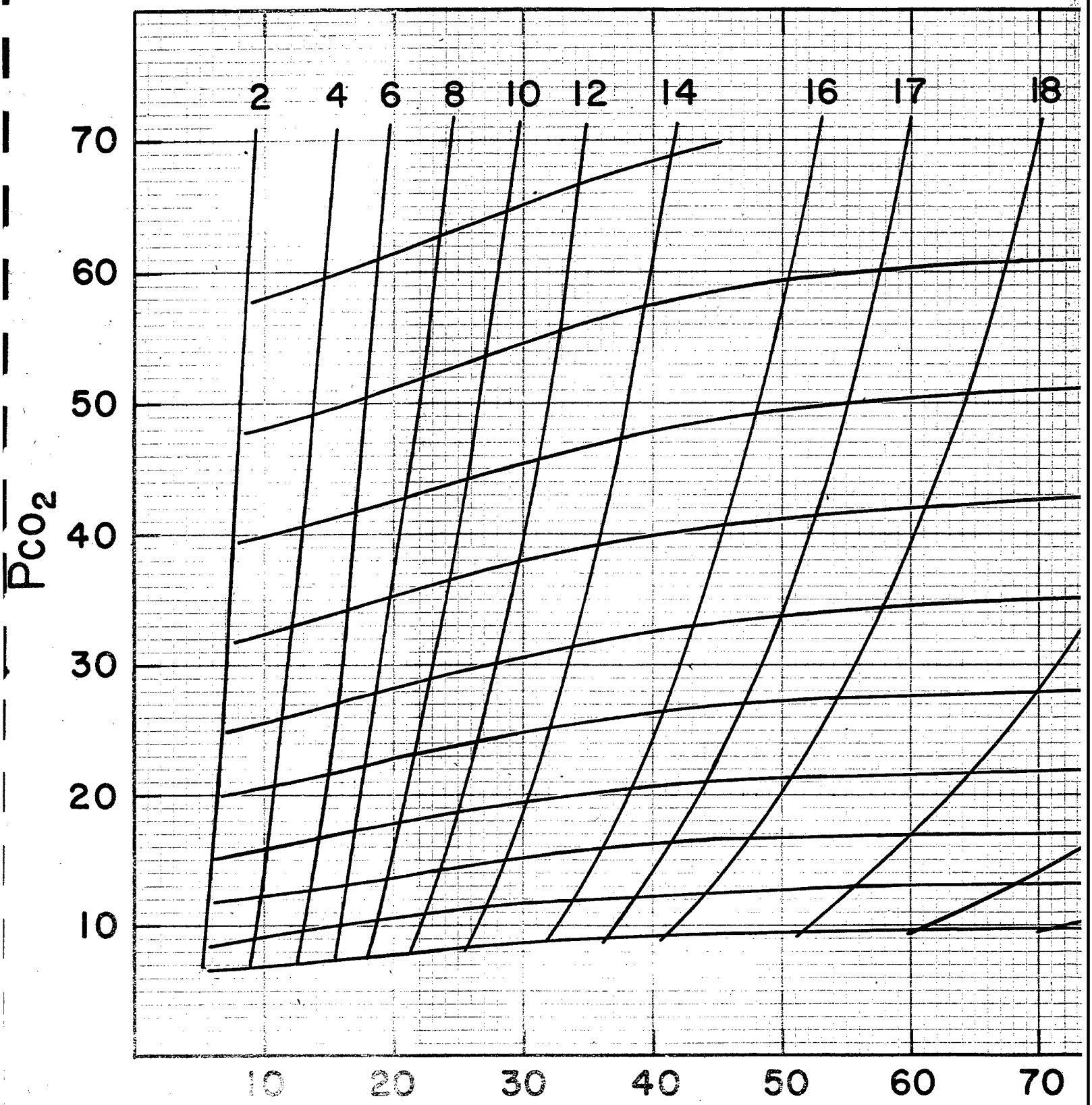
Combined O_2 and CO_2 dissociation curves of whole blood for man at sea level. Data obtained from Nomogram of Dill — see Diagram No. VI.

The oxyhemoglobin capacity is 20 vol. % (ml. STPD per 100 ml. of blood). The isopleths for various contents are indicated in red color. The slope of these isopleths represents the Bohr Effect.

The isopleths for CO_2 content represent the total CO_2 content of whole blood (ml. STPD per 100 ml. of blood) and are indicated in blue color. The slope of these isopleths represents the Haldane Effect.

The chart is useful in determining the CO_2 and O_2 contents of arterial blood if the CO_2 and O_2 tensions of the alveolar air are known, or vice versa if the alveolar-arterial O_2 gradient is disregarded or supplied.

MAN AT S



SEA LEVEL

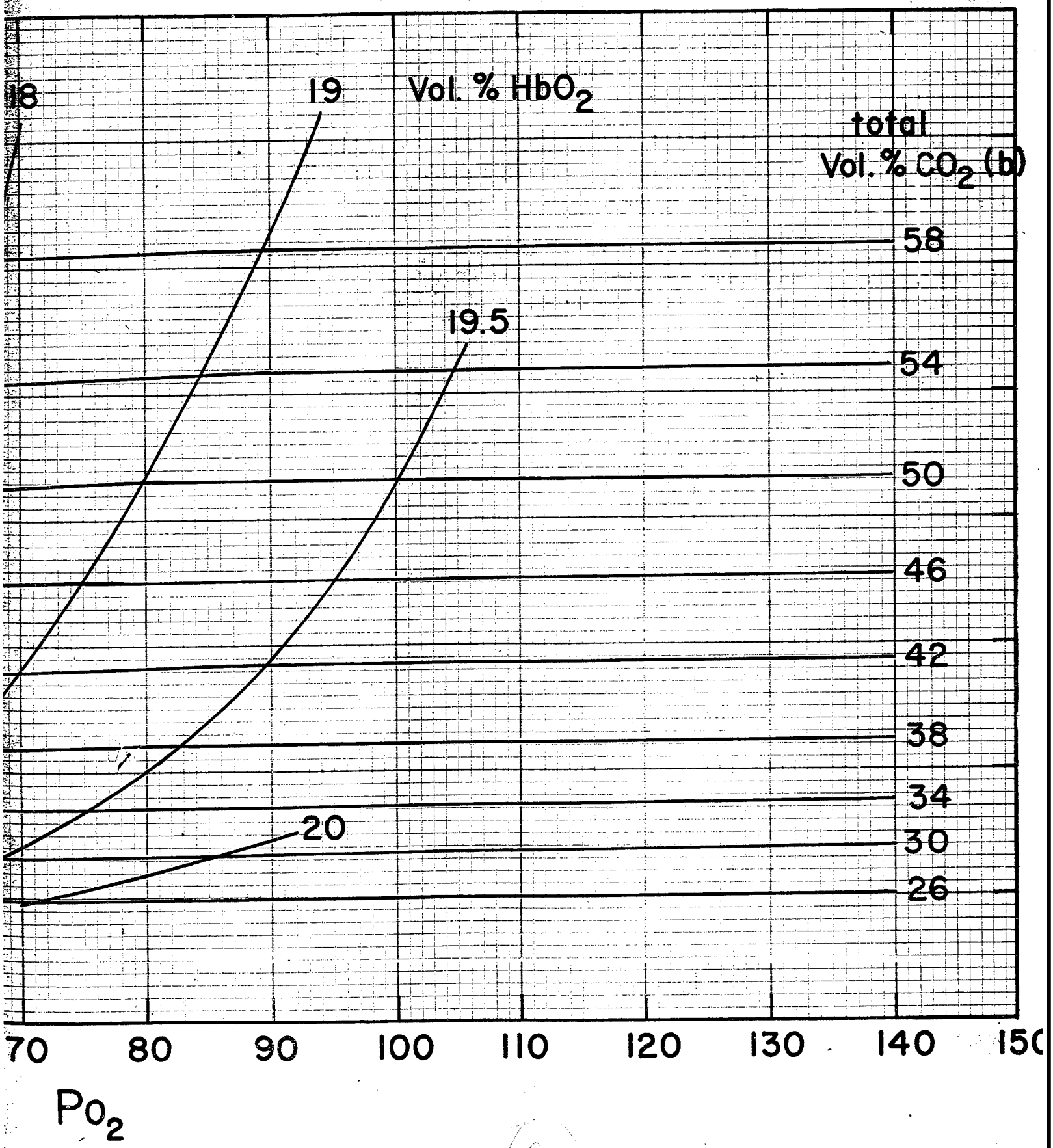
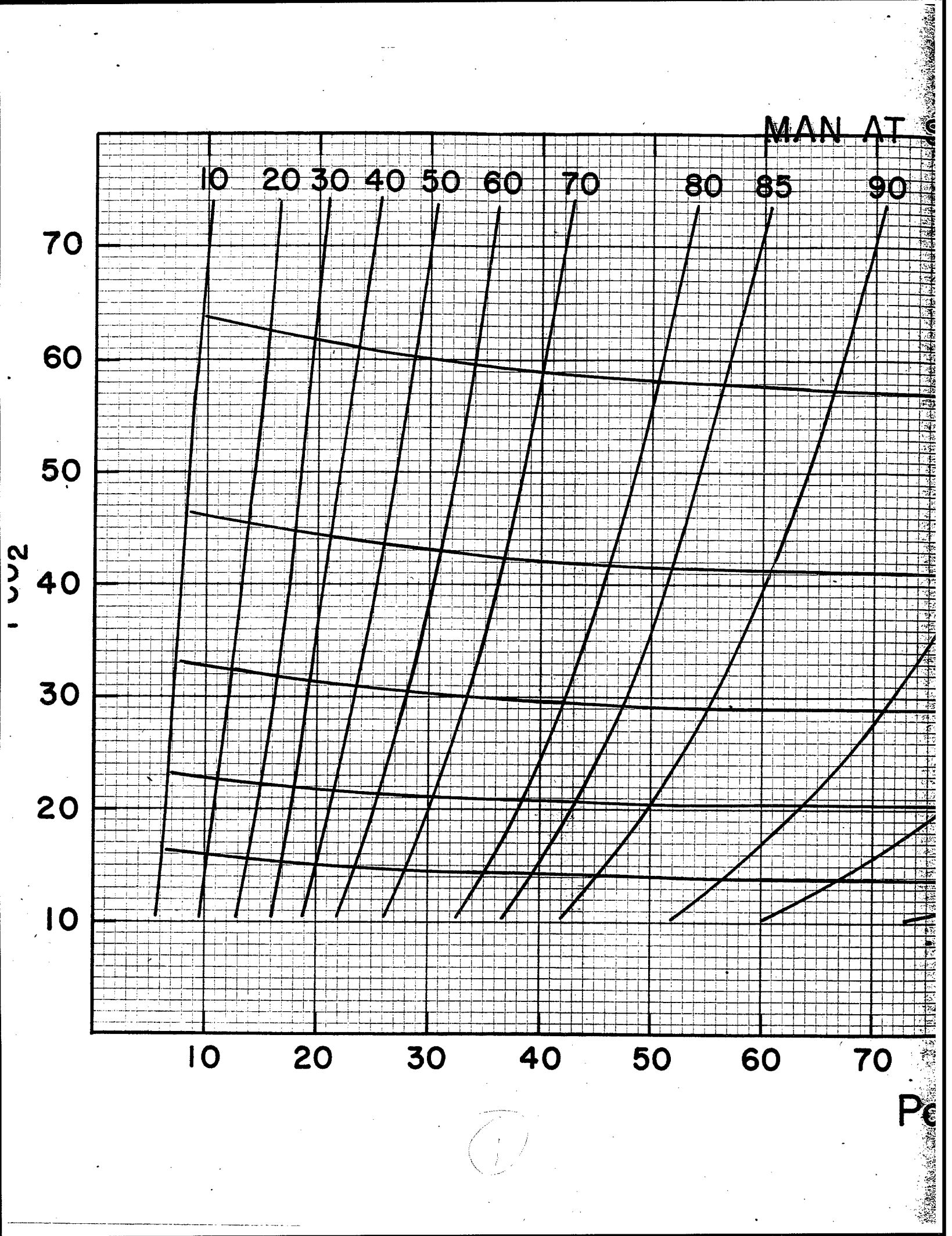

18
19
19.5
20
Vol. % HbO_2
total
Vol. % CO_2 (b)
58
54
50
46
42
38
34
30
26
70
80
90
100
110
120
130
140
150
Po_2

Diagram III

Combined oxyhemoglobin saturation and plasma pH curves for man residing at sea level. Data obtained from Nomogram of Dill.

The isopleths of oxygen contents from the previous Diagram II are converted to per cent oxyhemoglobin saturation — $\%\ H_{bo_2}$ and are indicated in red color.

The isopleths for serum pH are indicated in blue. These curves shift upwards at the left due to the Haldane Effect.


MAN AT
10
20
30
40
50
60
70
80
85
90
70
60
50
40
30
20
10
10
20
30
40
50
60
70

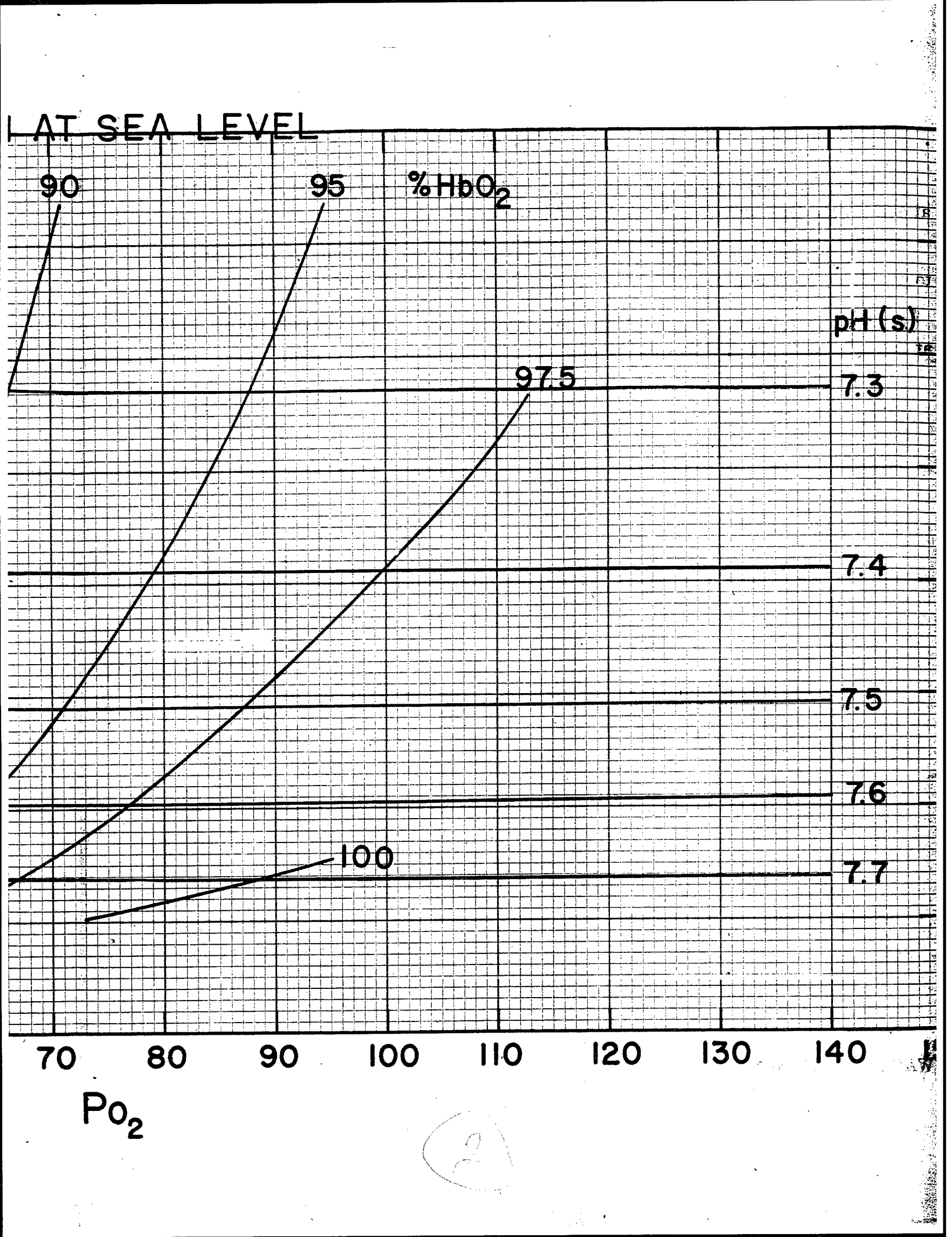
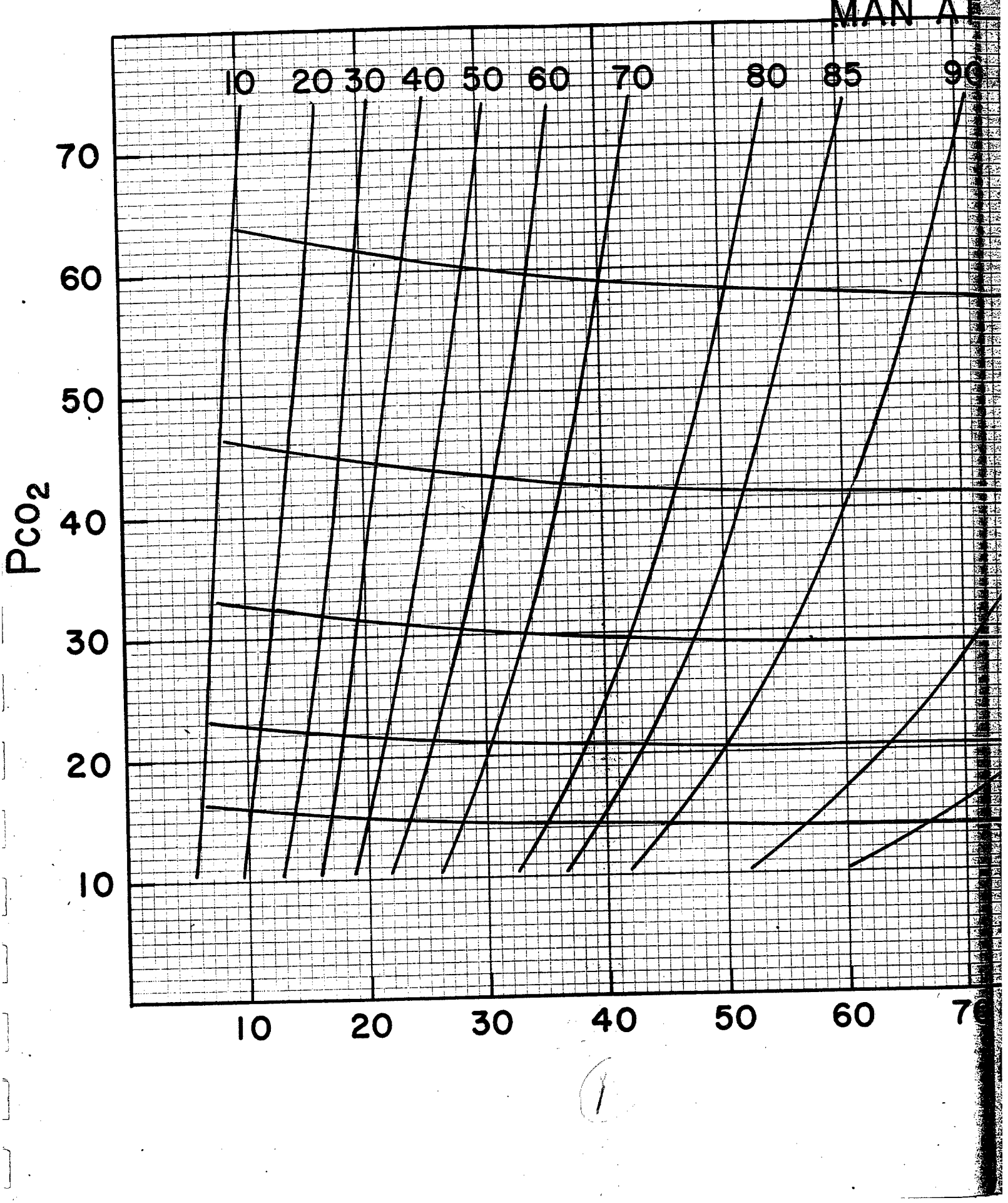

AT SEA LEVEL
90
95
%HbO2
97.5
100
pH (s)
7.3
7.4
7.5
7.6
7.7
70
80
90
100
110
120
130
140
PO2

Diagram IV

Combined O_2 and CO_2 dissociation curves of whole blood attained by permanent residents living at 17,500 ft. in the Andes at barometric pressure of 401 mm Hg. These miners have an alveolar pCO_2 of 25.6 and a pO_2 of 42.3 mm Hg. Data obtained from the Nomogram of Dill – Diagram VII.


MAN AT
10 20 30 40 50 60 70 80 85 90
70
60
50
40
30
20
10
P_{CO_2}
10 20 30 40 50 60

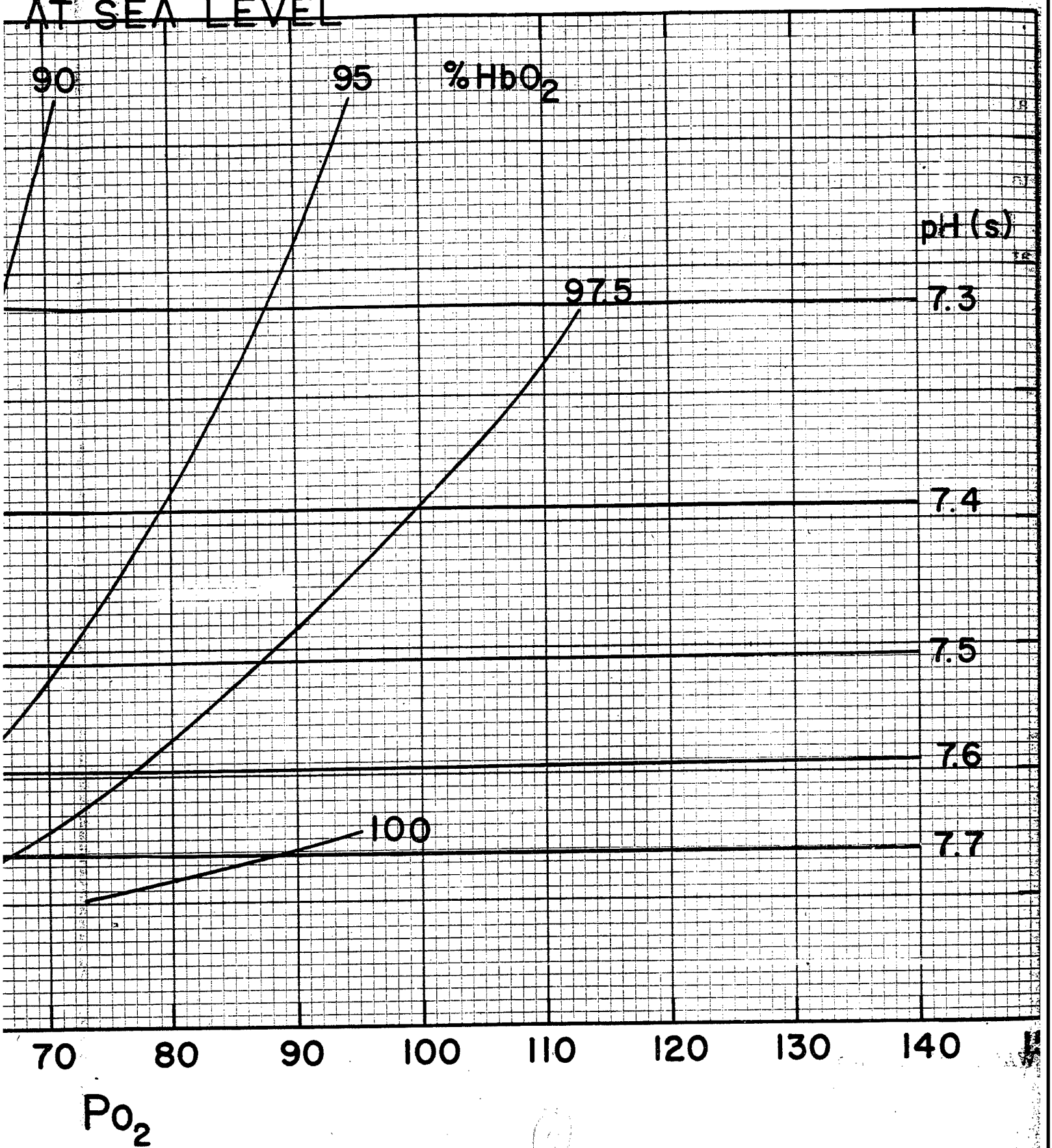
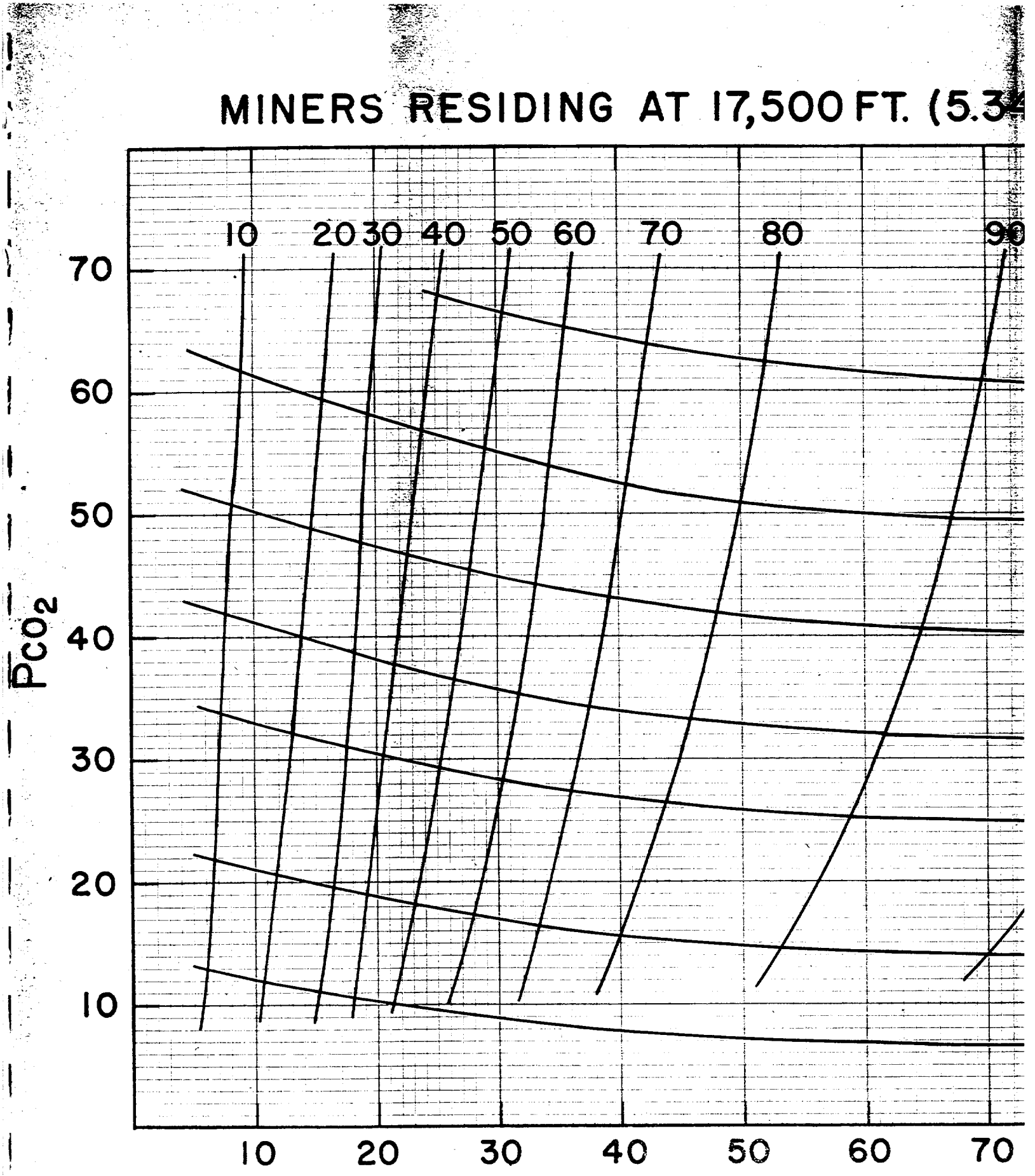
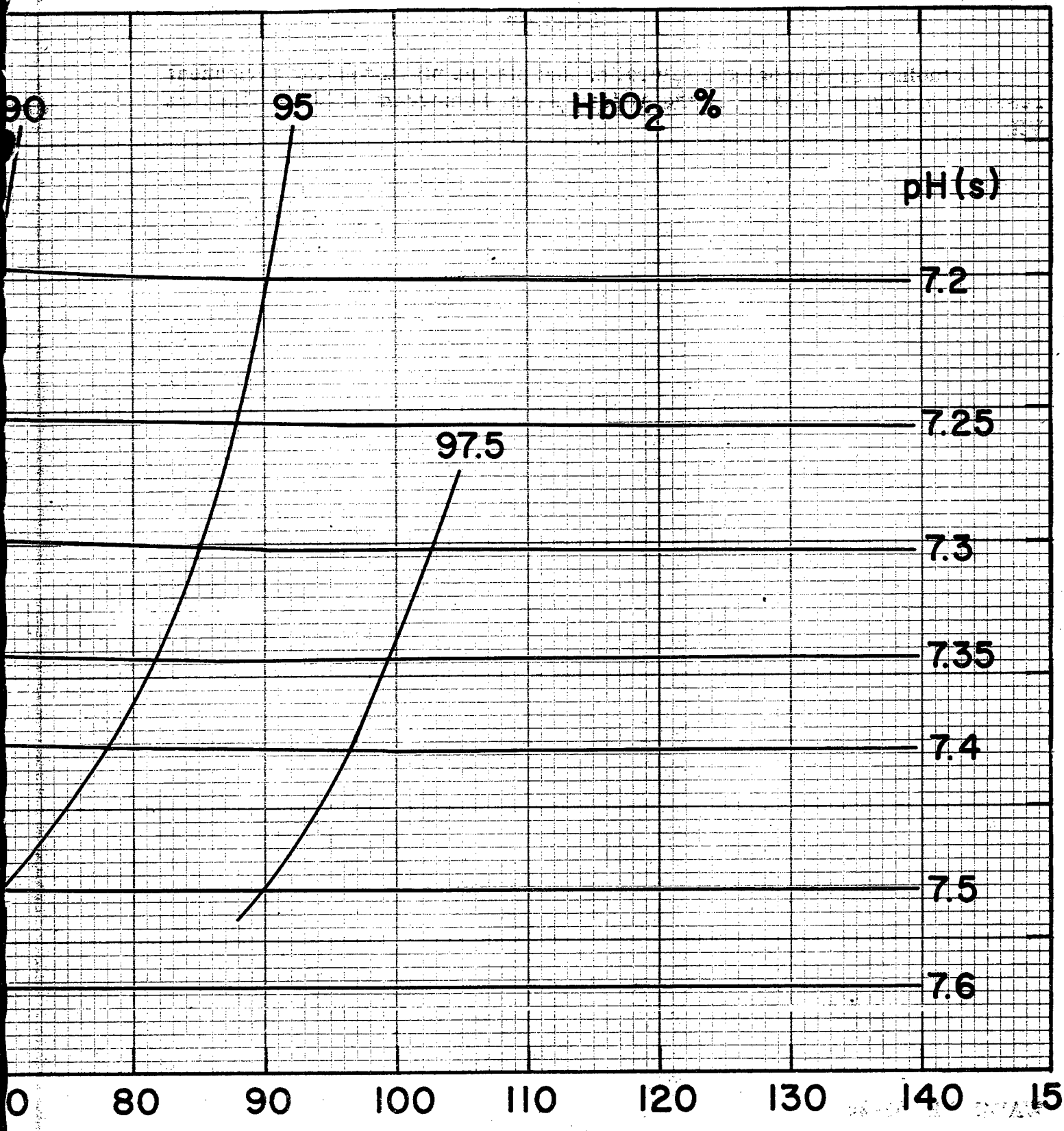

AT SEA LEVEL
90
95
%HbO2
97.5
100
pH (s)
7.3
7.4
7.5
7.6
7.7
70
80
90
100
110
120
130
140
PO2

Diagram V

Combined oxyhemoglobin saturation and plasma pH curves for permanent residents living at 17,500 ft. in the Andes. From Nomogram of Dill – Diagram VII.


MINERS RESIDING AT 17,500 FT. (5.3
10
20
30
40
50
60
70
80
90
70
60
50
40
30
20
10
P_{CO_2}
10
20
30
40
50
60
70

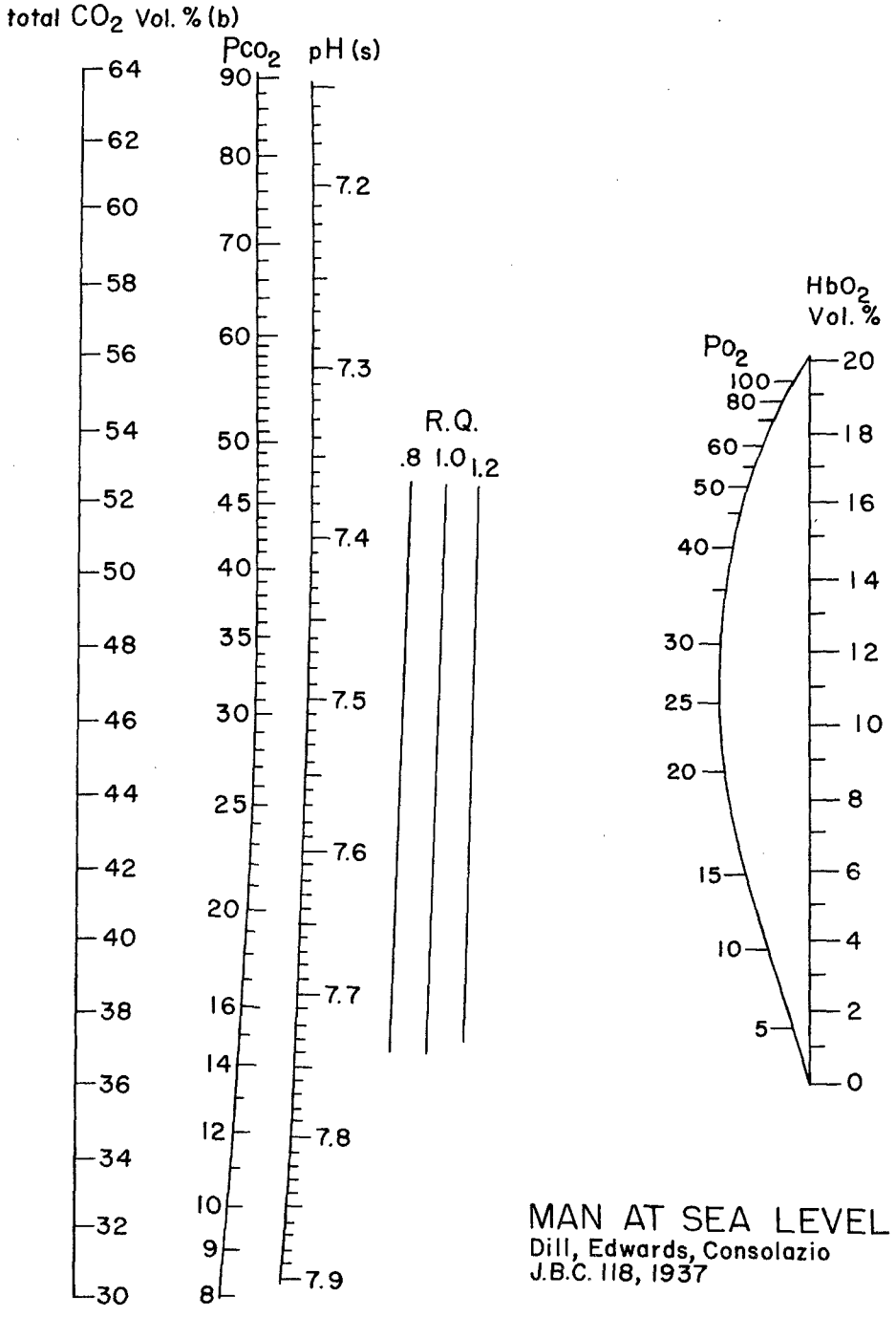
34 Km) AT A PRESSURE OF 401 mm Hg



(2)

Diagram VI

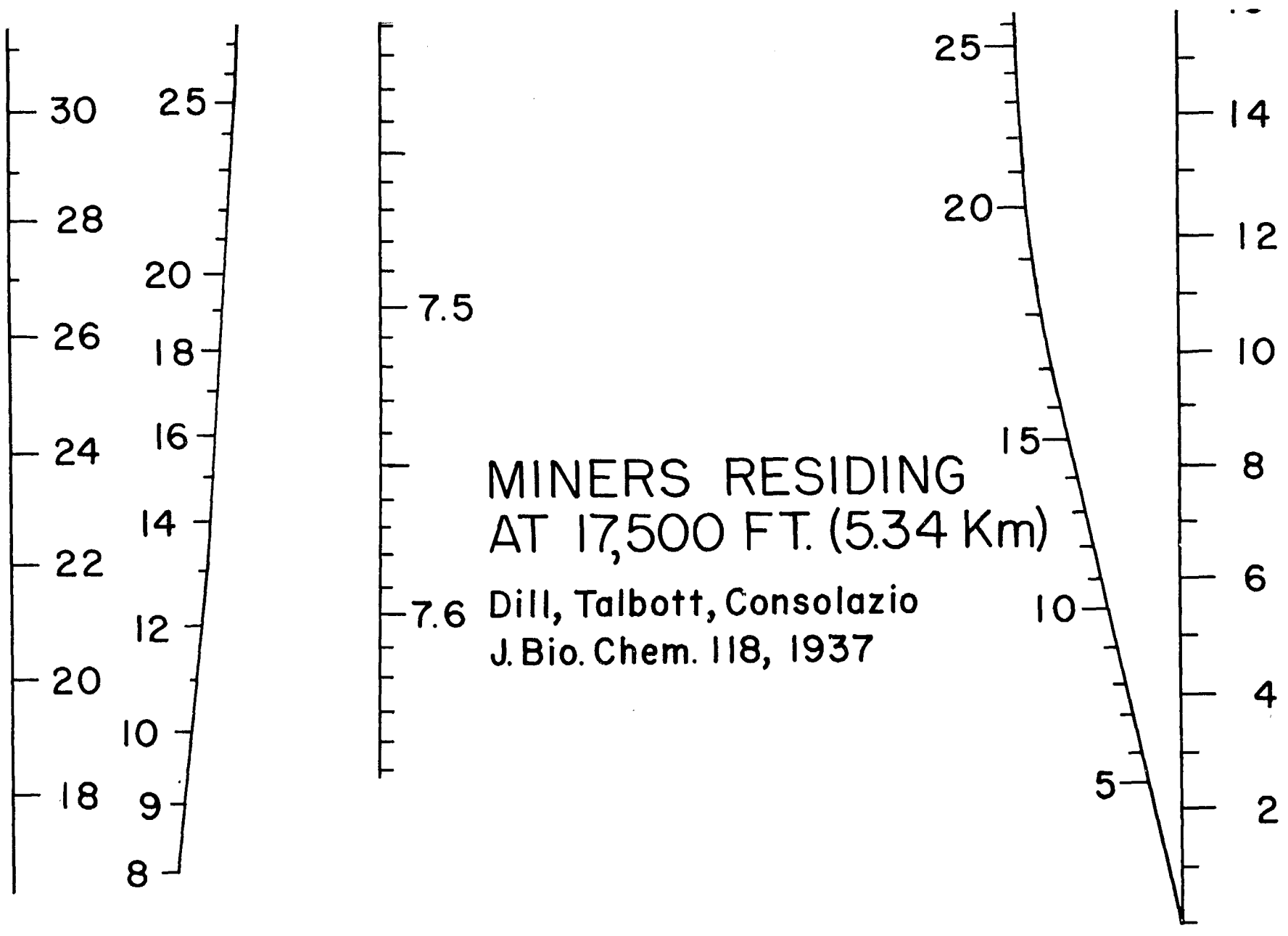
The blood Nomogram of Dill for man residing near sea level. The oxyhemoglobin values and CO_2 contents have been converted to vols. %. The R.Q. lines have been added.



MAN AT SEA LEVEL
Dill, Edwards, Consolazio
J.B.C. 118, 1937

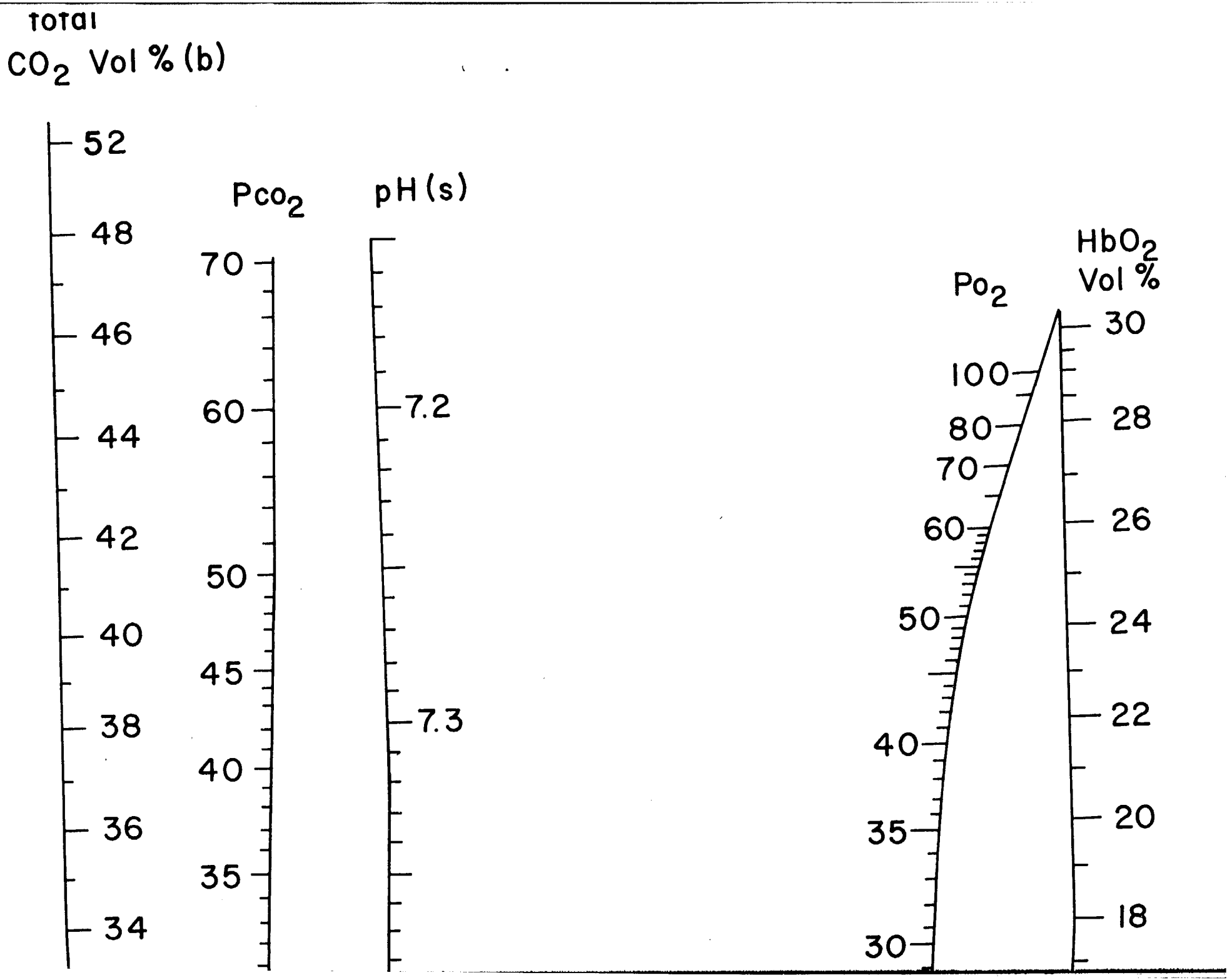
Diagram VII

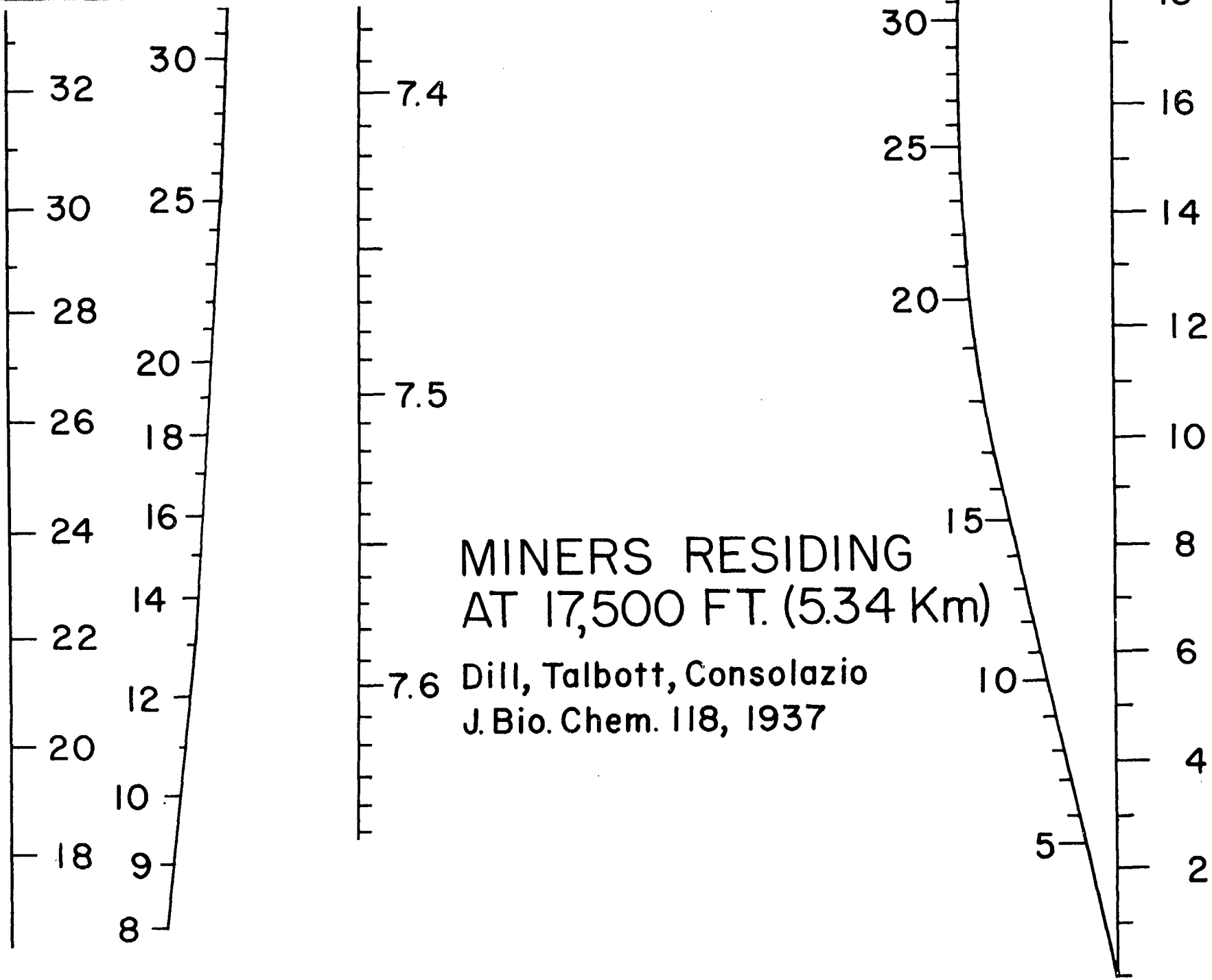
The blood Nomogram of Dill for permanent residing at 17,500 ft. altitude.



MINERS RESIDING
AT 17,500 FT. (5.34 Km)

Dill, Talbott, Consolazio
J. Bio. Chem. 118, 1937


total
CO_2 Vol % (b)
52
48
46
44
42
40
38
36
34
Pco_2
70
60
50
45
40
35
pH (s)
7.2
7.3
Po_2
100
80
70
60
50
40
35
30
HbO_2
Vol %
30
28
26
24
22
20
18



MINERS RESIDING
AT 17,500 FT. (5.34 Km)

Dill, Talbott, Consolazio
J. Bio. Chem. 118, 1937

Diagram VIII

Isopleths of gas Exchange Ratio. A transparent copy of this diagram is supplied (mounted on the back cover), which is designed to be superimposed upon a CO_2-O_2 diagram like Diagram II, so that the base line of the transparency coincides with the base line or O_2 axis of the diagram and so that the point P_{IO_2} from which the R lines radiate is at the correct value for the inspired oxygen pressure. As gas exchange occurs in the alveoli the composition of the gas changes is indicated by these lines according to the exchange ratio, R. In a steady state, R = the R.Q. or respiratory quotient. Due to the nitrogen in the lungs the (negative) slope of these lines is not exactly equal to $\Delta V_{CO_2}/\Delta V_{O_2} = R$ but is $R/(1-F_{IO_2}(1-R))$ in accordance with the alveolar air equation. The chart is a graphic representation of the alveolar air equation (see Equation 1). This chart applies only when O_2 fraction in the inspired air (F_{IO_2}) is .209, the $F_{ICO_2} = 0$, and the scale of ordinates and abscissae are equal. P_{IO_2} varies with the barometric pressure and is equal to (Pβ-47) .209. The less the N_2 in the inspired air, the less these lines radiate until at $F_{IN_2} = 0$ they all coincide at the R = 1 line (1).

The chart is useful (a) in determining the R.Q. when the composition of the inspired and the alveolar air or expired air is known, or (b) in determining the alveolar O_2 tension for a given R when the inspired air composition and the alveolar CO_2 tension are known. It can be applied to a subject breathing air at any altitude.

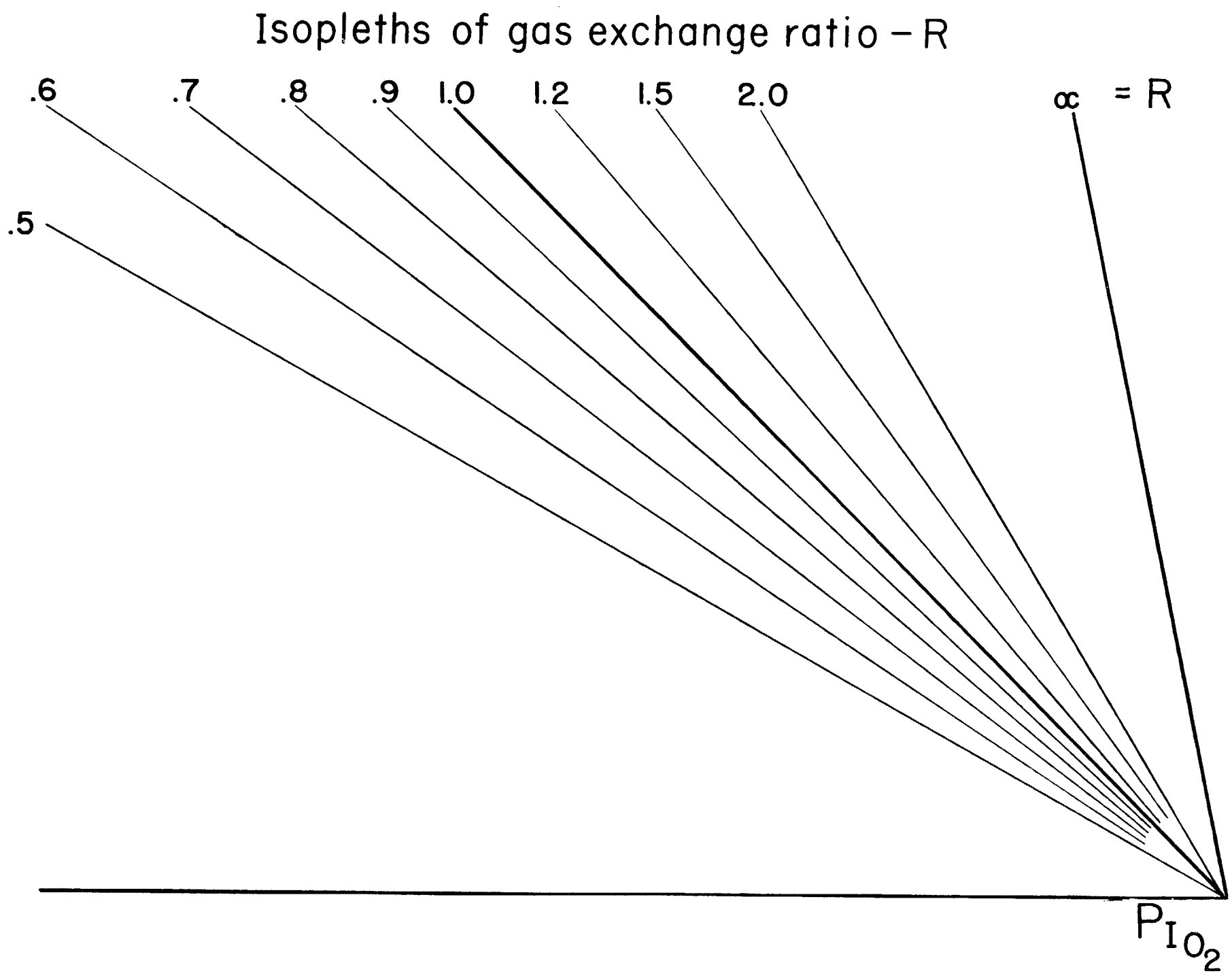

Isopleths of gas exchange ratio – R
.6
.7
.8
.9
1.0
1.2
1.5
2.0
∞ = R
.5
$P_{I_{O_2}}$

Diagram IX

Isopleths of Alveolar Ventilation. A transparent copy of this diagram (mounted on the back cover) is supplied to be used much like that of Diagram VIII. When the base line is properly superimposed on the O_2 axis of a CO_2-O_2 diagram with the point P_{IO_2} at the proper value for the inspired oxygen tension, the family of straight lines indicates the values of the alveolar ventilation (V_A) which would occur for a rate of oxygen consumption (V_{O_2}) of 100 ml., STPD, per minute. Thus for V_{O_2} = 300 ml. per minute, all values must be multiplied by 3. This family of lines is a graphic representation of Equation 2. It is applicable to a subject breathing air at any altitude provided the scale of the chart is 10 mm per inch. As the nitrogen content of the inspired air diminishes the (negative) slopes of these lines increase until in pure O_2 they coincide with the R = 1 diagonal (1).

If this chart and diagram VIII are superimposed simultaneously on diagram II, for example, there is a representation of 6 parameters, R, alveolar CO_2 and O_2 tensions, arterial CO_2 and O_2 contents, and the ventilation/oxygen consumption or $\dot{V}_A/\dot{V}_{O_2}$ ratio. Determination of any two of these parameters will fix the alveolar point and permit the values of all the others to be read from the chart. It is assumed only that there is such an entity as alveolar air of uniform composition. The values are independent of the size of the subject or the dimensions of his lungs.

$$\dot{V}_A = \frac{\text{L/min (B.T.P.S.)}}{\text{100 ml } O_2 \text{ uptake (S.T.P.D.)}}$$

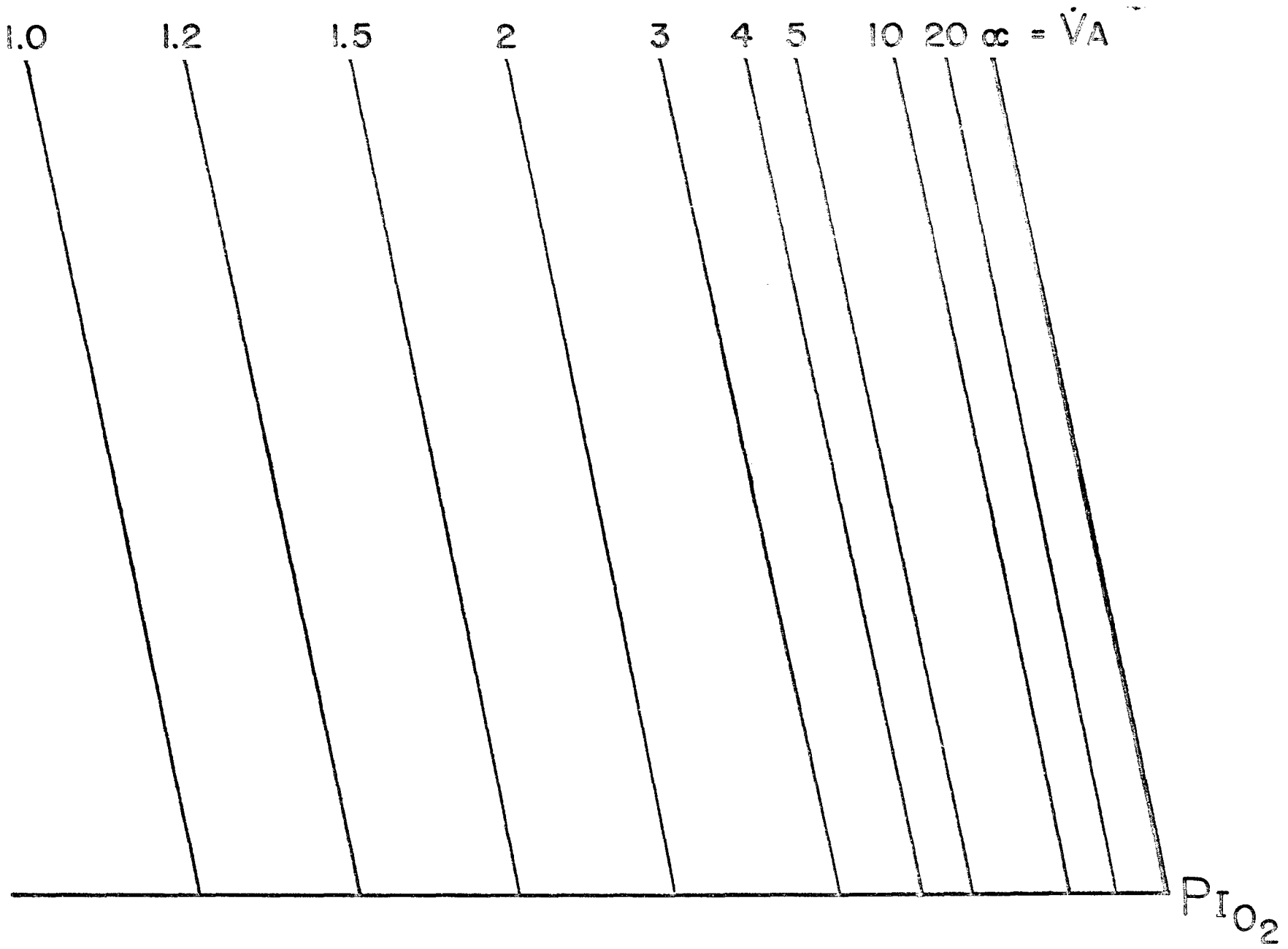
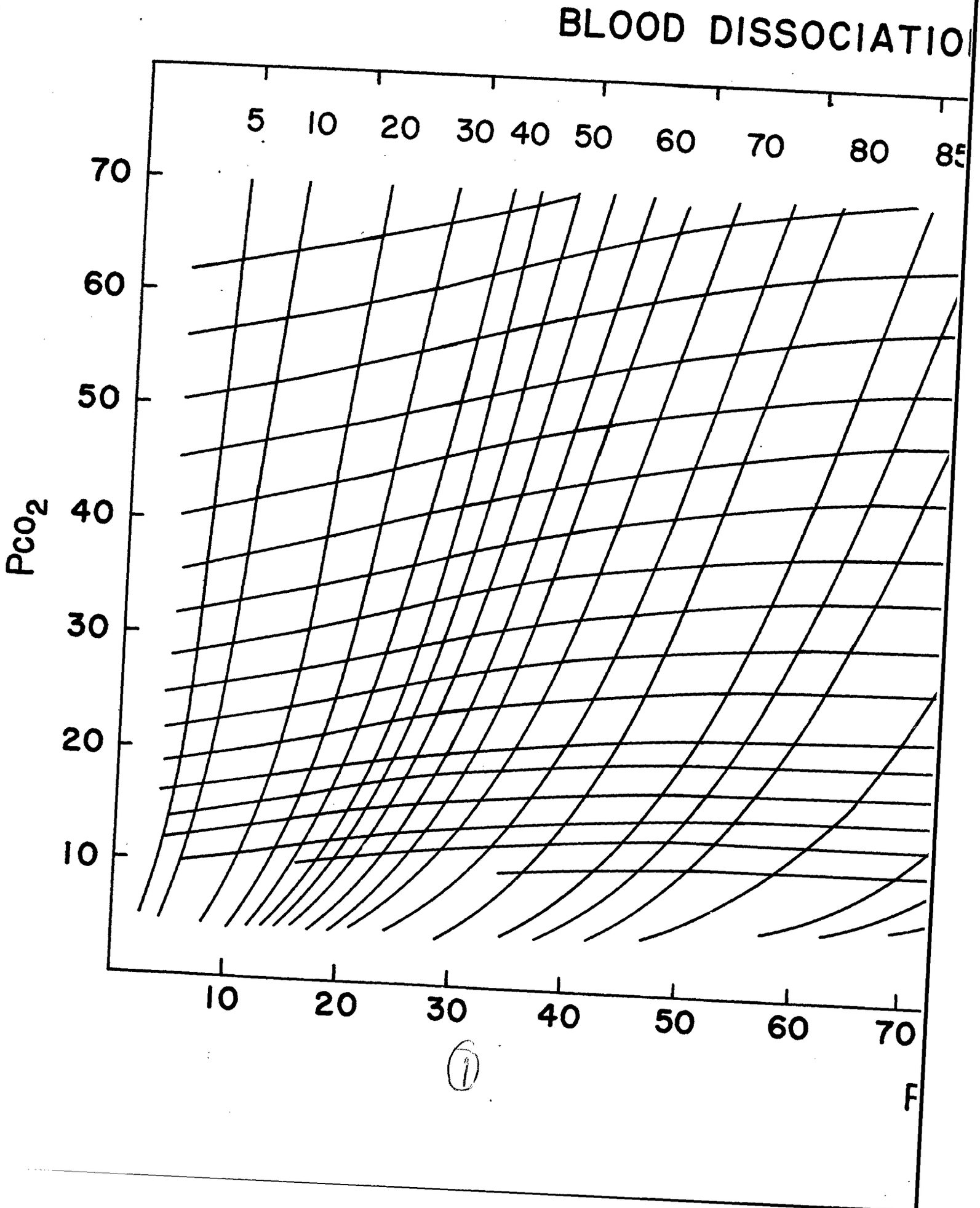
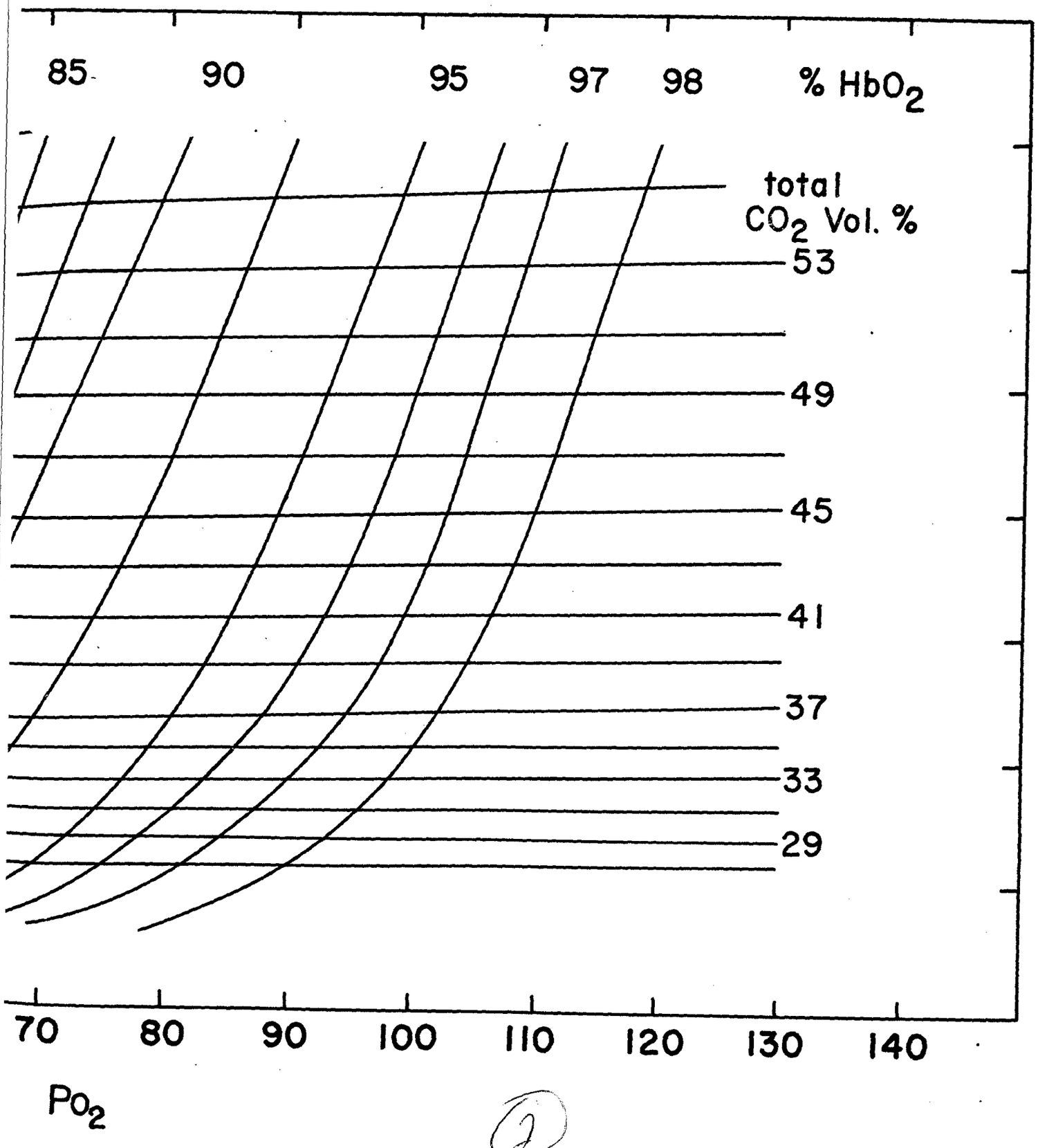


Diagram X

Combined oxyhemoglobin saturation and total blood CO_2 dissociation curves for the dog. These data were obtained by equilibrating dog blood with various O_2 and CO_2 tensions and analyzing for their O_2 and CO_2 content by the Van Slyke method. By extrapolation and interpolation of these data, as well as data previously obtained by A. Krogh, this composite chart has been drawn. The oxygen capacity of our dogs averaged 20 vols. %. (H. Rahn and H. T. Bahnson).


BLOOD DISSOCIATIO
5 10 20 30 40 50 60 70 80 85
70
60
50
40
30
20
10
P_{CO_2}
10 20 30 40 50 60 70
F

'ION CURVES OF THE DOG



(2)

CONSTRUCTION OF R AND V_A LINES

All equations apply to the gas pressures or volumes after the gases have been warmed and saturated with water vapor at 37° C. Therefore the total pressures of the dry gases in the lung are equal to the barometric pressure, P_B-47 mm Hg H_2O. The fraction of O_2, F_{IO_2}, is .209 in room air. Thus the inspired O_2 tension after it has been warmed and saturated is .209 (P_B-47) when room air is breathed, and (P_B-47) when pure O_2 is breathed. The fraction of CO_2, F_{IO_2}, in room air is considered to be 0.

In case of the alveolar ventilation equations the alveolar ventilation is expressed in l/min at B.T.P.S. (Body temperature, pressure, saturated), but the oxygen uptake is expressed in ml/min at S.T.P.D. (Standard temperature, pressure, dry). The difference in volume unit as well as changing fraction of gases to its partial pressure (in the derivation of the equation) introduces a constant .864.

R Lines

(a) When the inspired CO_2 tension is 0. The barometric pressure and the inspired O_2 fraction must be known. Assign any value to R and calculate the P_{AO_2} (from Equation 1) for any arbitrary P_{ACO_2} value. The intersection of the O_2 and CO_2 tension on the diagram connected to the inspired O_2 tension, P_{IO_2}, yields the desired R line. Or in other words all points on this line can only be the result of this particular exchange ratio, R. This equation applies to all O_2-N_2 mixtures, however the slope of any particular R line (except R = 1) varies with the O_2-N_2 ratio.

(b) When CO_2 is present in the inspired gas. In this case the procedure is similar but Equation 6 must be used and the CO_2 concentration of the inspired air must be known.

There is one exception where the slopes of the R lines breathing air can be used when breathing CO_2. This is the case where the CO_2 has been added to air. For discussion of this case see Applications of O_2-CO_2 Diagram, section (q).

V_A Lines

(a) When the inspired CO_2 tension is 0. The procedure is similar. The barometric pressure, the inspired O_2 fraction and the oxygen uptake, Vo_2, must be known. Assign any value to R and calculate P_{AO_2} (from Equation 2) for any arbitrary P_{ACO_2} value. Repeat this performance for a different P_{ACO_2} value. Connect the 2 intersections on the O_2-CO_2 diagram which yields the desired V_A line. All V_A lines are parallel to each other. When V_A is infinity, it intersects the abscissae at the P_{IO_2} point. This line is the same as that for infinite R. This equation applies to all O_2-N_2 mixtures, however the slope of the V_A lines varies

with the O_2-N_2 ratio. For the total ventilation , V_E, the product of (dead space x frequency) must be added.

Equation 3 is a very useful and much simpler equation. It expresses V_A in terms of R and P_{ACO_2}, where $\dot{V}_{O_2} \times R = \dot{V}_{CO_2}$. As long as V_{CO_2} is constant the V_A lines are merely <u>horizontal</u> lines across the O_2-CO_2 diagram and they do not require any O_2 values. They are therefore also independent of the inspired O_2 value.

(b) When CO_2 is present in the inspired gas. In this case the procedure is similar to the above procedure except that equation 7 or its alternate solution (in terms of O_2 and CO_2 only) must be used.

There is one very useful exception where the V_A lines breathing room air are the same as when CO_2 is breathed. This is the case when CO_2 has been added to the room air. For discussion of this case see Application of O_2-CO_2 Diagram, section (q).

EQUATIONS

1. Alveolar air equation (1). Values of the alveolar O_2 tension, $P_{A_{O_2}}$, are expressed in terms of the exchange ratio, R, the inspired O_2 tension, $P_{I_{O_2}}$, and the alveolar CO_2 tension $P_{A_{CO_2}}$. The inspired fraction of O_2 is $F_{I_{O_2}}$ and the inspired CO_2 tension is considered to be zero.

$$P_{A_{O_2}} = P_{I_{O_2}} + \left\{\frac{P_{A_{CO_2}} \cdot F_{I_{O_2}} \cdot (1 - R)}{R}\right\} - \frac{P_{A_{CO_2}}}{R}$$

or it may be rearranged to solve for R: $$R = \frac{P_{A_{CO_2}} (1 - F_{I_{O_2}})}{P_{I_{O_2}} - P_{A_{O_2}} - F_{I_{O_2}} \cdot P_{A_{CO_2}}}$$

2. Alveolar ventilation equation (1).

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{0.864 \dot{V}_{O_2} (1 - F_{I_{O_2}})}{\dot{V}_A} - F_{I_{O_2}} \cdot P_{A_{CO_2}}$$

where $\dot{V}_{O_2}$ = cc_{O_2} per min. STPD

$\dot{V}_A$ = lit/min BTPS alveolar ventilation (i.e., total ventilation less dead space ventilation.

3. Alveolar ventilation may also be expressed in terms of alveolar pCO_2 and the exchange ratio, R.

$$\dot{V}_A = \frac{0.864 \dot{V}_{O_2} \times R}{P_{A_{CO_2}}}$$

4. Ventilation - perfusion equation (2). By combining the Fick equation for blood flow with the alveolar ventilation equation the alveolar gas concentration may be expressed in terms of blood flow through the lung in lit/min, $\dot{Q}$ as well as $\dot{V}_A$.

Thus $$P_{A_{CO_2}} = \frac{\dot{Q}}{\dot{V}a} \; 0.864 \, R \, (Ca_{O_2} - C\bar{v}_{O_2})$$

where $Ca_{O_2} - C\bar{v}_{O_2}$ is the arterial-venous O_2 difference in ml/lit.

5. Alveolar air and alveolar ventilation equations in terms of N_2. These are similar to equations 1 and 2 expressed in terms of alveolar N_2, $P_{A_{N_2}}$, when air is breathed.

5. (Continued)

$$P_{An_2} = \frac{.791\ P_{Aco_2}\ (1-R)}{R} + P_{In_2}$$

$$\dot{V}_A = \frac{0.683\ \dot{V}o_2\ (1-R)}{P_{An_2} - P_{In_2}}$$

6. Alveolar air equation when CO_2 is in the inspired gas mixture (1).

$$P_{Ao_2} = \frac{P_{Io_2} \cdot R + P_{Aco_2} \cdot F_{Io_2}\ (1-R) + P_{Ico_2} - P_{Aco_2}}{F_{Ico_2}\ (1-R) + R}$$

where F_{Ico_2} is the fraction of the inspired CO_2

and P_{Ico_2} is the CO_2 tension of the inspired gas.

7. Alveolar ventilation equation when CO_2 is in the inspired gas mixture (1). When the ventilation is expressed in terms of R and the alveolar and inspired CO_2 for a given O_2 uptake we have

$$\dot{V}_A = \frac{0.864\ \dot{V}o_2\ (R + F_{Ico_2}\ (1-R))}{P_{Aco_2} - P_{Ico_2}}$$

$\dot{V}_A$ expressed in terms of O_2 and CO_2 only may be found elsewhere (1).

ALTITUDE-PRESSURE TABLE

(1) Altitude Ft.	(2) P_B mm Hg	(3) (P_B-47) mm Hg	(4) $.209$ (P_B-47) mm Hg
0	760	713	149
2000	707	660	138
4000	656	609	127
6000	609	562	118
8000	564	517	108
10000	523	476	100
12000	483	436	91
14000	446	399	83
16000	412	365	76
18000	379	332	69
20000	349	302	63
22000	321	274	57
24000	294	247	52
26000	270	223	47
28000	247	200	42
30000	226	179	37
32000	206	159	33
34000	187	140	29
36000	170	123	26
38000	155	108	23
40000	141	94	20
42000	128	81	17
44000	116	69	14
46000	106	59	12
48000	96	49	10
50000	87	40	8
63000	47	0	0

(All pressure figures rounded off to the nearest mm).

P_B = Barometric Pressure - U.S. Standard Atmosphere

47 = P_{H_2O}, vapor pressure, at 37° C.

(P_B-47) = Total pressure of the dry gases after the inspired gas has been saturated with water vapor. It is also equal to the inspired O_2 tension, P_{Io_2}, when pure oxygen is inspired.

.209 = Fraction of O_2 in dry air at any pressure

$.209\ (P_B-47)$ = inspired O_2 tension, P_{Io_2}, when air is breathed.

CONVERSION FACTORS: 1 Atmosphere = 14.7 p.s.i. = 760 mm Hg = 29.9 inches HG
1 Foot = 0.305 meter

APPLICATIONS OF THE O_2-CO_2 DIAGRAM

The O_2-CO_2 diagram (1) allows the simultaneous visualization of the various parameters which determine the gas tensions in the blood and the lung. The whole O_2 and CO_2 transport between the inspired gas tensions and the venous blood gas tension can be described and the changes which must occur whenever one or more parameters are altered can be quantitatively predicted. The observed gas tensions in the lung and blood are primarily a function of: 1. the inspired O_2 tension, 2. the rate at which the air pump works, the alveolar ventilation, and 3. the rate of the heart pump or cardiac output.

The following applications are designed to illustrate the practical operations which are required in using the preceeding diagrams to represent these problems of gas transport on the O_2-CO_2 diagram.

a.) Alveolar Air - Determination of ventilation and R from the composition of the alveolar air.

For general orientation we may take a subject with an alveolar O_2 and CO_2 tension of 100 and 40 mm Hg, respectively, when the barometric pressure is 747 mm Hg (see Figure 1). The moist, inspired O_2 tension (P_{IO_2}) will be equal to (747-47) .209 or 146 mm Hg. The transparent chart (No. VIII) for R, the gas exchange ratio, and for V_A, the alveolar ventilation (No. IX) placed at this value indicated that this alveolar gas tension is the result of an exchange ratio (R.Q.) of .85 and an alveolar ventilation of 1.83 L/min for an O_2 consumption of 100 cc/min (S.T.P.D.). If we assume an oxygen uptake of 300 cc, then the alveolar ventilation would be 1.83 x 3 or 5.5 L/min (B.T.P.S.). V_A chart cannot be used on Figure 1 where scale is reduced. Replot on Work Diagram I instead.

b.) Expired Air

Expired air may be regarded as a mixture of inspired air and alveolar air and consequently, on the CO_2-O_2 diagram, the composition of expired air must lie somewhere on the straight line which connects the inspired point and the alveolar point, the exact position depending on the relative amounts of dead space air and alveolar air. If E represents the expired air in Figure 1, then in accordance with the Bohr equation the linear distances AE/ AI = dead space / tidal volume, and the distance EI represents alveolar volume. The greater the dead space the greater the distance between A and E. The chart demonstrates that if the composition of the expired and inspired air is known, the R diagonal can be drawn. The point representing the alveolar air on this line can be determined if the dead space and the tidal volume are known. In this indirect way the composition of alveolar air can be determined without the necessity of obtaining a sample for analysis.

c.) Arterial and Venous Blood Gas Tensions

For alveolar CO_2 and O_2 tensions of 40 and 100 mm, respectively, the

arterial tensions may be estimated as 40 mm and 95 mm, respectively. This assumes an average alveolar-arterial gradient ($P_{A_{O_2}}$-$P_{a_{O_2}}$) of 5 mm and no difference between the alveolar and arterial CO_2. Using these values the arterial point is represented in Fig. 1 as point a. The combined O_2 and CO_2 dissociation curves of the blood (Diagram II) indicate that at this arterial tension for O_2 and CO_2 we have an O_2 and CO_2 content of 19.4 and 48.0 vols. %, respectively, or if we glance at the blood pH and oxygen saturation chart (Diagram III), we find an O_2 saturation of 97% and a pH of slightly above 7.4.

From this arterial point one may now determine the mixed venous blood ($\bar{v}$) tensions or contents. Since the exchange ratio, R_a, in the lungs in our example is .85, R_b for the blood must also be .85. The dotted line between a and $\bar{v}$ in Figure 1 is the blood R line of .85. The arterial-venous content difference for CO_2 and O_2 between any point on this line and the fixed arterial point has a ratio of .85. (This line can be obtained by placing a straight edge on the proper arterial O_2 and CO_2 tensions of the nomogram (Diagram VI). By pivoting the straight edge around the point where it intersects R = .85 pairs of simultaneous pO_2 and pCO_2 values for this particular blood R value can be read off and plotted).

The mixed venous blood must therefore be somewhere on this R_b line, the exact point being determined by the cardiac output. If the blood flow is 6 L/min. (the oxygen uptake being 300 cc), the A-V difference for O_2 is 5 vol. %. The venous point is therefore at the intersection of the blood R line and the O_2 content isopleth of 14.4 vols. % (19.4-5.0). The oxygen saturation and pH of the venous blood can be obtained from the other chart (Diagram III). The total tension available may be divided into fractions the most important being the inspired-alveolar fraction, the magnitude of which depends upon the pulmonary ventilation, and the arterial-venous fraction which depends upon the cardiac output. In the steady state both depend also upon the metabolic rate. In addition one might recognize a pulmonary diffusion fraction, if the arterial blood and alveolar air are not in complete equilibrium, and a tissue diffusion fraction. Each of these fractions can vary independently but in determining them one must start with the inspired air which is the fixed point in the system and work backwards.

Mixed venous blood as found in the pulmonary artery is a mixture of many components from various organs which differ widely in O_2 and CO_2 content. This is illustrated in Figure 2 for a man at rest. The arterial blood, represented by a solid dot is assumed to have a pO_2 of 100 mm, a pCO_2 of 40 mm and an O_2 content of 19.5 vols. %. From this point a family of blood R lines have been drawn (as described above) anticipating the various respiratory quotients to be encountered from 1.0 in the brain to nearly 0.7 in resting muscle. The venous blood of each organ must be represented by a point located somewhere on the blood R line appropriate to that organ. The distance of any point from the arterial point is determined by the ratio of its (O_2) metabolic rate to its perfusion rate or the A-V oxygen content difference. The individual values for various organs have been

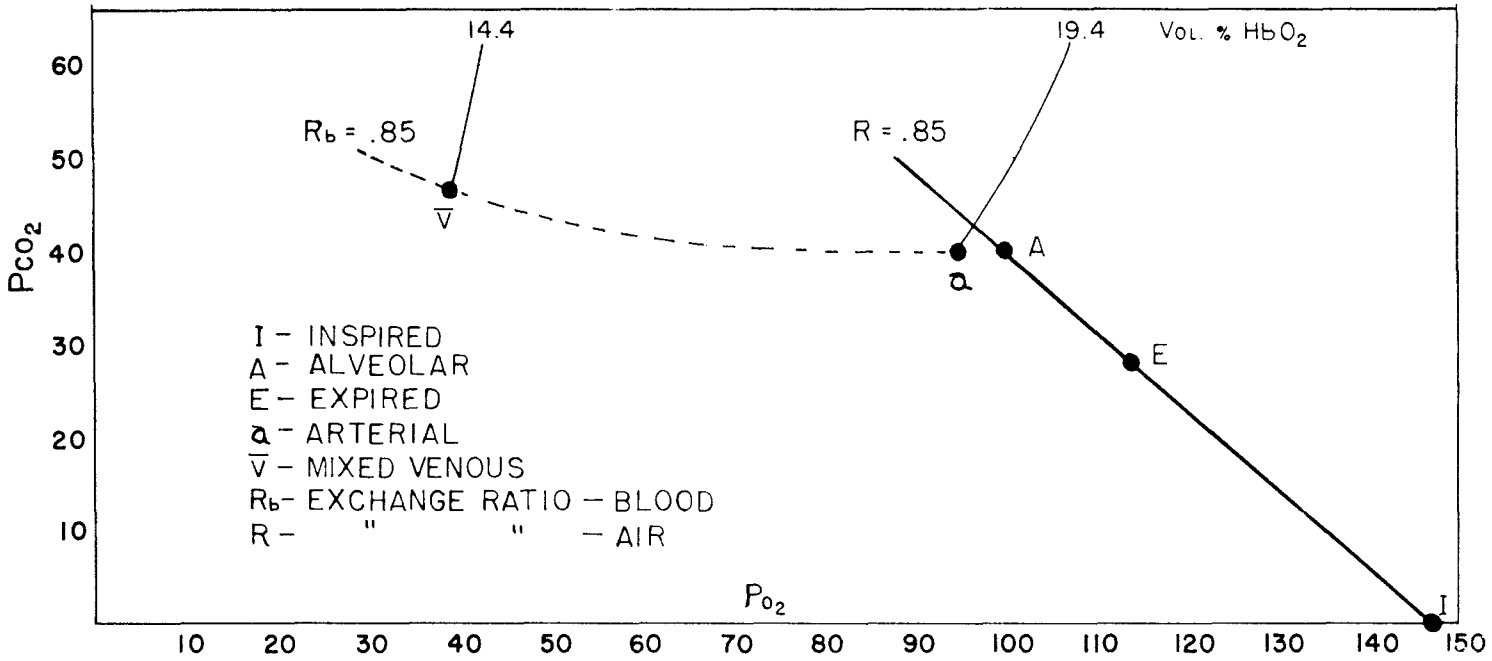
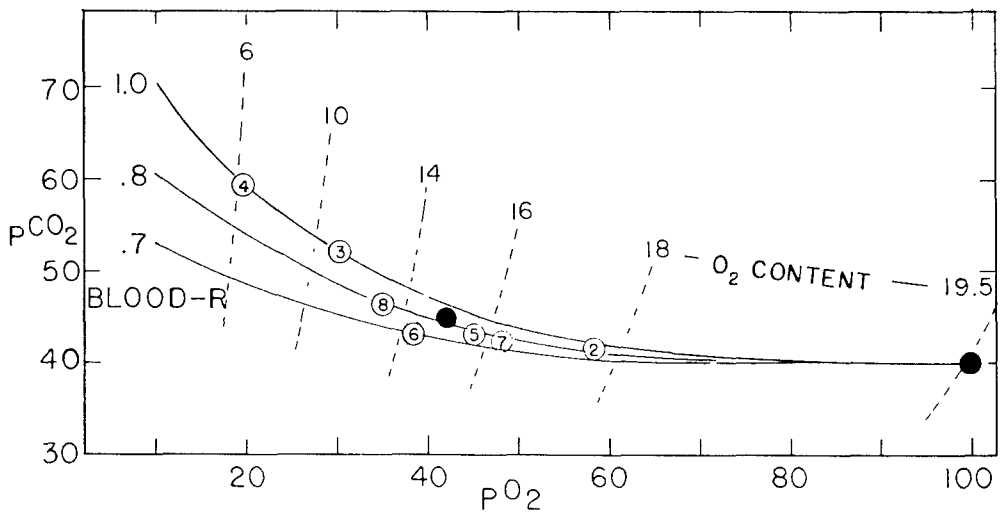


FIG. 1



	Organs	Wt.-kg	$\dot{V}_{O_2}$-ml	$\dot{Q}$-lit	R.Q.	$(A-V)_{O_2}$-vols%	Venous O_2-vol%
(1)	Lung	1.20	-	-	-	-	-
(2)	Kidney	.27	22	1.33	.86	1.65	17.85
(3)	Brain	1.50	68	.64	1.00	8.10	11.40
(4)	Heart	.33	26	.20	.97	13.00	6.50
(5)	G.I.Tract, Liver, Spleen	3.20	54	1.50	.80	3.6	15.90
(6)	Muscle	40.00	50	1.00	.70	5.0	14.50
(7)	Con. Tissue, Skin, Fat	22.00	20	.63	.80	3.2	16.30
(8)	End.Glands, Marrow	1.50	30	.50	.85	6.0	13.50
	Total or Weighted Means	70.00	270	6.00	.85	4.5	15.00

FIG. 2 VENOUS BLOOD GAS TENSIONS

derived from various sources in the literature as indicated below Figure 2. The resultant mixed venous point, indicated by the other solid dot, is the sum of the total O_2 consumed by each of the organs (i.e., its A-V O_2 difference x its blood flow) divided by the total flow or cardiac output.

d.) Ventilation - Perfusion Ratio

For a given composition of the mixed venous blood and inspired air the alveolar or arterial gas tensions are determined by the ratio of alveolar ventilation / perfusion or the V_A/Q ratio, (See Equation 4), and are independent of the metabolic rate. This concept can be applied to the whole lung or to an individual alveolus. In the former case Q, the perfusion rate is equal to the cardiac output and V_A to the total alveolar ventilation.

Equation 4 can be solved graphically (2) and is illustrated in Figure 3. It is necessary to fix the two points which represent the inspired gas tensions and the mixed venous gas tensions (See solid dots). Radiating from each of these points is a family of R lines, the pulmonary R lines from the inspired air point and the blood R lines from the mixed venous point. The blood R lines are determined as described above except that one starts with the straight edge at the pCO_2 and pO_2 of the mixed venous point on the nomograms. The R lines for .6, 1.0, 1.5 and 3.0 are indicated in Figure 3. Clearly there is only one point where a given blood R line intersects the alveolar R line of the same value. The tensions of O_2 and CO_2 indicated by this point represent therefore the only values at which blood and alveolar air can exchange at this particular exchange ratio. For example, gas and blood can only exchange at an R = 1.0 when the alveolar composition has an O_2 and CO_2 tension of 112 and 37 mm, respectively. (In such an ideal case it is assumed that no arterial-alveolar gradients exist.) Equation 4 allows one to calculate the V_A/Q ratio of 1.5 which would be necessary for this exchange.

When the intersections of the various possible blood and gas R's are plotted, they can be connected to form the heavy solid line between the inspired and venous point, shown in Figure 3. This line represents all the possible combinations of O_2 and CO_2 tensions which could exist in any alveolus, each depending on a particular V_A/Q ratio. Some of these values have been indicated by the large numerals opposite various R line intersections. An alveolus with no perfusion or infinite ventilation is represented by the inspired air point and an alveolus with no ventilation or infinite perfusion rate is indicated by the venous point.

e.) Alveolar-Arterial N_2

The O_2-CO_2 diagram has so far omitted any reference to the N_2 tensions in the alveolar air. Actually the changes which occur in alveolar or arterial N_2 are reflected in the O_2-CO_2 diagram. This fact can best be appreciated by making first an extension of this diagram to include the N_2 and water vapor as shown in Figure 4.

On the abscissa we have the inspired gas tensions, $P_{Io_2} + P_{In_2} + P_{H_2O} = P_B$, the barometric pressure (760 mm Hg). If now the metabolic CO_2 is added and O_2 is taken up in the expired or alveolar air, the P_{n_2} in the expired or alveolar air no longer remains equal to the inspired nitrogen, P_{In_2}, except when R = 1.0. In the latter case the CO_2 added is equal to the O_2 uptake and the net volume of the gas remains the same. However, when R is less than 1.0, that is when the O_2 uptake exceeds the CO_2 output, the inspired N_2 becomes concentrated by the volume shrinkage. On the other hand, with an R greater than 1.0, the CO_2 output exceeds the O_2 uptake and thereby dilutes the inspired N_2 and increases the inspired gas volume.

Figure 4 illustrates 3 different alveolar gas concentrations representing R values of .5, 1.0 and 2.0. (These large R differences were chosen simply to magnify the N_2 changes to be represented on the very small scale of the abscissae). One will note that the horizontal distance (from 0 to the P_B line) through each alveolar point + the vertical distance must always be equal to the total barometric pressure. The absolute tensions of the lower, middle, and upper alveolar points are indicated in the table below including the changes which occur between the inspired and alveolar N_2 as well as the factor by which the volume of the inspired air changes. This factor is equal to (P_{In_2}/P_{An_2}). Thus, for example, the inspired volume of 1000 ml is reduced to 935 ml in the lung under the conditions of the upper alveolar air point. At altitude this factor increases inversely with the total pressure since P_{In_2} becomes reduced but the difference between P_{In_2} and P_{An_2} remains the same for comparable R and CO_2 values.

	P_{CO_2}	P_{O_2}	P_{N_2}	P_{H_2O}	P_B	ΔP_{N_2}	Vol. cor. Factor (P_{In_2}/P_{An_2})
Inspired gas	0	149	564	47	760		
Lower Pt. R = 1.0	30	119	564	47	760	0	1.00
Middle Pt. R = 2.0	40	125	548	47	760	-16	1.03
Upper Pt. R = 0.5	50	60	603	47	760	+39	0.935

It is now important to point out that the changes of the P_{In_2} can be directly obtained for any alveolar point by simply measuring the horizontal distance between this point and the R = 1.0 line. This interval represents the partial pressure of N_2 gained or lost from the inspired N_2. For practical purposes, therefore, it is not necessary to extend the O_2-CO_2 diagram in order to evaluate the changes in N_2. This can be further verified by placing the R chart on Figure 1. One will note that the horizontal distance between the alveolar point A and the R- 1.0 line is 8 mm. Therefore, the alveolar P_{N_2} is equal to P_{In_2} + 8. It will also be noted that a similar procedure for the expired air composition (point E - Figure 1) will yield

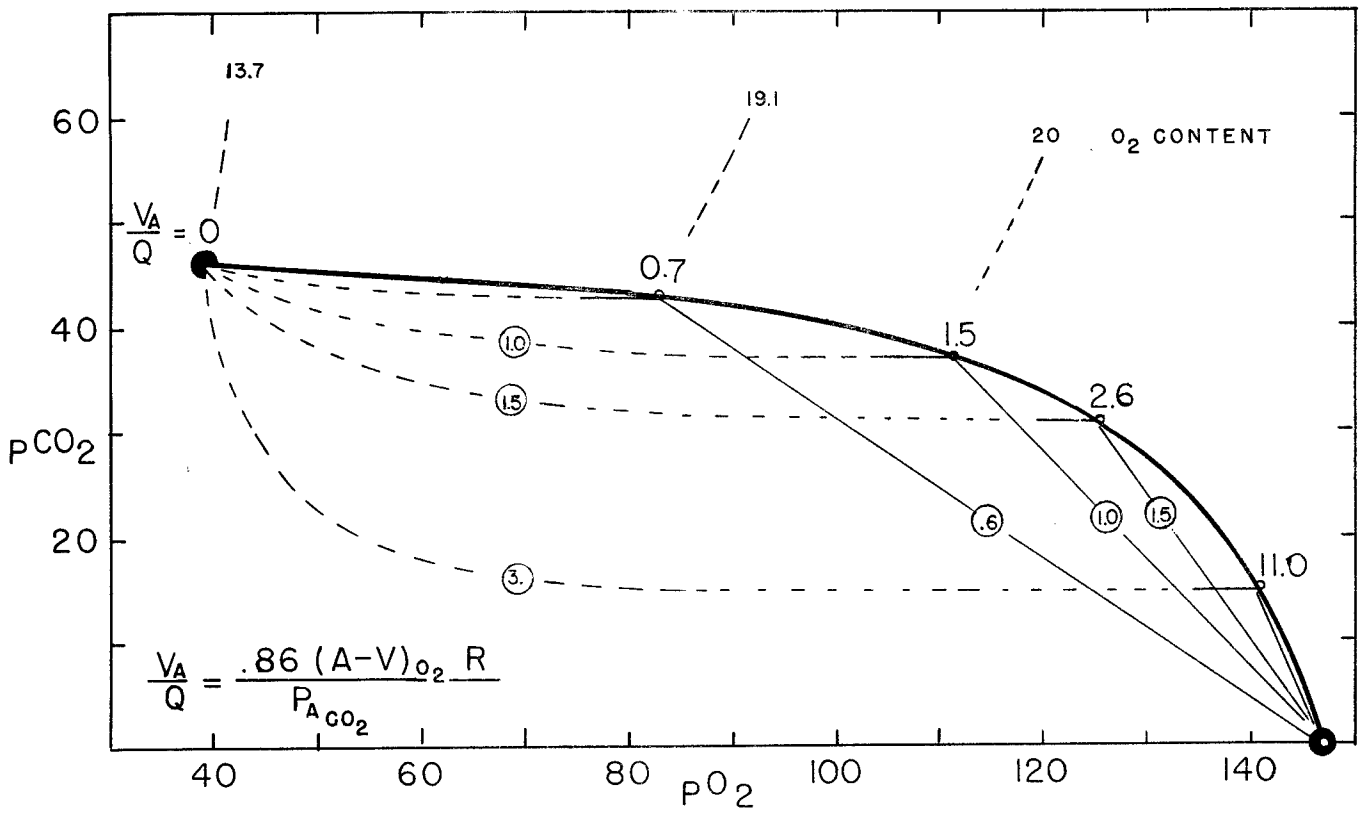


FIG. 3 VENTILATION–PERFUSION RATIOS

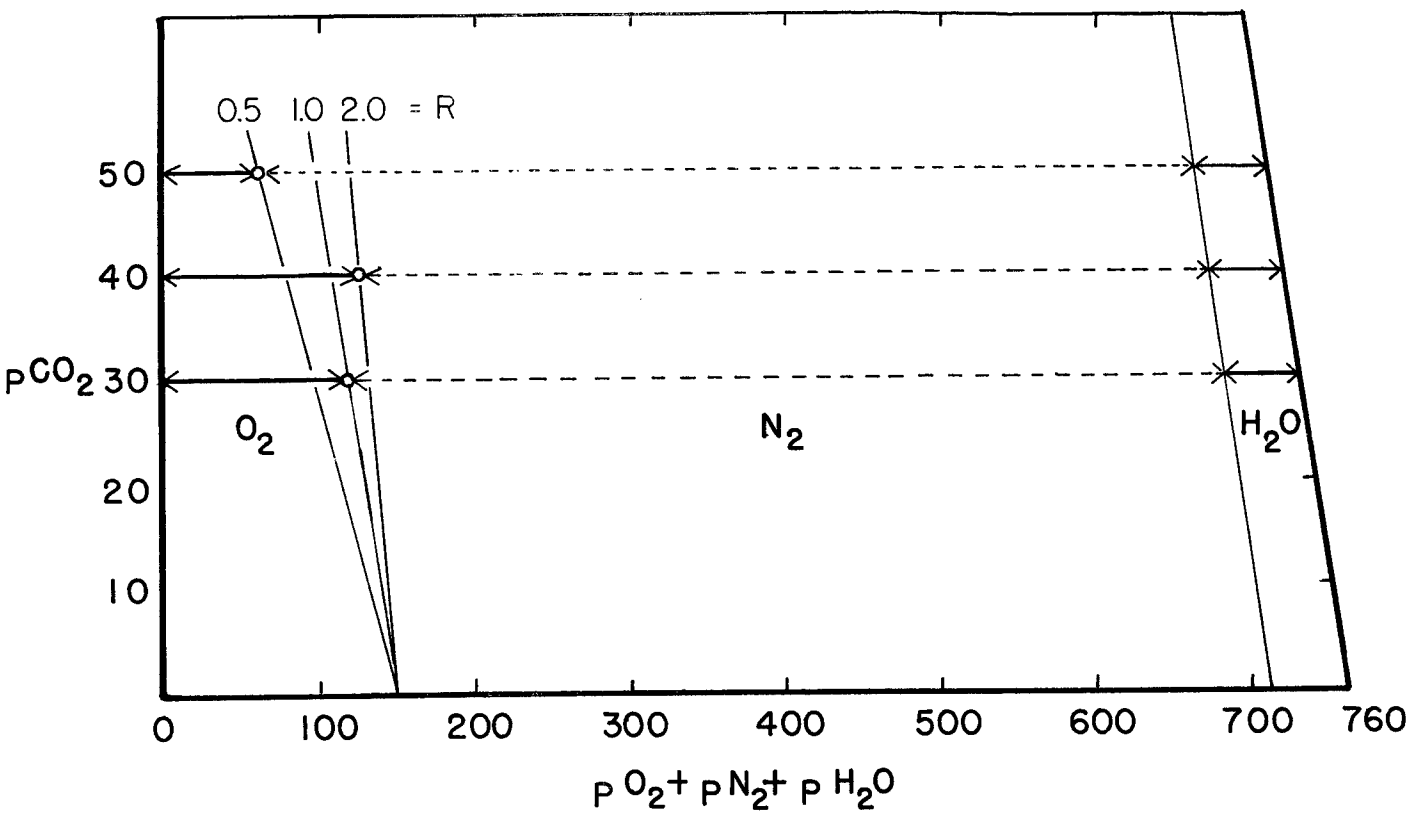


FIG. 4 THE $O_2 - CO_2 - N_2$ DIAGRAM

a smaller N_2 tension than found in the alveolar air. Thus the P_{An_2} is not only a function of R but of P_{CO_2} as well (see Equation 5). During the unsteady state large fluctuations in alveolar N_2 may be encountered. Some of these are indicated under the section (p), entitled the N_2-CO_2 Diagram.

f.) Breathing of Pure O_2 at Altitude

When the inspired gas is pure O_2, the ventilation and R.Q. isopleths of diagrams VIII and IX are all coincidental with the R = 1 diagonal having a slope of -1. The alveolar point must lie on this diagonal regardless of the actual exchange ratio. This is necessary because with only two gases present, in addition to water vapor, the sum of their tensions must always be equal to P_B-47. For every altitude or every value of P_B, therefore, there must be a single "altitude diagonal" starting from the inspired pO_2 tension and having a slope of -1 (1). Several such altitude diagonals are shown in Figure 5. The curve connects the alveolar points which have been observed as average values on each of these diagonals or at each of these altitudes. For any altitude the intersection of the appropriate altitude diagonal with this curve will identify the CO_2 and O_2 tensions of the average alveolar point. With the aid of diagrams II and III the corresponding values of HbO_2 %, CO_2 and O_2 contents and pH can be read off. Diagrams VIII and IX are not applicable when pure O_2 is used as the inspired gas.

When breathing pure O_2 at barometric pressures less than 196 mm (33,000 ft), the inspired O_2 tension is less than at sea level breathing air. At altitudes below this the use of O_2 in partial or complete substitution for air will restore the alveolar pO_2 to normal values. At altitudes higher than this the alveolar pO_2 will be below normal in spite of the use of pure O_2 unless pressure breathing is used.

g.) Pressure Breathing

When pressure breathing is instituted, the pressure is theoretically applied to both the CO_2 and O_2 of the lung. But the respiratory center does not tolerate a higher CO_2 tension. Thus for practical purposes all the pressure is applied to the O_2 tension and the alveolar point moves to another altitude diagonal (3,4) without change in pCO_2. In Figure 5 the subject has an alveolar air at point A at 46,000 ft. With 22 mm Hg pressure breathing his alveolar point moves over 22 mm Hg to the 42,000 ft. diagonal to point B. Since pressure breathing is usually accompanied by an additional hyperventilation, he moves down the altitude diagonal to point C. The corresponding changes in the arterial blood gas content resulting from: 1. positive pressure alone, and 2. from the additional hyperventilation can be readily seen on diagrams II and III.

h.) Hypoxia at Air Breathing Altitude

At an air breathing altitude (Figure 6) which has the same inspired O_2 tension as an oxygen breathing altitude (for example, 46,000 ft. on O_2 and 22,000 ft.

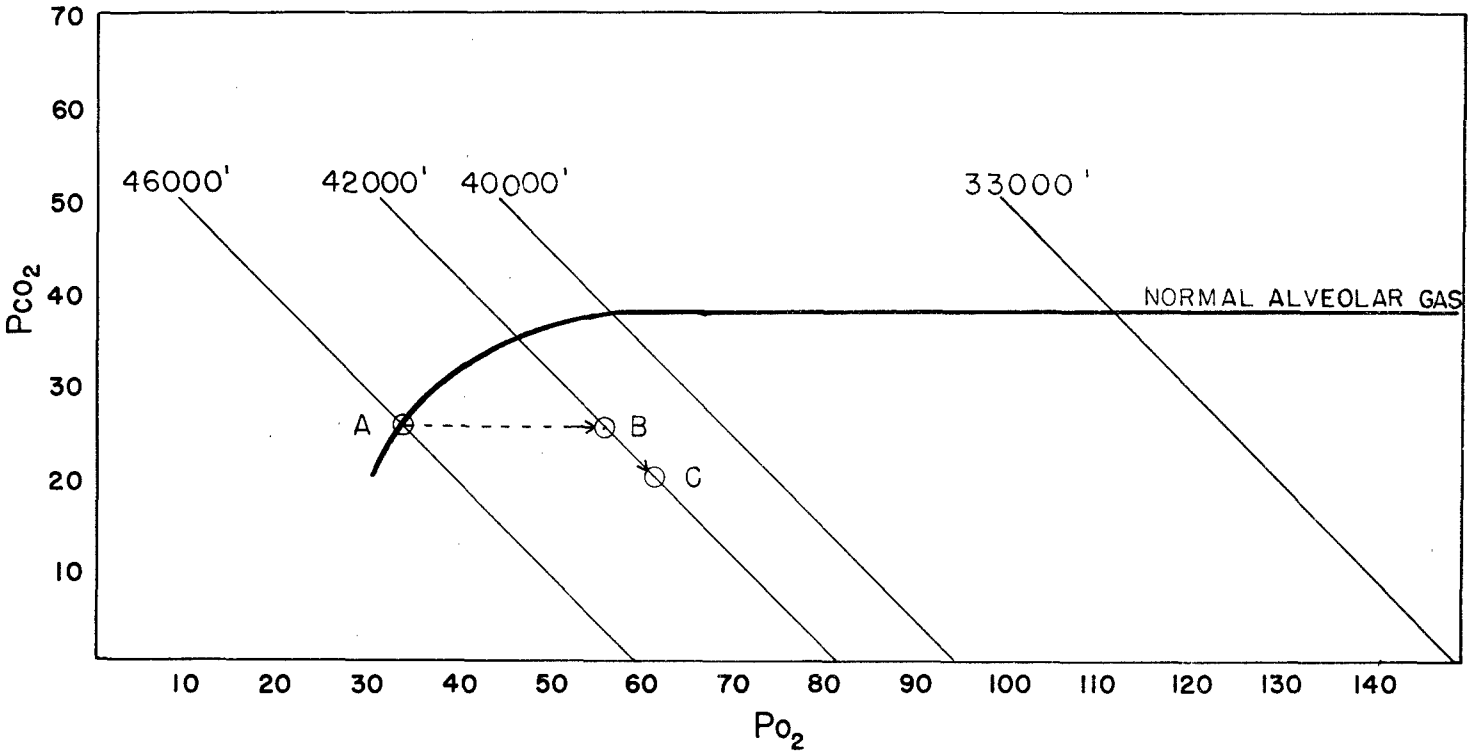


FIG. 5 ALTITUDE DIAGONALS – PRESSURE BREATHING

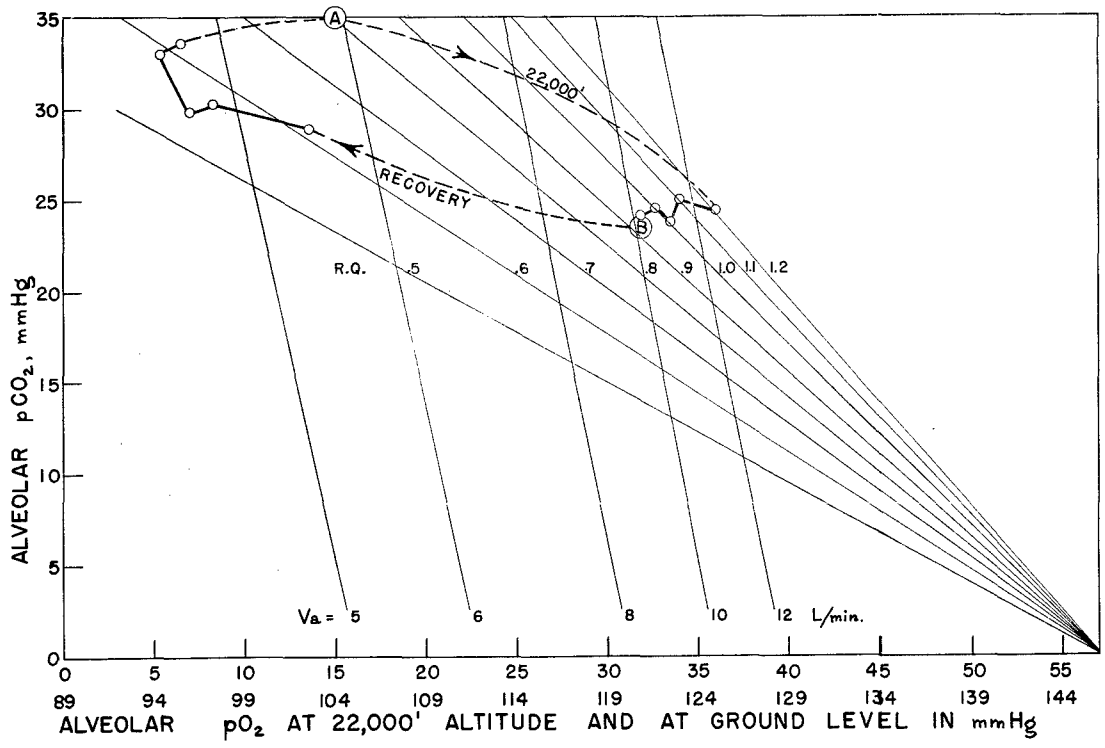


FIG. 6 ACUTE EXPOSURE TO 22000'

on air, P_B = 105 and 321, respectively), the alveolar point is no longer bound to the R = 1.0 line because of the presence of N_2. Instead we have a family of altitude diagonals, each one depending upon the R and the alveolar ventilation. Only when the R breathing air is equal to 1, all other things being equal, will the alveolar pO_2 be the same at these two altitudes. At any other R on air the alveolar O_2 will be lower or higher, depending upon an R lower or higher than 1, respectively. Upon acute exposure to low O_2 the ensuing hyperventilation blows off CO_2 stores of the blood and tissues and thus raises temporarily the R. The steady state at 22,000 ft. is not reached in less than 30 minutes. Figure 6 describes the changes observed in man upon exposure to 22,000 ft. altitude (5). Point A would represent the alveolar concentration man would have if he maintained his normal alveolar sea level ventilation of 6 1/min and R. = .8. The open circles represent at five-minute intervals the observed concentrations which are produced by the anoxic hyperventilation. At the end of 5 minutes (first point) the alveolar ventilation has more than doubled with a reduction in pCO_2 and an R value of 1.2. If this new ventilation were maintained the alveolar point would slowly move down on the particular ventilation isopleth with the exhaustion of the CO_2 stores until the R line of 0.8 was reached at a pCO_2 of 16 mm with the establishment of a new steady state. Actually the initial acapnia counteracts the hypoxic drive and the alveolar ventilation is slowly reduced to about 10 1/min after 30 minutes of exposure with an R value of slightly over 0.9 at point B. The predicted H_bO_2 saturation at point A would have been 30% but the observed alveolar values predict an H_bO_2 of 70%. (Actually the ear oximeter indicated a value of 65%. This would indicate an A-a gradient of about 3 mm O_2).

After 30 minutes' exposure (point B) the subjects were quickly recompressed to ground level and the recovery pathway is indicated from point B to A. The reduced ventilatory drive to less than 5 1/min allows for the gradual recovery of the previously lost CO_2 stores with R values below 0.6.

i.) Acclimatization to Altitude

When after an acute exposure to anoxia the steady state has been reached (1/2 - 1 hour), then the alveolar air values must come to rest somewhere along the R = .85 diagonal of that particular altitude (if the true metabolic R.Q. is 0.85). In Figure 7 the upper curve represents the alveolar values found at various altitudes after the steady state is attained (6).

If man now remains longer at these altitudes, as has been verified by residence in the mountains, he very slowly increases his ventilation. Thus the CO_2 is lowered over several days, and the alveolar point progresses down along the R.Q. = .85 diagonal with proportional increase in alveolar pO_2 until the acclimatized curve of Figure 7 is reached. The degree by which his blood oxygen saturation increases during this acclimatization process can be predicted from the oxygen saturation curves since they are not appreciably altered by the slow increase in

hemoglobin. On the other hand the pH, O_2 and CO_2 content isopleths are no longer valid and require new nomograms for their construction. The only complete data available for permanent residents are those of Dill et al obtained on miners living in the Andes at an altitude of 17,500 ft. (P_B = 401). The diagrams, Nos. IV, V, and VII, include their nomogram as well as two O_2-CO_2 diagrams with the isopleths for O_2, CO_2 blood content and pH and H_bO_2 saturation. The average alveolar pO_2 and pCO_2 tensions for these people are 42 and 26, respectively. The inspired O_2 tension at this altitude is .209 (401-47) or 74 mm Hg. The R chart (Diagram VIII gives these people at rest an R of .8. The V_A chart yields an alveolar ventilation of 2.7 L/min/100 ml of O_2 uptake. This is a 50% increase over what would be required if they maintained their pCO_2 at 40 mm Hg. Furthermore, it can be seen that their arterial O_2 content of 23.5 vols. % is actually above that for man at sea level in spite of the fact that their saturation is only 79%. The pH is just slightly above 7.4.

j.) Equivalent Altitudes

The problem of equivalent altitudes breathing air and oxygen can be best appreciated by placing, for example, the R chart at the inspired pO_2 of 94 in Figure 5 which is also equal to the inspired pO_2 of 40,000 ft. when O_2 is breathed. As has been pointed out above the alveolar gas is restricted to the slope of -1 as long as O_2 is breathed. Breathing air an inspired pO_2 of 94 will be found at 11,200 ft. where P_B = 497 and P_{Io2} = .209 (497-47). But in this case man is not restricted to the R = 1 line, but can theoretically be at any R depending upon his ventilation. In fact as pointed out in section (h) his R will vary considerably with acute exposure until he reaches his new steady state. For example, at this particular air altitude with a pCO_2 of 40 mm and an R of 0.7 the alveolar point will actually be on the 42,000 ft altitude diagonal for pure oxygen. With an R greater than 1 he will at an O_2 altitude less than 40,000 ft and only when his R = 1.0 may his equivalent altitude be regarded as the same as that predicted from the inspired oxygen tension.

The advantage of a high R breathing air compared to breathing O_2 at equivalent inspired O_2 tensions can actually be demonstrated in survival studies of animals acutely exposed to very low O_2 tensions (7).

k.) Psycho-motor Performance at Altitude

Man's performance at altitude is affected by the composition of the arterial or alveolar gases. At each altitude there exists an optimum alveolar gas composition for the best performance. This optimum may vary for different types of performance. The effects of anoxia and acapnia seem to be additive rather than antagonistic in their effects (8,9). Figure 8 indicates the approximate boundaries of normal and impaired performance as well as the normal alveolar gas composition encountered with changes in altitude. The arterial gas composition in any performance region may be approximately gaged by reference to Diagrams II

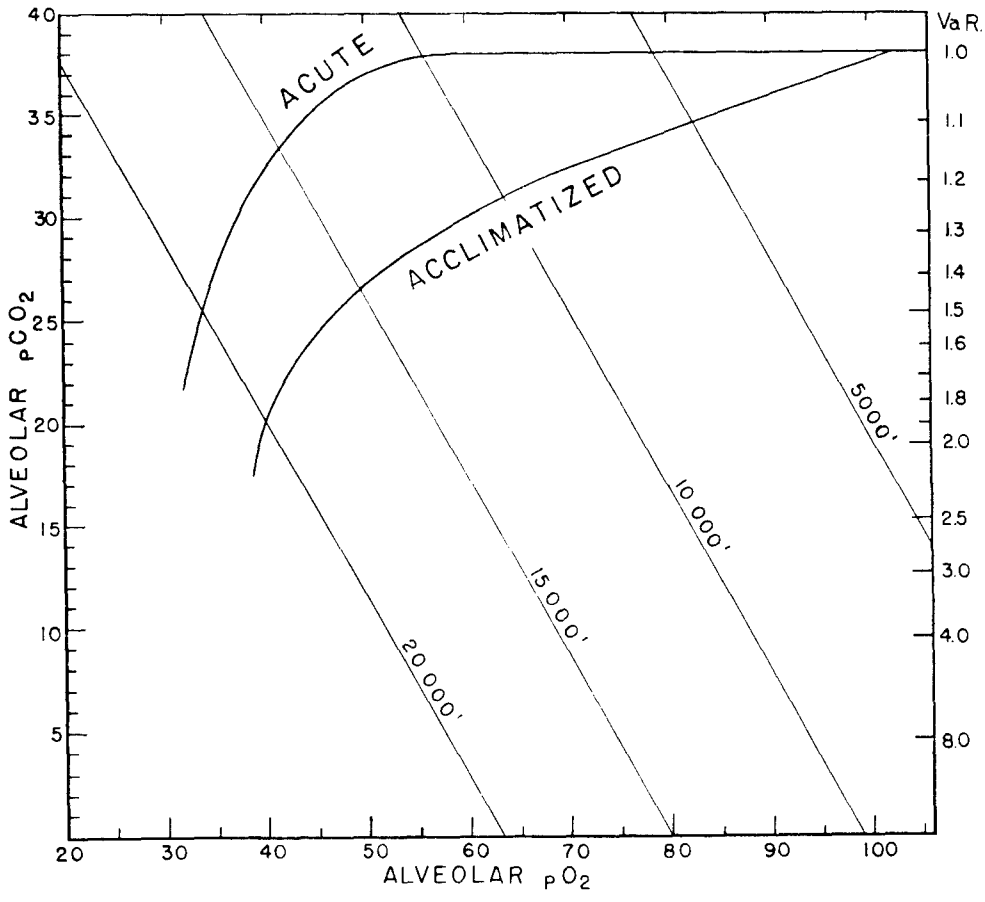


FIG. 7 ACCLIMATIZATION TO ALTITUDE

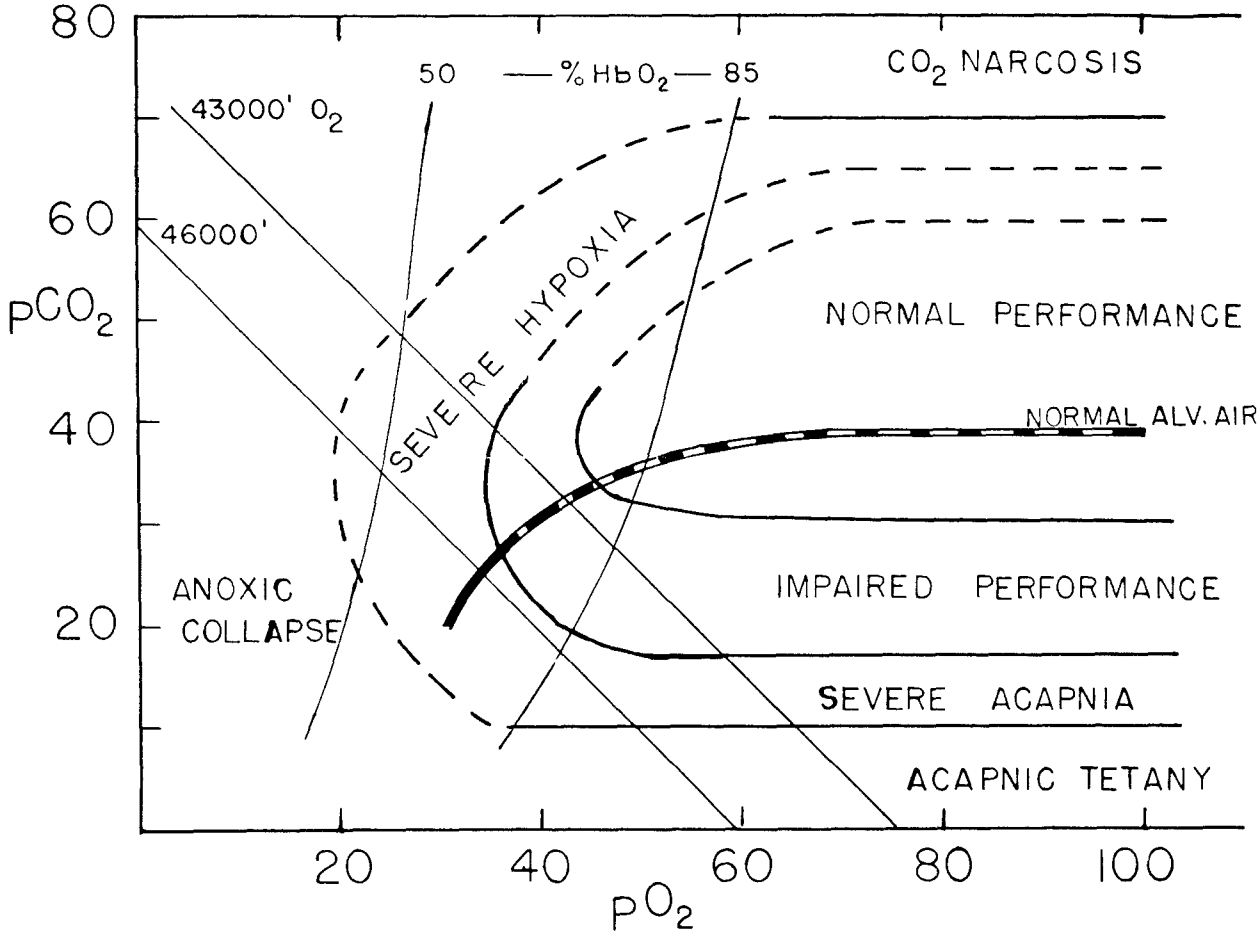


FIG. 8 PERFORMANCE AND ALTITUDE

and III. Two oxygen saturation isopleths and two altitude diagonals have been added for orientation.

1.) Oxygen Transport and Cardiac Output at Altitude

By means of the O_2-CO_2 diagram it can be shown that the hyperventilation and lowered alveolar pCO_2 which occurs at altitude is advantageous for the transport of oxygen because it permits the maintenance of the same mean venous oxygen tension with minimum increase in cardiac output.

This is demonstrated in Figure 9. The vertical line at a pO_2 of 30 mm represents the venous oxygen tension which is to be maintained. On this line 5 sample points are selected. The CO_2 and O_2 contents of each of these points can be determined from the background grid of more or less horizontal and vertical lines. The corresponding alveolar points are connected to the venous points by broken lines. Each alveolar point is 6 vols. % of O_2 higher and 5 vols. % of CO_2 lower than the venous points. This assumes, therefore, that the exchange ratio is 0.83 and the A-V oxygen difference is 6 vols. % with a cardiac output taken as 100%. The heavy curve to the right on which the alveolar points lie represents the alveolar requirement for a venous pO_2 of 30 mm.

The meaning of this curve is better demonstrated in Figure 10 where similar alveolar requirement curves are shown for different cardiac outputs between 100 and 300% of normal. The same venous pO_2 can be maintained with a lower alveolar pO_2 if the cardiac output is increased above the normal value. Suppose further that the alveolar point is at the upper intersection of the 120% cardiac output curve and the 42,000 foot altitude diagonal. The subject is breathing pure oxygen, the arterial saturation is 85% and the alveolar pCO_2 about 35 mm. If he now increases his ventilation, the alveolar point will travel down the 42,000 foot diagonal to the right. In so doing it will come closer to the 100% cardiac output curve and further from the 120% cardiac output curve. Thus the same venous pO_2 can now be maintained with a cardiac output which has decreased from 120 to about 110% of the normal. Indeed the 93% saturation line appears to pass through the minimum or bend of each of these alveolar requirement curves. Thus it can be seen that for the transport of oxygen (1) hyperventilation will minimize the cardiac output requirement so long as the percentage saturation is not higher than 93% and (2) the higher the altitude the lower the value of the alveolar pCO_2 which is minimum for cardiac output and therefore optimum for O_2 transport.

The same problem can also be approached from a consideration of the position of the venous point as illustrated in Figure 11. The alveolar point may be considered as located somewhere along the R.Q. diagonal of approximately 0.8 at an inspired pO_2 of 80 mm and an altitude, breathing air, of about 18,000 feet. Three such sample points have been selected from which blood R = .8 lines (dotted) have been drawn. These are so drawn that the CO_2 increases 0.8 vols. % for every O_2 decrease of 1 vol. %. Points on these dotted curves which are 5 vols. % O_2 lower than the alveolar points are arbitrarily connected by the 100% cardiac output curve.

O_2 TRANSPORT & CARDIAC OUTPUT

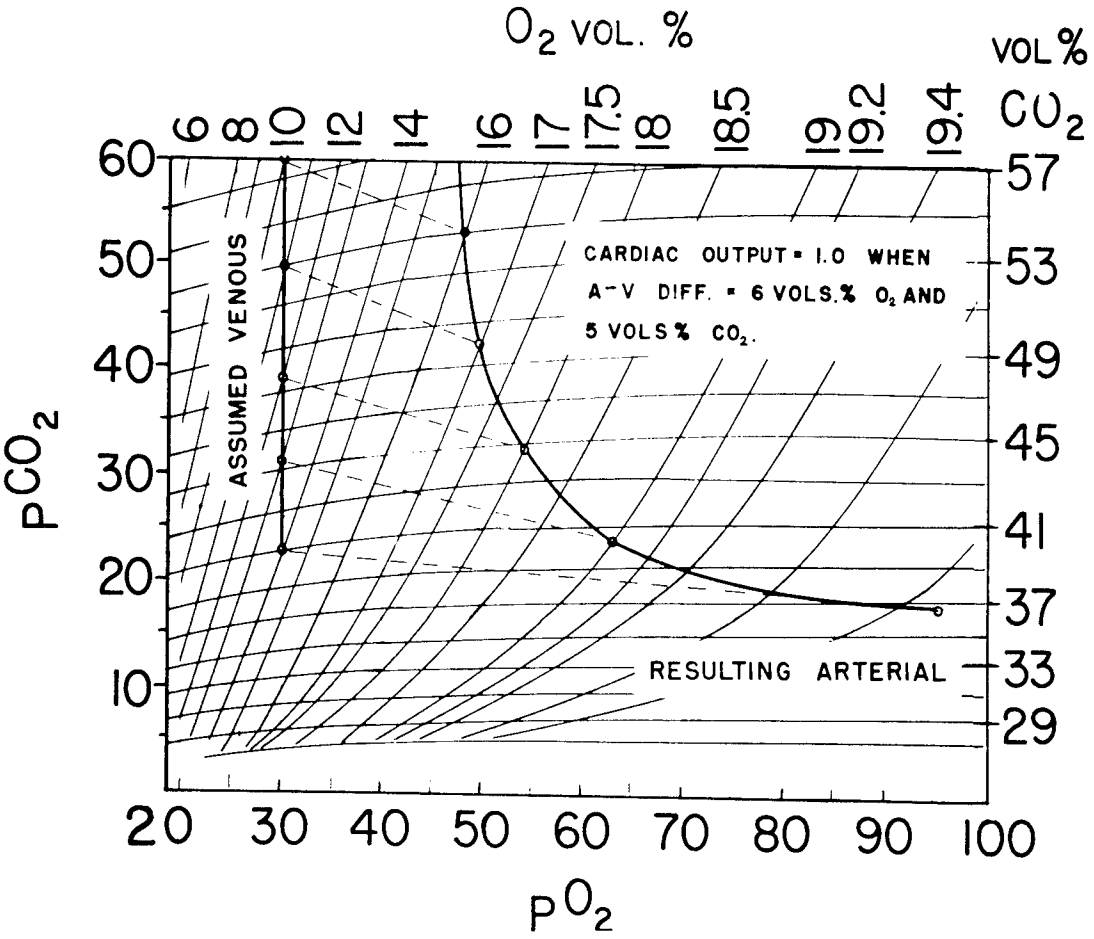


FIG. 9

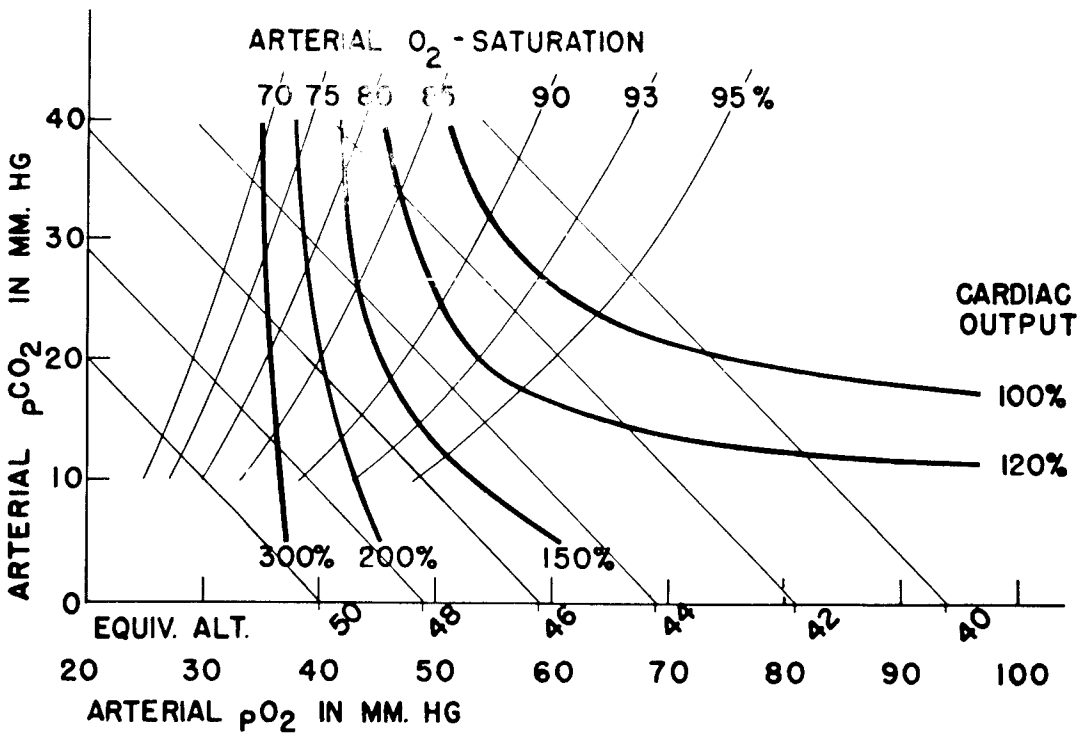


FIG. 10

Similarly the 50% cardiac output curve lies at an A-V O_2 difference of 10 vols. %. This family of curves shows for this altitude, therefore, (1) how much the venous pO_2 can be increased by an increase in cardiac output without change in the ventilation, or (2) what change in the venous point can be expected if the ventilation is changed without change in the cardiac output, and (3) that increase in ventilation will increase the venous pO_2 until the alveolar pCO_2 falls to about 20 mm after which there is either no change or a slight fall (as indicated on the 50% cardiac output curve). (At ground level the venous pO_2 falls if hyperventilation causes any fall of alveolar pCO_2 below the normal value as shown below in Figure 14.)

Similar venous point curves can be drawn for different altitudes as illustrated in Figure 12. Six different altitude diagonals are illustrated each with a value of R= 0.8. The corresponding venous point curves are illustrated at the left, each labelled with the appropriate value of the inspired oxygen tension, varying from 50 to 149 mm. The points on each of the altitude diagonals where the arterial saturation falls below 100% is indicated by a circle. Dotted lines from these points to the 75% saturation line indicate the corresponding venous points where the A-V differences are all 5 vols. % and the A-V CO_2 differences are 4 vols. %. These are the points where the venous point curves coincide with the 75% saturation line. The solid circles on the venous point curves represent the points which correspond to the average alveolar points observed at each of the altitudes indicated — the corresponding alveolar points are not indicated in order to avoid making the diagram too complicated. From this chart it can be concluded (1) that for a given cardiac output and A-V oxygen difference the maximum venous pO_2 can be obtained at an alveolar pCO_2 which is lower as the altitude increases and (2) that the venous pO_2 increases with increasing ventilation to a maximum value and then decreases slightly and (3) at altitudes where the inspired pO_2 is 100 mm or less, the venous pO_2 can be increased by an increase of ventilation beyond that which normally occurs. (Note that the venous point curves move further to the right below the solid circles except at $P_{Io_2} > 100$ mm.)

A slightly different representation of venous points and tissue points at a altitude is illustrated in Figure 13 where again six different 0.8 altitude diagonals have been drawn (for air breathing). Each of these terminates at the average observed alveolar point lying on the alveolar curve. From these alveolar points dotted lines are drawn to the venous points. Each of these dotted lines represents a blood R.Q. line with an A-V oxygen difference of 5 vols. % and an A-V CO_2 difference of 4 vols. %. These venous points correspond to the solid circles in Figure 9 and indicate the value of the venous gas tensions if there is no increase in the cardiac output above the normal ground level value. From the venous points so selected other dotted lines are drawn to the tissue curve which is supposed to be always 20 mm pO_2 lower than the venous value, this being the assumed minimum gradient which will suffice for adequate supply of oxygen to the tissues. The slope of the dotted lines representing this diffusion gradient is such that it would suffice for the diffusion of 5 vols. of oxygen to 4 vols. of CO_2 and it depends upon the molecular weight of the molecules and the solubilities of the gases in the tissues.

O_2 TRANSPORT & CARDIAC OUTPUT AT ALTITUDE

FIG. 11

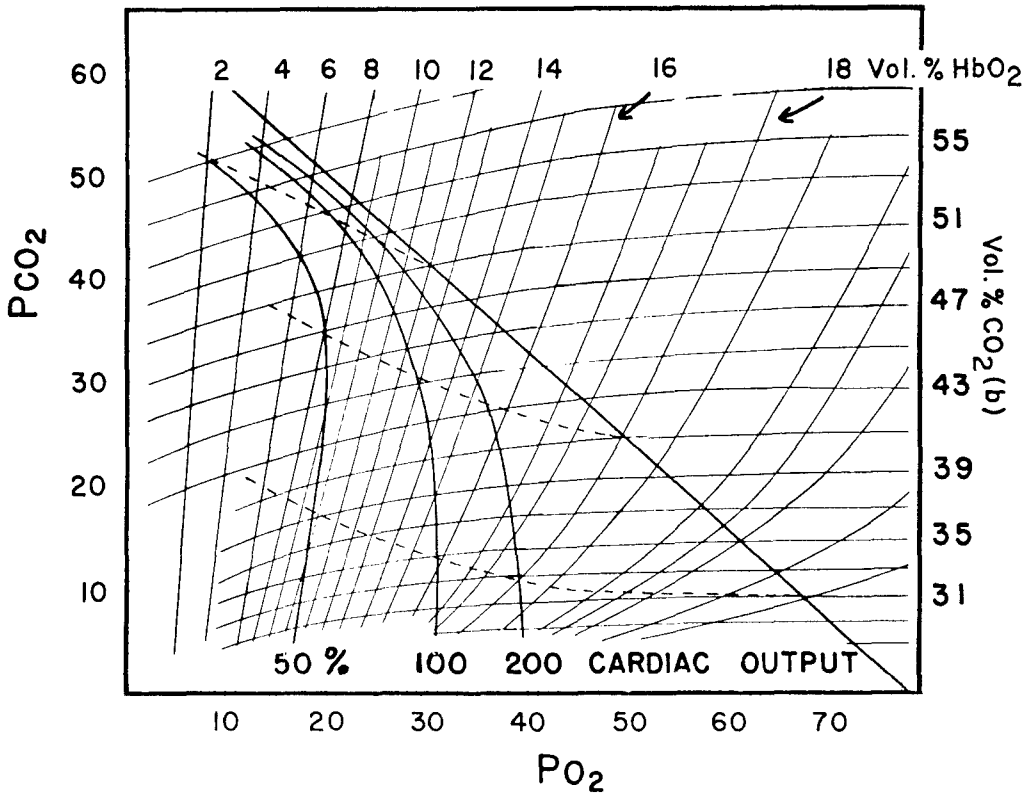


FIG. 12

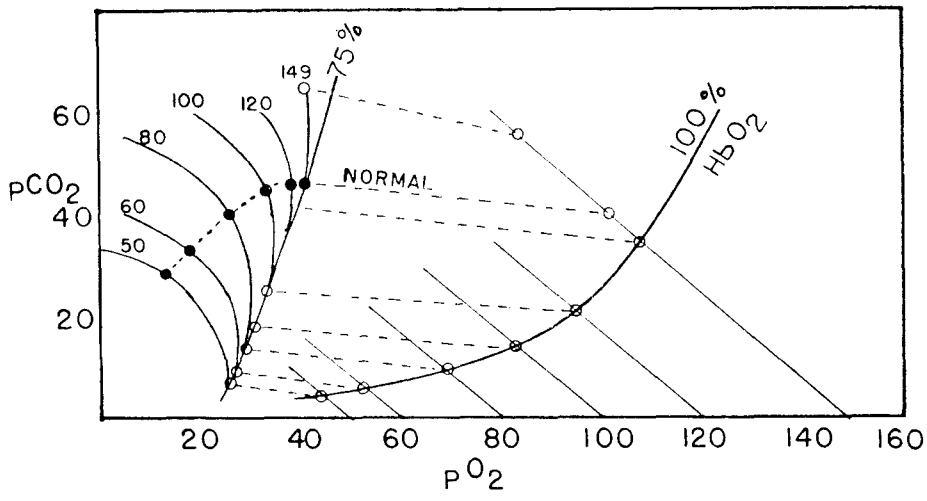
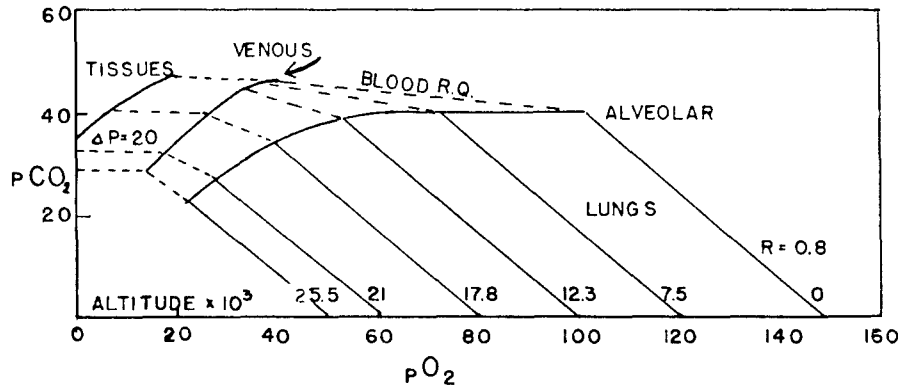


FIG. 13



On account of the high solubility of the CO_2 compared to that of oxygen the lines appear almost horizontal and all of the same slope. From these curves it can be seen that without increase in the cardiac output or excessive hyperventilation (i.e., greater than normal amount) the tissue pO_2 will fall to zero and symptoms of severe anoxia may be expected at altitudes higher than about 18,000 feet. If more than 20 mm oxygen gradient is required, anoxia would occur at still lower altitudes.

In conclusion these considerations show that so far as the transport of oxygen is concerned some additional hyperventilation at altitude is likely to be beneficial. It is not to be feared because of the falacious argument that the decrease in pCO_2 prevents the unloading of oxygen in the tissues. This does not prove by itself that a further lowering of the alveolar pCO_2 will improve the performance or the maintenance of consciousness at altitude. One of the compensations for low O_2 is an increase in cardiac output and cerebral flow and a lowered pCO_2 antagonizes this compensation. It is difficult to predict, therefore, with certainty the net effect of further increase in ventilation. Performance tests indicate, however, that anoxia and acapnia appear to be additive in their effects and that the optimum pCO_2 is ordinarily lower than the value attained by the average person at altitude. If, therefore, in a given individual at altitude it is found that the performance seems to improve with an increase in alveolar pCO_2 and a corresponding decrease in pO_2, it probably means that (1) his ventilation was previously increased above the optimum, or (2) that the cardiac output was low and was markedly improved by the increased carbon dioxide.

m.) Gas Transport at Ground Level Breathing Air

It is furthermore of interest to focus upon the gas transport at groundlevel, particularly where the ventilation or the cardiac output may become insufficient. This situation is met in first aid resuscitation, prolonged resuscitation in respirator cases and during anesthesia in the operating room. Figure 14 illustrates the O_2 and CO_2 transport when air is breathed at a barometric pressure of 760 mm Hg. The inspired oxygen is 149 mm. It is assumed that (1) the metabolic rate remains constant, (2) the R.Q. is .8, and (3) there is no alveolar-arterial gas gradient. The alveolar gas tensions must lie somewhere on the R = .8 line. A CO_2 of 35 mm has been arbitrarily chosen as a normal value produced by a normal alveolar ventilation designated as 100%. The gas tensions produced by 1/2 and 2 times the normal ventilation (controlled by a respirator or manually by an anesthetist) are indicated by solid squares. Other values will fall on the R line according to the alveolar ventilation equation. The alveolar values are here assumed to equal the arterial values. One may now, as outlined previously, plot all the possible venous gas tensions corresponding to the various arterial tensions existing on the R = .8 line. If we choose an A-V O_2 difference of 5 vols. % as a normal cardiac output, the mixed venous gas tensions will have values indicated by the dotted line designated as 100% cardiac output. The values for 1/2 and 2 times the normal cardiac output are likewise indicated.

Consideration of Figure 14 indicates that for a given cardiac output the highest venous oxygen tensions are found when the ventilation and alveolar pCO_2 are normal. Even hyperventilation like hypoventilation causes then a decrease in the venous oxygen tension.

Further it is evident that at groundlevel the venous pO_2 is largely controlled by the cardiac output and is relatively independent of the ventilation while the venous CO_2 tensions and pH are largely uninfluenced by the cardiac output but vary widely with changes in ventilation. Thus, at normal cardiac output change in ventilation from 50 to 200% decreases the venous pCO_2 56 mm but varies the venous pO_2 only $\pm$ 4 mm. Conversely, at normal ventilation rate a change in cardiac output from 50 to 200% increases the venous pO_2 27 mm and decreases the venous pCO_2 only 7 mm. At high altitudes when the inspired oxygen tension becomes a limiting factor, the changes in venous pO_2 due to ventilation become relatively more important. It is, of course, largely the shape of the oxygen dissociation curve which maintains the venous pO_2 relatively constant in spite of wide variations of ventilation. Thus, at normal cardiac output change in ventilation from 50 to 200% may change the arterial pO_2 60 mm, while the venous pO_2 changes only 6 mm. The CO_2 dissociation curve does not have this property.

These examples are obviously idealized conditions where the R.Q. remains the same. Actually with sudden depressions in ventilation rather marked changes occur which lower the R values and therefore shift the alveolar and arterial values to the left on this diagram. Such conditions are illustrated in the following chapter. Likewise, it might be pointed out that this analysis considers the whole body as a single capillary bed, whereas each organ has its own venous gas tensions and blood flows as illustrated in Figure 2, and the distribution of the blood between these different circulations may be altered so as to permit one organ, such as the brain, to prosper at the expense of other less essential tissues. All predictions based on this type of analysis are necessarily subject to modification by such special circumstance.

n.) Hypoventilation

Alveolar hypoventilation can be observed (1) by an increase in the external dead space, (2) by an increase in the resistance to breathing, and (3) by depression of the respiratory center (anesthesia). In either case hypoventilation involves a displacement of the alveolar or arterial point to a lower iso-ventilation line. Acute reduction in alveolar ventilation increases the pCO_2 and lowers the pO_2. Since the storage capacities in blood and tissues for the CO_2 are so much larger than that for O_2, the CO_2 tension will initially rise very much less than the O_2 will drop with a resultant large change in R until the steady state is reattained (10,11). Figure 15 illustrates the respiratory depressant action of a single standard dose, i.v., of sodium pentobarbital in a dog on the oxygen and CO_2 transport (12). The large circles indicate the alveolar, arterial and mixed venous blood gas tension before the anesthetic was given. The solid points indicate the changes during the following three hours at half hour intervals. Placing the R chart

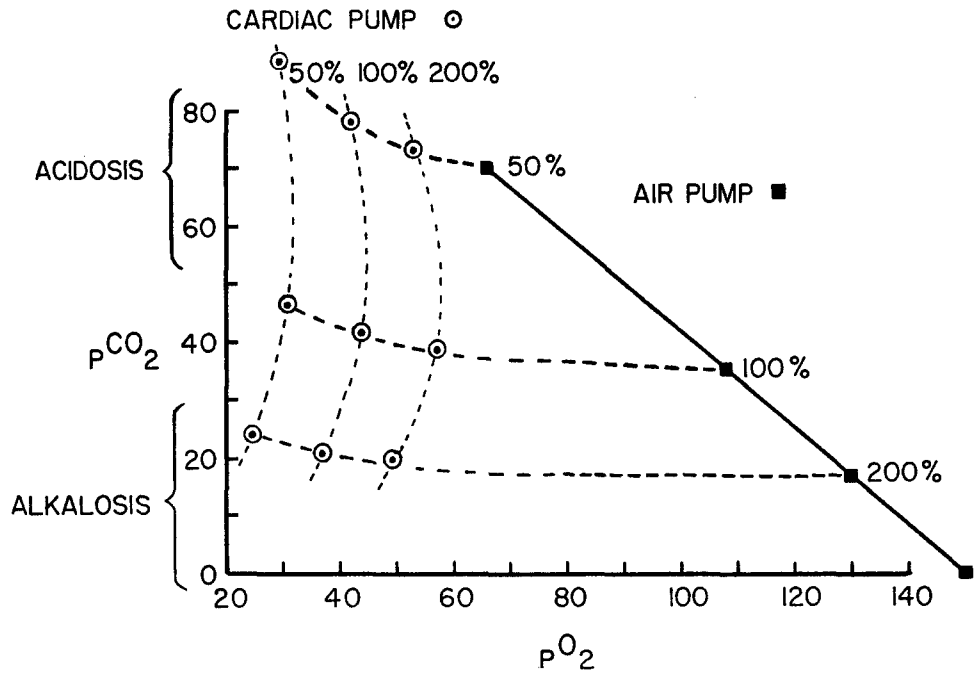


FIG. 14 GAS TRANSPORT AT GROUND LEVEL

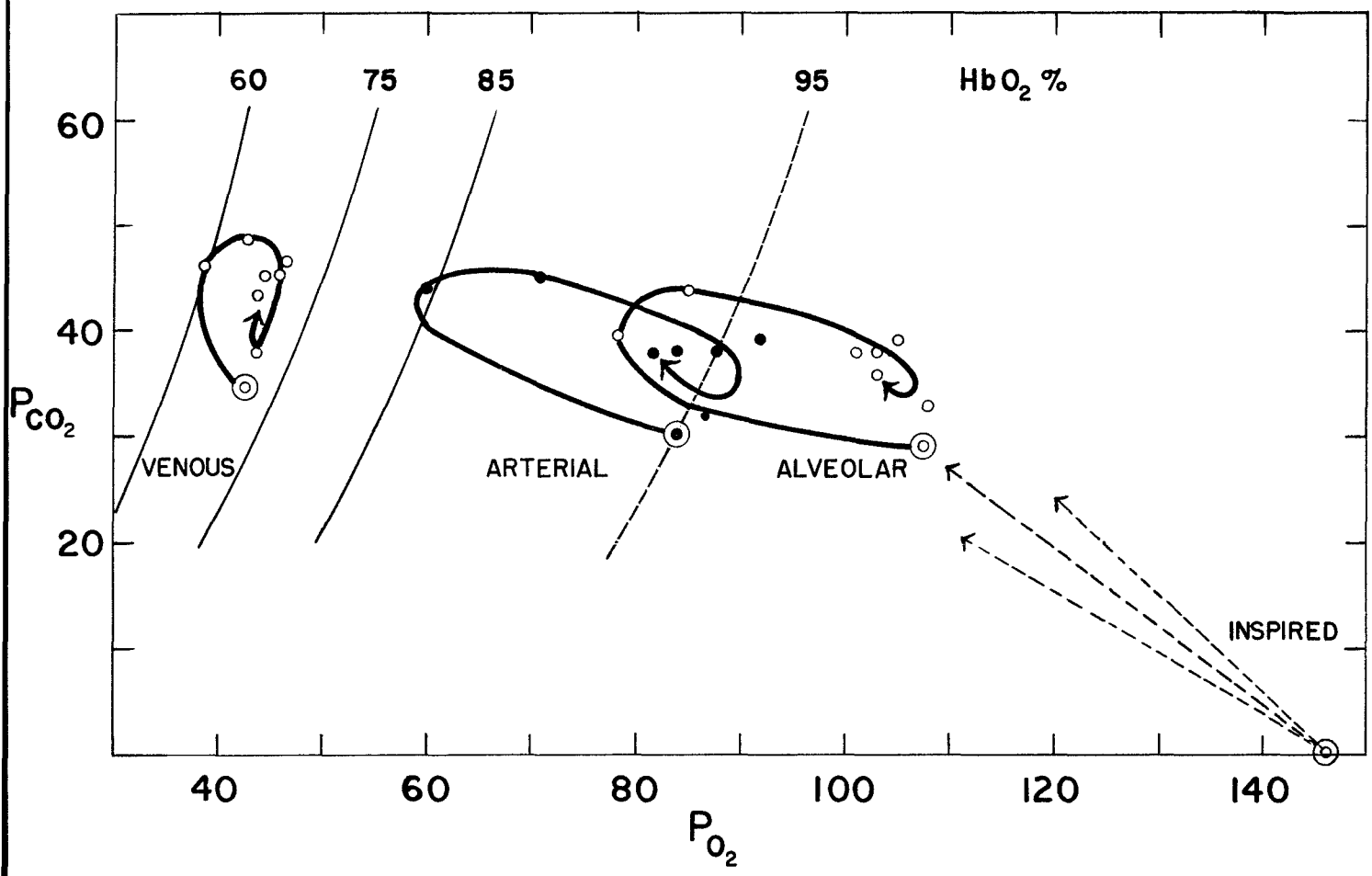


FIG. 15 GAS TRANSPORT DURING ANESTHESIA

on this diagram one will see the initial depression of R with anesthesia and finally a recovery with relatively high R values when the anesthetic wears off. The arterial tensions follow the alveolar values but with a large A-a O_2 gradient typical for dogs. The H_bO_2 saturation is reduced to 85% 30 minutes after the induction. It will be noted that the mixed venous tensions do not change very much over the whole period because the cardiac output remains unaltered and the slope of the oxygen dissociation curve is relatively steep in this region. In anesthesia as in hyperventilation (Figure 6) the alveolar point moves in clockwise direction along an alveolar air loop on the pCO_2-pO_2 diagram. The two loops however are located in opposite directions from the normal point.

o.) Breathing Air in Submarines or Other Closed Spaces

When a man is enclosed in an air-tight space, the oxygen percentage gradually diminishes as the carbon dioxide percentage rises until at a certain point death occurs. The changing composition of the air can be represented on a pCO_2-pO_2 diagram by a straight line comparable to an R.Q. diagonal. In this case when the space is strictly closed and the volume is large compared to the man the negative slope of the line is equal to the R.Q. of the man. If, on the other hand, the space is open to the outside through a pipe so that air is admitted or expelled to maintain constant pressure, then the equation must be modified slightly to cover this dilution. If further the volume becomes smaller and approaches the volume of the man, then the slope becomes less because of the CO_2 stored in the body. Quantitative aspects of this situation are illustrated in Figure 16. When there are 10,000 or more liters of volume surrounding the man then the pO_2 will fall from the initial 149 mm to 100 mm in 30 or more hours and the pCO_2 at an R.Q. of 0.8 will rise to 39 mm = 0.8 (149-100). If, however, there are only 100 liters of gas surrounding the man, the pO_2 will fall as before to 100 mm in only 0.3 hours at the same basal rate of oxygen consumption while the pCO_2 may rise only to 19.5 mm or only half as much as before. This will be the case if half of the CO_2 produced is stored in the tissues. If the body can store as much CO_2 with a rise of pCO_2 of 1 mm as would be required to raise the pCO_2 of 100 liters 1 mm, then we say that the man's "equivalent volume for CO_2" is 100 liters. This seems to be a reasonable value to assume for short term experiments. For more prolonged experiments a considerably larger value could be assumed because of the more slowly reacting storage capacity of the bones (13).

In a submerged submarine the habitability of the closed space can be improved by constant removal of CO_2 by soda lime or other absorbant and the simultaneous addition of oxygen. The effect of the continuous absorption of CO_2 at a given rate without the addition of oxygen can be illustrated quantitatively by Figure 17. Here the rate of removal of CO_2 is expressed as a clearance or the number of liters of air cleared of CO_2 per minute per man. At a clearance of 12 liters per minute per man and a given rate of gas exchange as indicated on the chart the pCO_2 will rise along the lower curve but will never become much greater than 15 mm. At about this level the rate of production of CO_2 becomes just equal

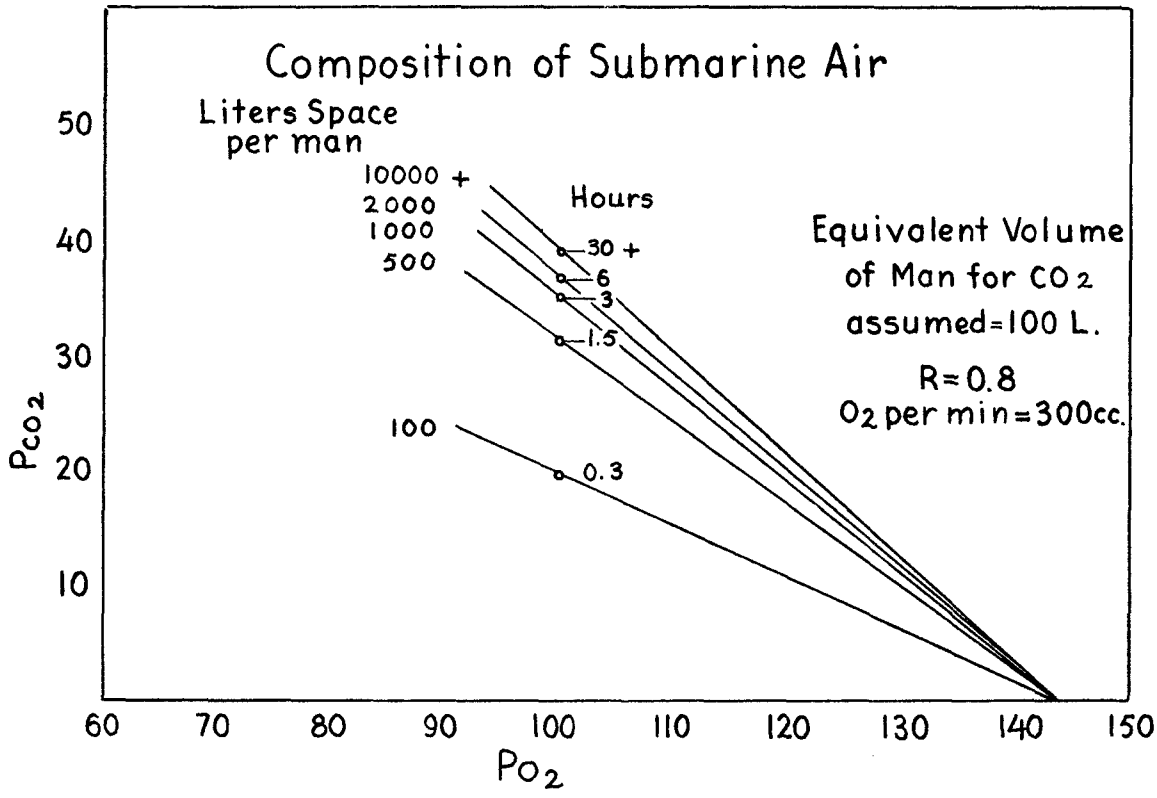

Composition of Submarine Air
Liters Space per man
10000 +
2000
1000
500
100
Hours
30 +
6
3
1.5
0.3
Equivalent Volume of Man for CO2 assumed=100 L.
R=0.8
O2 per min=300cc.
PCO2
PO2
50
40
30
20
10
60
70
80
90
100
110
120
130
140
150

FIG. 16

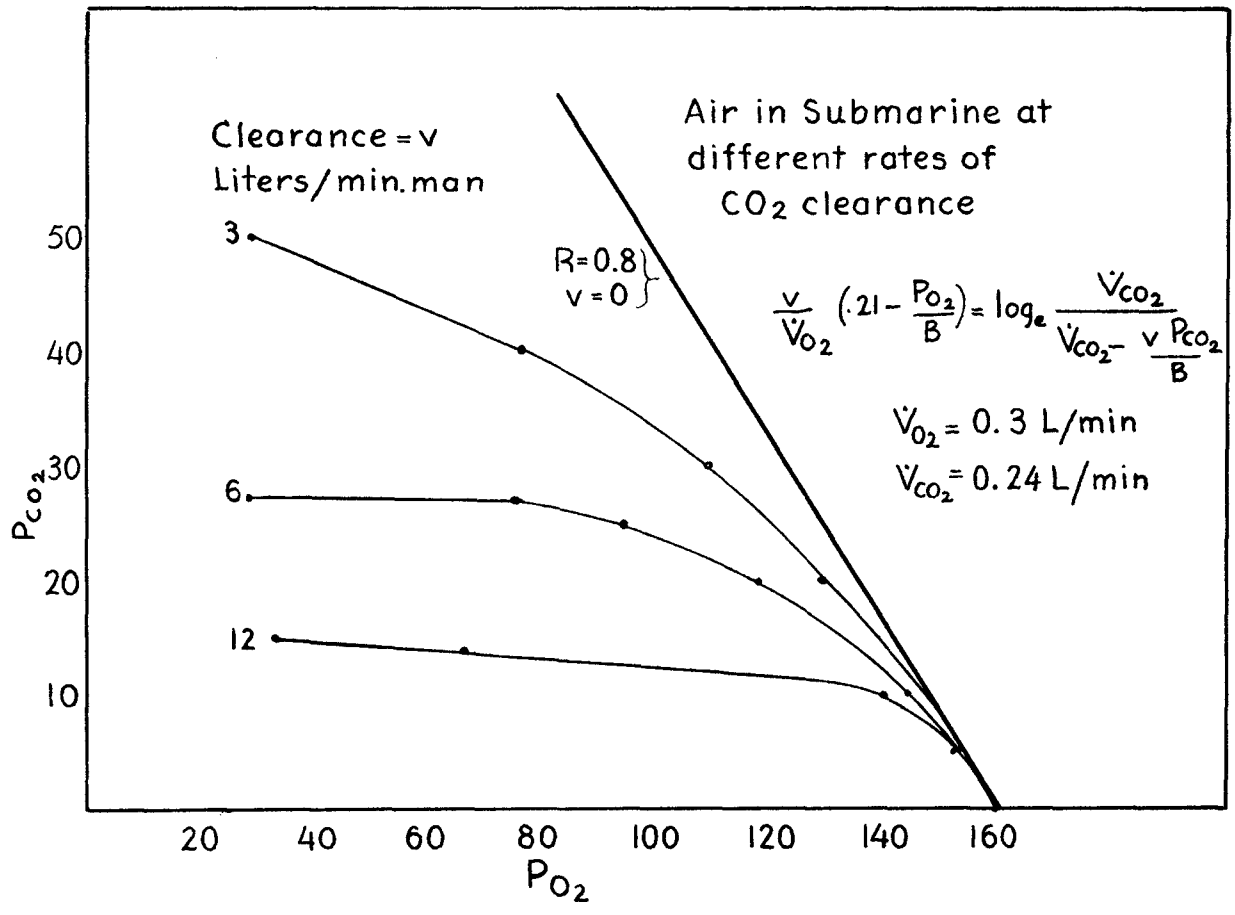

Clearance = v Liters/min.man
3
6
12
R=0.8
v=0
Air in Submarine at different rates of CO2 clearance
$\frac{v}{\dot{V}_{O_2}}\left(.21-\frac{P_{O_2}}{B}\right)=\log_e\frac{\dot{V}_{CO_2}}{\dot{V}_{CO_2}-\frac{v\,P_{CO_2}}{B}}$
$\dot{V}_{O_2}$ = 0.3 L/min
$\dot{V}_{CO_2}$ = 0.24 L/min
PCO2
PO2
50
40
30
20
10
20
40
60
80
100
120
140
160

FIG. 17

to the rate of production. The time required to reach this point depends upon the volume of the submarine and the number of men. Time values are not indicated on this chart and the equation of the curves given in Figure 11 does not contain time as one of the parameters. The shape of the curves, in other words, is independent of the time. It is only the rate of progress along the curve which depends upon time. At lower rates of clearance the pCO_2 rises higher. When the clearance is zero, the composition of the air changes according to the 0.8 R.Q. diagonal, as indicated previously.

A general summary of possible changes in the composition of the air in a submarine or other closed space is diagrammed in Figure 18. The 0.8 diagonal indicates the changing composition of the air as a result of respiration by the occupants of the ship. The arrow indicates the composition after 3.1 hours if there are 1000 liters per man and each man consumes 0.3 liters of oxygen per minute with an R.Q. of 0.8. There will then be 4% CO_2 in the air and the alveolar ventilation will be twice normal (VR = 2). With this point for inspired air the simultaneous composition of the alveolar air can also be indicated for this ventilation rate. It will lie on the dotted line of slightly steeper slope. On this line the pO_2 for a given pCO_2 is slightly greater because fresh air containing more oxygen is continuously added in amounts equal to the difference between the volume of oxygen consumed and the volume of CO_2 given off.

If now the submarine is continuously ventilated with fresh air at a rate of 6 liters per man per minute, then the composition of the air will be maintained indefinitely at the 4% CO_2 point. If this ventilation is further increased, the point representing the composition of the submarine air will move down along the 0.8 diagonal. If the ventilation is increased to 12 liters per man per minute, the composition of the submarine air will be stabilized at 2% CO_2. Every time the ventilation is doubled the CO_2 content of the air will be halved. At infinite ventilation rate the submarine air remains of the same composition as "pure" outdoor air. If at the 4% CO_2 point an effort is made to improve conditions by the addition of pure oxygen (without the escape of any contaminated air — i.e., at constant volume) the composition will change along a straight line drawn from the 4% point to the pure O_2 point at 0% CO_2 and 760 mm pO_2. Mixtures on this chart always lie along the straight line connecting the two subject points.

Again starting at the 4% CO_2 point the habitability of the submarine can be improved by mere absorption of CO_2. If this is done in a strictly closed vessel, the pO_2 will not change, but if fresh air is allowed to enter in proportion to the loss of CO_2 the composition changes along the arrow, as indicated, with a slight increase in the pO_2. With a decrease of pressure in the submarine (such as that produced by the activities of the snorchel pump when the inlet valve closes) the partial pressures of both CO_2 and O_2 decrease along a line drawn from the 4% point to the origin where partial pressures of both O_2 and CO_2 are zero.

Finally it would be possible to improve conditions in this submarine by pumping the air through a CO_2 absorber at a rate of say 12 liters per minute. In

this case the CO_2 would fall along the curved line stabilizing at 15 mm pCO_2 in 2 hours at the point where the CO_2 production just equals the CO_2 absorption. Unless oxygen is supplied, however, the pO_2 will continually fall until consciousness is lost. If this same clearance rate is maintained from the time breathing in this closed space is first begun, the composition changes along the curved dotted line as indicated previously in Figure 17.

If breathing in the closed space continues as indicated in Figure 16 without any ventilation or absorption of CO_2, the pO_2 may be expected to reach a dangerously low level of 50 mm when the pCO_2 reaches 75 mm or about 10% CO_2. Since 10% CO_2 produces narcosis by itself, it is difficult to say whether death will eventually result from hypercapnia or anoxia. Since these two hazards are additive rather than antagonistic in their effects, it is probable that both contribute to the eventually lethal effects.

p.) The N_2-CO_2 Diagram

In section (e) it was shown that the alveolar N_2 is a function not only of the exchange ratio but also of the concentration of CO_2 found in the alveolar gas. This relationship is given by Equation 5 and is plotted as the N_2-CO_2 diagram in Figure 19. The R lines radiate from the inspired nitrogen, P_{In_2}. The R = 1.0 line is perpendicular indicating that P_{In_2} remains unchanged in the alveolar air at any pCO_2. R values less than 1 will yield P_{N_2} values greater than P_{In_2}, (+), and vice versa (-). In addition the iso-ventilation lines are superimposed on Figure 19 similar to the ventilation lines of the transparent chart (Diagram IX). The alveolar ventilation equation (Equation 5) is expressed in terms of P_{N_2}, R and oxygen consumption.

Figure 19 shows the typical pathway observed when the alveolar ventilation is reduced by increasing the apparatus dead space by 1300 cc (upper curve) (10). The solid dot indicates the normal resting alveolar gas tension. The solid line shows the alveolar pathway during the next 10 minutes which returns to an R of .8 and a pCO_2 of 46. Upon recovery (dotted line) the retained CO_2 is blown off, R increases temporarily to 1.2 and finally returns to the original starting values. The maximal N_2 concentration difference between dead space breathing and recovery is 28 mm or approximately 4% N_2 in the alveolar air. Even greater differences in P_{An_2} can be observed with hyperventilation followed by recovery. The lower loop shows the effects of 10 minutes of controlled breathing at a rate of slightly over 6 L of alveolar ventilation per 100 cc of O_2 uptake (10). The R values initially approach 1.8 and the alveolar values parallel the iso-ventilation line slowly approaching the new steady state (R = .8) as the CO_2 reserves are blown off. With recovery (dotted lines) the ventilation is reduced followed by very low R values and tremendous rise in P_{An_2}.

The equations (No. 5) have been derived on the assumption that no N_2 is taken up or given off by the blood. On the other hand it is quite apparent from the pathways in Figure 8 that such a transfer of N_2 must take place and invalidate to

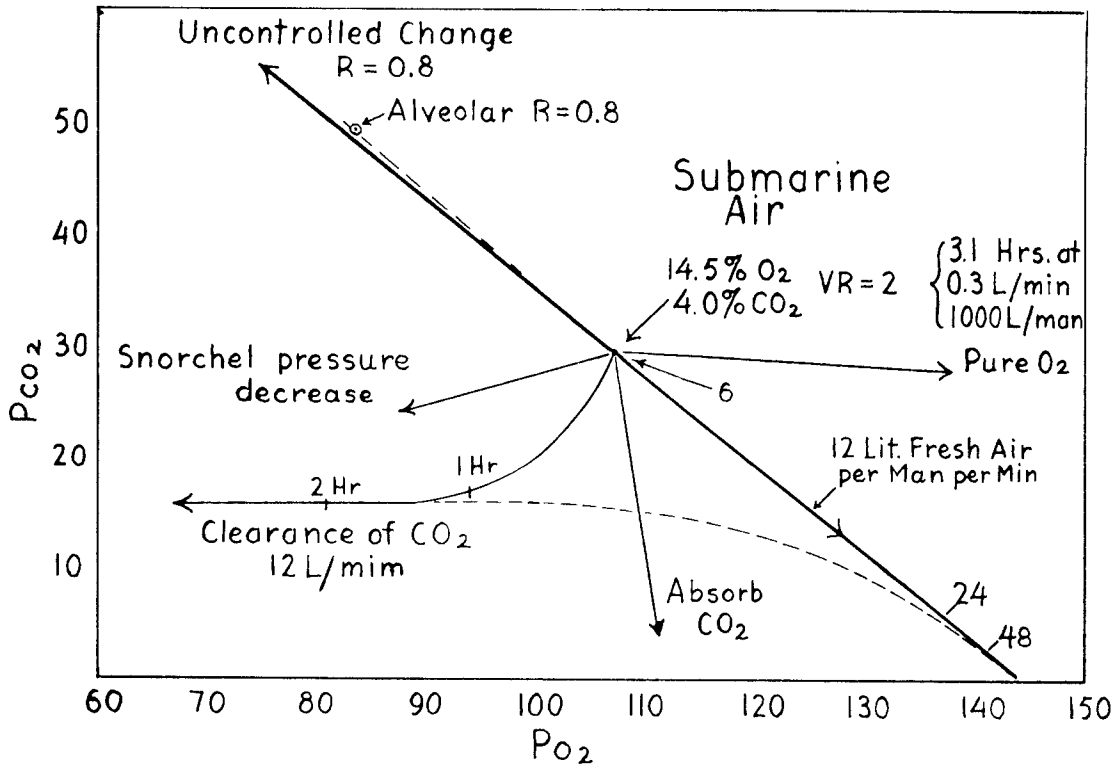


FIG. 18

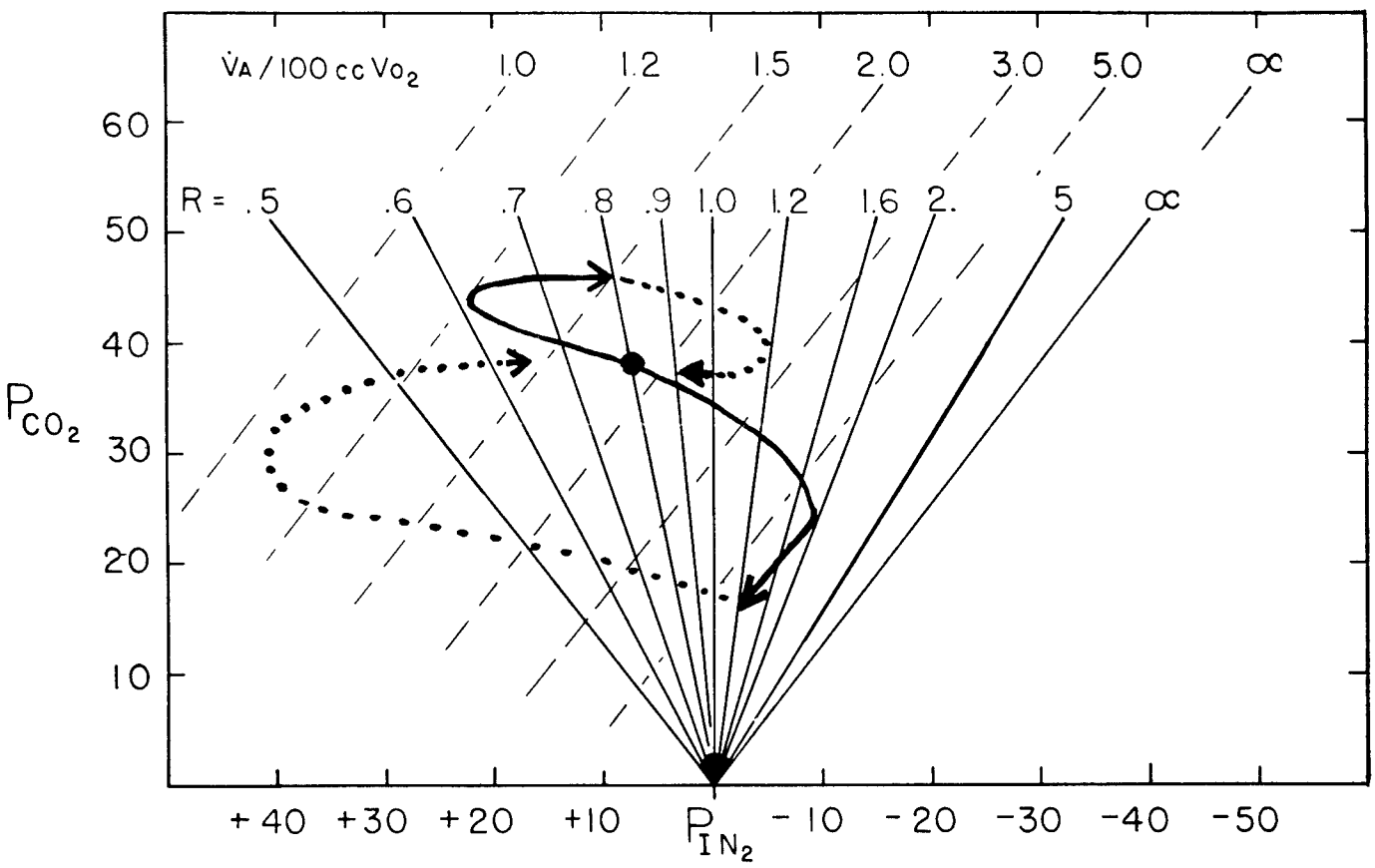


FIG. 19 THE $N_2 - CO_2$ DIAGRAM

some extent these equations during the unsteady state. However, the transfer is quite small and amounts to 1.0 cc N_2 per minute per 10 mm ΔP_{N_2} for a cardiac output of 6 liters. Therefore, this transfer is inconsequential in altering the pN_2 calculated for the static N_2 state.

q.) CO_2 Inhalation

So long as the inspired air contains no CO_2 and the subject breathes air the ventilation and R diagrams, Nos. VIII and IX, are applicable and no further calculations are necessary. When the O_2 fraction of the inspired air is not 0.209 and the CO_2 fraction is not zero, the R diagonals and the iso-ventilation lines must be calculated by Equations 6 and 7, respectively.

In one special case, however, it is possible to use the transparent charts for R.Q. and ventilation lines provided herewith. This is the case where the CO_2 is increased by merely adding CO_2 to air as if a CO_2 tank were leaking into the inspired air. In this case the decrease in pO_2 is always 0.209 of the increase in pCO_2 and the slopes of the R lines remain unchanged irrespective of the amount of CO_2 added. Likewise the iso-ventilation lines (for constant O_2 intake) remain identical. This being so Diagram IX can be used for ventilation and Diagram VIII can be used for R. For the latter the origin of the R diagonals on the transparency placed over the proper pCO_2 and pO_2 values of the inspired air and the correct R can then be determined for any alveolar point.

This is illustrated in Figure 20. The original gas mixture (air) is at point H, the alveolar point at A on the 0.8 R diagonal. When CO_2 is added to the inspired air, this mixture changes along the line HGFE. Four identical sets of R.Q. diagonals are drawn with origins at H, G, F, and E. These could be traced from the transparent Diagram VIII if it were placed successively at these four points.

On the same chart is drawn a set of iso-ventilation lines as in the transparent Diagram IX. In this special case these lines apply to all the inspired air points along the line HGFE and can therefore be used without change for all 4 sets of R diagonals. From these lines it appears that the ventilation is 1.73 lit/min for each 100 cc of O_2 consumed per minute if the alveolar point is at A and the inspired air at H and the R.Q. = 0.8. To maintain the same alveolar pCO_2 at point K in the second set of R.Q. diagonals with the inspired air point at G, the ventilation would have to be 3.46 lit/min or twice as large. Actually the respiratory centers cannot entirely compensate for the 2.8% of CO_2 which is inspired and the ventilation increases only to 3.1 lit/min with the alveolar point at B. This is calculated from Gray's equation $V_AR = 0.4\ pCO_2 - 15$ which gives the alveolar ventilation ratio V_AR in terms of the alveolar pCO_2. Similarly if the inspired air point is at E the ventilation would have to be infinite to keep the alveolar $pCO_2 = 40$. Actually the alveolar point will be at C on the observed line ABCD with a ventilation of about 8 lit/min per 100 cc O_2 consumed. Finally when the inspired $CO_2 = 8.4\%$ at E, the alveolar point after complete equilibration will be at D with 8.4% CO_2 and a ventilation rate of about 18 lit/min per 100 cc O_2 intake.

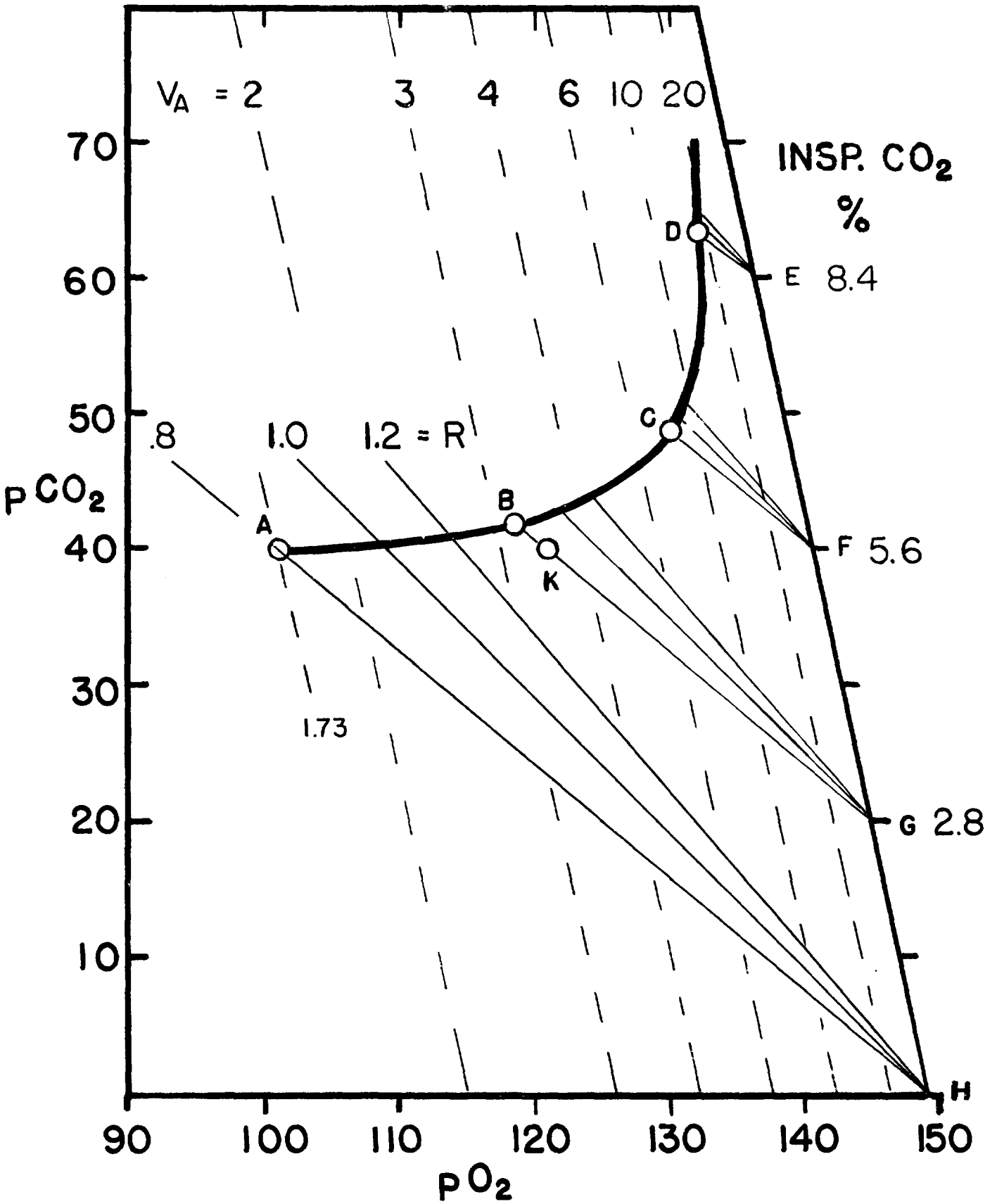


FIG. 20 CO_2 IN THE INSPIRED AIR

Thus as CO_2 slowly accumulates in the inspired air the alveolar point moves along this line ABCD, each point on that line (in the steady state) being on the 0.8 diagonal of a set of R.Q. diagonals which is to be thought of as moving up the inspired air line HGFE. Further as the inspired CO_2 increases, the ventilation increases and the alveolar and inspired air points move closer together.

Similarly, of course, any other set of R.Q. diagonals for an inspired oxygen fraction different from that in air could be used along the corresponding HGFE line for CO_2 dilution. If, however, CO_2 is added to air in exchange for the O_2 or for the N_2, or in any way which does not dilute both N_2 and O_2 equally, a new set of R.Q. diagonals will have to be calculated by Equation 6 and a new set of iso-ventilation lines by Equation 7.

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