

MATERNAL-FETAL BLOOD GAS TRANSPORT

by

Miles John Edwards, B.A.


A THESIS

Presented to the Department of Physiology
and the Graduate Division
of the University of Oregon Medical School
in partial fulfillment
of the requirements for the degree of
Master of Science

June 1956

APPROVED:

...  ...
(Professor in Charge of Thesis)

...  ...
(Chairman, Graduate Council)

Acknowledgement

The author is indebted to Dr. B. B. Ross for advice and assistance, to the nursing staff in the obstetrical unit of Emanuel Hospital for their cooperation in collection of blood samples, and to Mrs. Duane Denney for typing this manuscript.

TABLE OF CONTENTS

INTRODUCTION	1
REVIEW OF THE LITERATURE	2
METHOD	17
RESULTS	26
DISCUSSION AND CONCLUSIONS	77
SUMMARY.	81

LIST OF TABLES

		Page
Table I.	Effect of Time of Gestation on Human Fetal Blood Gas Values	9
Table II.	Fetal Blood Gas Contents in Human Umbilical Vessels	9
Table III.	Human Maternal Blood Gas Contents in Uterine Vessels	12
Table IV.	Scholander Analyses on Gas Mixtures . . .	27
Table V.	Blood Gas Values of First Fetal Group. .	29-34
Table VI.	Blood Gas Contents of First Fetal Group with Carbon Dioxide Contents Related to A Reference Value	36-39
Table VII.	Blood Gas Contents of First Fetal Group, Not Corrected for Acid Produced During Tonometry	40
Table VIII.	Corrected Blood Gas Contents and Partial Pressure for First Group of Fetal Blood Determinations	42
Table IX.	Blood Gas Values on Second Fetal Group .	46-49
Table X.	Final Values Second Group Fetal Blood . .	50
Table XI.	Blood Gas Values for Maternal Blood . .	64-66
Table XII.	Final Maternal Blood Gas Values	67-68
Table XIII.	Serum pH Values Determined from Carbon Dioxide Contents and Partial Pressures on Maternal Blood	72

LIST OF FIGURES

FIGURE 1	Tonometer system utilized for blood gas equilibration	18
FIGURE 2	Demonstration of diminishing carbon dioxide combining powers with time and temperature	23
FIGURE 3	Demonstration of the need for keeping blood cold	24
FIGURE 4	Oxygen and carbon dioxide dissociation curves established for the first fetal group of blood determinations	44
FIGURE 5	Graphical correction of the carbon dioxide contents obtained in the second group of fetal blood determinations . . .	52
FIGURE 6	The carbon dioxide content decrease in volumes per cent for each per cent oxygen saturation increase at constant partial pressure of carbon dioxide plotted against carbon dioxide content. .	55
FIGURE 7	Method by which the carbon dioxide and oxygen contents are predicted for the population of the first group of fetal blood determinations from those contents actually obtained from the second group of fetal blood determinations . . .	57
FIGURE 8	Normal adult nomogram	58
FIGURE 9	Graphical estimation of the intervening carbon dioxide contents and partial pressures in fetal blood	60
FIGURE 10	Graphical estimation of the intervening oxygen contents and partial pressures in fetal blood	61
FIGURE 11	Completed nomogram for fetal blood . . .	62

FIGURE 12	Means of estimating the carbon dioxide dissociation curves knowing one carbon dioxide content at one carbon dioxide partial pressure and the oxygen capacity	70
FIGURE 13	Completed nomogram for maternal blood. . .	74
FIGURE 14	Fetal blood dissociation curves on O_2 - CO_2 diagram	75
FIGURE 15	Maternal blood dissociation curves on O_2 - CO_2 diagram	76

INTRODUCTION

The mammalian fetus functions as a parasite, deriving all its needs from its mother, the host. The respiratory function of the fetus is dependent upon the maternal pulmonary function, the qualities and circulation of both the maternal blood stream and the fetal blood stream, and the placenta, where transfer of the respiratory gases occurs between the two blood streams. The entire physiological state, including respiration, of the fetus has long defied the precise study given to other phases of physiology. The respiratory physiology of the pregnant mammal is not well understood.

In this study, an attempt has been made to measure carefully the relationship between the contents and partial pressures of oxygen and carbon dioxide in blood samples taken from both the mother and the fetus at term. These dissociation curves are plotted on the recently developed O_2 - CO_2 (1) diagram.

REVIEW OF THE LITERATURE

Past work dealing with the problems of fetal respiration has, by and large, been inadequate and frequently contradictory. This has been largely due to the inaccessibility of the intra-uterine organ and the difficulty in maintaining it in its normal physiological state during the manipulations necessary for study. For this review, the published work has been subdivided into the four groups listed below.

- (1) Qualities of the fetal and maternal blood dealing with oxygen and carbon dioxide transport.
- (2) Oxygen capacities and oxygen and carbon dioxide contents found in maternal and fetal vessels.
- (3) The placenta.
- (4) Fetal and maternal blood flow.

Qualities of the Fetal and Maternal Blood Dealing with Oxygen and Carbon Dioxide Transport. It has long been established that there are qualitative differences between the hemoglobin produced by the fetus (fetal hemoglobin) and that produced after birth (commonly called adult hemoglobin) (2-8). This is true for all mammals studied. The difference in hemoglobin has even been detected in non-mammalian species, such as the frog and chicken (9,10). In mammals, differences have been observed in crystal structure (4,6), solubility (4-6), resistance to alkali denaturation (4),

and affinity for oxygen (3,7,8). In all mammalian fetuses except man, fetal hemoglobin will associate with a greater amount of oxygen, at like partial pressures of oxygen, than will the adult form, although the two hemoglobins have identical oxygen capacities. On the conventional oxygen dissociation curve, these fetal hemoglobin curves lie to the left (and/or above) of that of the adult. In humans, however, the fetal hemoglobin curve lies to the right of that of the adult, indicating less affinity for oxygen at the same partial pressure (3,4,7).

One group of investigators (7) reported that the human fetal and maternal oxygen dissociation curves became identical when their ionic environments were equalized by dialysis of hemolyzed blood. Admitting that the two were chemically different, they argued that the differences in oxygen affinity were entirely attributable to the ionic environment of the hemoglobin. The conclusion of these investigators has not been generally accepted.

For all mammals, including man, the oxygen dissociation curves of fetal erythrocytes lie to the left of those of the adult (3,6,11-13). There is an influence of the stroma or membrane of the red blood cell that markedly alters the affinity of oxygen by hemoglobin (3) but does not alter the oxygen capacity. Both fetal and adult erythrocytes diminish the oxygen uptake of their contained hemoglobins, but this effect is much more pronounced in the adult cells. Regardless of the oxygen affinities of liberated

hemoglobin, the erythrocytes of the fetus have a greater affinity for oxygen than do those of the adult, at like partial pressures. Again, the oxygen capacities are identical.

In addition to the difference in displacement of the fetal and maternal oxygen dissociation curves, there is a difference in their curvature (11-14). The fetal curve is steeper, having a greater affinity for oxygen between 25 and 65 mm. Hg partial pressure of oxygen than does the adult blood (13). Above 65 mm. Hg and below 25 mm. Hg partial pressure of oxygen, the fetal blood has decreased affinity for oxygen, compared to adult blood (13). This, it is argued, enables fetal blood to take up oxygen more readily at the placenta where the partial pressures of oxygen are between 25 and 65 mm. Hg (13). The decreased affinity of fetal blood, below a partial pressure of oxygen of 25 mm. Hg, is believed to allow the blood to give up oxygen more readily at tissue partial pressures of oxygen. In fetal sheep, the oxygen dissociation curve becomes more similar to that of adult blood in both oxygen affinity and curvature, as pregnancy progresses (11).

Increased hydrogen ion concentration, influenced by both carbon dioxide and non-volatile acids, decreases hemoglobin's affinity for oxygen (2,11-16). Much has been written of the "acidosis" of pregnancy (2,11-14,17,18). Direct pH measurements on maternal blood have not shown this acidosis (19,20). Kaiser (21) noted a pH of 7.38 in

maternal venous blood. In blood-gas equilibration studies, the oxygen dissociation curves of maternal blood were shifted to the right, suggesting increased hydrogen ion concentration. These, however, were performed under conditions of constant partial pressures of carbon dioxide (2,11-14). By the constant partial pressure of carbon dioxide, any in vivo respiratory compensation of acidosis would be obscured. Therefore, the displacement of the maternal curve to the right does not alone indicate maternal acidosis. Non-volatile cations must, however, be increased. Equilibration studies done at constant pH showed no displacement of the maternal oxygen dissociation curve (12).

Increasing the non-volatile acid content in any blood causes a lowering of the carbon dioxide dissociation curves, with decreasing affinity of blood for carbon dioxide. Such decreased carbon dioxide affinity has been noted in the bloods of both the mother and the fetus, in man and other animals (13,14,18-20,22). For the goat, the carbon dioxide curves are depressed to a greater extent in the maternal blood than in the fetal blood (2,18). In the human, however, the carbon dioxide affinity is less in the fetal blood than in that of the mother (13,14). Both are equally depressed in the sheep (23).

Most studies suggest that the "non-volatile" component of the blood consists of lactic and pyruvic acids in the fetus (24-27). One report lists an average maternal

2. 10. 1945
 buffering ability
 in mat. blood due to
 H₂CO₃

blood lactate content greater than that in fetal blood (27). Ketone bodies have not been found in the blood of newborns (26). Others found an increased chloride ion concentration in the blood of the newborn (28). Low serum sodium concentrations were found in two premature infants (14). Whatever the cause, both the fetus and the mother have decreased carbon dioxide combining powers.

In humans, the blood pH of the mother is normal or slightly lowered (19-21), the fetal blood pH being more markedly lowered (21). The mother, then, is either in a state of ^{partially} compensated metabolic acidosis or ^{over-} compensated respiratory alkalosis. She, therefore, must be hyperventilating, either as a compensatory or primary phenomenon. Alveolar partial pressures of carbon dioxide were found to drop early in pregnancy from the non-pregnant adult "normal" of about 40 mm. Hg (19,20). At six months gestation, the alveolar partial pressure of carbon dioxide stabilized at 32 mm. Hg (20). There it remained until labor when it transiently decreased still further (19). Within a few days after delivery, the alveolar partial pressure of carbon dioxide returned to 40 mm. Hg (19-20). Alkali reserve (carbon dioxide combining power) determinations showed changes occurring in a corresponding fashion (19-20). The serum pH did not change (19-20). An interesting possibility has been suggested as an explanation of the mechanism responsible for these changes, though no proof is given (20). This postulates a hormonal cause of an initial hyper-ventilation resulting in respiratory ^{alkalosis} ~~acidosis~~ (20). The

evidence in support of the postulate rests in two observations. First, alveolar partial pressure of carbon dioxide levels undergo cyclic changes during the menstrual cycle, being lowest during the luteal phase, when progesterone is secreted in greatest amounts. Secondly, this must be a hormonal effect because the drop in alveolar partial pressure of carbon dioxide and alkali reserve occurs early in pregnancy (first few weeks) when the fetal mass is negligible. This is a striking challenge to the notion that acidosis is primarily responsible. The issue remains unsettled.

Oxygen Capacities and Oxygen and Carbon Dioxide Contents Found in Maternal and Fetal Blood Vessels. The actual concentrations of the respiratory gases found in maternal and fetal blood streams show great variation and proper evaluation of the published data is very difficult. Proper technique and careful handling of both the tissues and blood vessels concerned is of paramount importance. Any undue tension created by opening the uterus at caesarean section tends to embarrass uterine blood flow, resulting in low oxygen and high carbon dioxide contents in the blood of both the fetal umbilical artery and vein (29). In addition, even the slightest trauma to the fetal umbilical artery may result in vasospasm, causing diminished fetal placental blood flow. This would result in increasing the arterio-venous difference of the blood in the umbilical vessels. The umbilical vein blood (physiologically arterial) would

have an increased oxygen and decreased carbon dioxide content as compared to the normal status. The converse would apply to fetal umbilical artery blood, the oxygen content being decreased and the carbon dioxide content being increased. This would artificially alter the important maternal-fetal perfusion-perfusion relationship.

The usual means of determining blood oxygen and carbon dioxide contents has been by the VanSlyke method (30). The contents are usually expressed in volumes per cent. Direct measurement of the partial pressures of these gases in blood is much more difficult and unreliable. The bubble-equilibrium technique of Riley (31) has been awkward and inexact. However, improvements are being made. In the past, partial pressures have been indirectly determined from blood gas contents by use of dissociation curves.

Studies on both human (32,33) and sheep (29) fetuses indicate the fetal umbilical vein oxygen contents remain generally constant through the last third of gestation. The oxygen capacities, however, rise markedly, with the result that a corresponding drop in oxygen percentage saturation occurs (Table I). It is therefore argued that oxygen percentage saturations are a better index of the availability of oxygen to the fetus than are oxygen contents (29,32,33). The increasing hemoglobin concentration, or increased oxygen capacity, manages to compensate for the presumed hypoxia. This is considered to be analogous to compensatory polycythemias found in adults in hypoxic states.

Table I

Effect of Time of Gestation
on Human Fetal Blood Gas Values

Week of Gestation	22	29-30	39-40 (term)	⁴³ (post-mature)
Oxygen capacity (vols. %)	below 20	19.2-20.4	19.8-22.2	22.2-26.8
Oxygen content (vols. %)	12.5-14.0	12.5-14.0	10.8-12.7	7.8-9.7
Oxyhemoglobin (per cent saturation)	75%	70%	slightly below 60%	30% or less

Table II

Fetal Blood Gas Contents
in Human Umbilical Vessels

	Umbilical Artery	Umbilical Vein
Carbon Dioxide (vols. %)	46.1	41.1
Oxygen (vols. %)	6.6	13.1
Oxyhemoglobin (per cent saturation)	31.5	63.2
Oxygen Capacity (vols. %)	--21.3	

It is felt that the fetus outgrows its placenta late in pregnancy (29), with fetal post-maturity possibly leading to damaging degrees of anoxia (29,32,33).

Blood gas contents have been determined at caesarean section under spinal or local anesthesia (29,32-40) or at vaginal delivery following labor (33-35,38,40-42). Blood gas contents determined at caesarean section are preferable to those done at vaginal delivery in two respects. First, it is possible to obtain blood samples from the maternal uterine artery and vein. Secondly, there is no preceding labor, a possible source of error.

The effect of labor on fetal blood oxygenation is uncertain. Haselhorst and Stromberger (38-40) noted much higher fetal blood oxygen saturations following labor, either at caesarean section or vaginal delivery, than were measured at caesarean section preceding labor. On this basis, it was argued that labor contractions improved maternal circulation in the uterus. Walker (33) found the fetal blood oxygen saturations unaffected by labor. In complete contrast to these results, Eastman (34) noted that the oxygen content of fetal blood was diminished about three volumes per cent by labor. This was attributed to the impairment of maternal uterine circulation by the labor contractions. The issue, therefore, remains unsettled.

Unfortunately, most investigators have ignored blood carbon dioxide contents, being preoccupied with oxygen. This makes it difficult to fully understand several

important questions, including fetal respiratory quotients, acid-base status, and the general respiratory picture of which carbon dioxide transport is an essential part. In Table II are listed the results of Clemetson (41), which fortunately include carbon dioxide contents. His oxygen contents lie within the range established by others (32-34, 36,39,40,42). Unfortunately, because these were taken at vaginal delivery (41), simultaneous maternal uterine blood gas contents are not available.

The blood of pregnant women undergoes a decrease in oxygen capacity or hemoglobin concentration (34,36,39), relative to that of the non-pregnant adult. Eastman (34) reported a mean oxygen capacity (15 pregnant women at term) of 15.4 volumes per cent, with 18.9 volumes per cent being quoted as normal for non-pregnant women. Other investigators (36,39) report similar results, which are included in Table III. An iron deficiency is believed to cause the anemia (43).

The oxygen and carbon dioxide contents of maternal arterial and uterine venous blood samples have been determined at caesarean section (34,36,37,39) (Table III). It can be appreciated that precise knowledge of the maternal uterine blood gas contents has not yet been obtained.

The Placenta. Actual exchange of respiratory gases between the blood streams of the mother and the fetus occurs at the placenta (44). The two circulations are separated by a thin barrier of from one to six cell layers depending on the species. The extent to which this

Table III

Human Maternal Blood Gas Contents
in Uterine Vessels

	Eastman	Haselhorst and Stromberger	Dieckman and Kramer
Oxygen Capacity (vols. %)	15.4	15.82	13.91
Arterial Oxygen content (vols. %)	14.7	14.22	
Oxyhemoglobin (per cent saturation)	95.0	89.95	
Arterial Carbon Dioxide (vols. %)		43.81	
Venous Oxygen content (vols. %)	11.0	9.04	9.00
Oxyhemoglobin (per cent saturation)	71.3	57.25	64.9
Venous Carbon Dioxide (vols. %)	43.3	50.42	41.42

separation impedes transfer of respiratory gases is unknown. The extent of obstruction of the transfer of respiratory gases is a factor in determining the partial pressure gradients of carbon dioxide and oxygen necessary to effect adequate transfer. Some investigators have obtained blood samples from the maternal and fetal afferent and efferent vessels, analyzed them for oxygen and carbon dioxide contents, and calculated the partial pressures of oxygen and carbon dioxide from their contents in the blood samples on dissociation curves. These, however, are only analyses of blood gas contents of the afferent and efferent vessels to each side of the placental barrier, not partial pressures at the barrier itself.

In the placenta of all mammals, the fetal blood lies within the endothelium of blood vessels. In some mammals, the maternal placental blood also lies within blood vessels. It has been demonstrated that the blood flows within the maternal and fetal vessels occur in an opposite direction (45). Opposite flow is an advantage to the fetus whose blood equilibrates with incoming oxygenated maternal arterial blood just prior to its return to the fetus by the umbilical vein (45). In the other mammals, including man, the maternal placental blood lies within sinuses, into which the fetal villi protrude. The velocity of the maternal blood flow is presumably low and a more stagnant situation may therefore be considered to exist on the maternal side of the placenta. It has been argued that the maternal blood

has directional flow, even within the sinuses, opposite to that of the fetal blood (46). This concept of directional flow in the maternal blood sinuses has little evidence to support it.

The blood gas composition of the sinus maternal blood equilibrating with the blood of the fetus is intermediate between that of the afferent artery and the efferent vein. The relative rates of blood flow in the maternal and fetal placental circulations should influence the compositions of the equilibrating blood. A higher maternal-fetal perfusion-perfusion ratio would be expected to shift the blood gas composition of the equilibrating maternal blood towards that of the incoming arterial blood. This would elevate the blood oxygen and lower the blood carbon dioxide contents. Conversely, a lower maternal-fetal perfusion-perfusion ratio would cause a lowering of blood oxygen content and elevation of blood carbon dioxide content. A comparison can be made with the ventilation-perfusion concept of pulmonary respiration (1).

Fetal and Maternal Blood Flow. Until recently, no reliable estimates of uterine or umbilical blood flow have been made. Recently, however, the nitrous oxide uptake technique has been developed and adapted to the studies of uterine blood flow (47,48). This technique is based on two principles. First, the solubility of nitrous oxide is the same in the uterine tissues (fetus, placenta, amniotic fluid, and myometrium) as it is in the blood plasma.

Second, the Fick principle states that the uptake of a given substance is equal to the blood flow multiplied by its arterio-venous difference. By use of an equation involving calculus, uterine blood flow is calculated (47). These studies were made at caesarean section with hysterectomy, with the mother breathing nitrous oxide (49,50). Serial blood samples were taken from a uterine vein and a peripheral artery and analyzed for oxygen, carbon dioxide, and nitrous oxide. In eleven initial caesarean sections, the mean uterine blood flow was about 750 cc. per minute (49). In a later study at thirteen caesarean sections, the mean uterine blood flow was found to be about 518 cc. per minute (50). The arterio-venous blood oxygen differences were 4.7 volumes per cent for the maternal uterine arterial and venous blood, and 4.5 volumes per cent for the blood of the fetal umbilical vessels (50). These investigators assumed for their calculations that the oxygen uptakes of the myometrium, placenta, and fetus occurred in proportion to their relative weights (50). Comparing the arterio-venous differences and making the assumption that oxygen uptakes by the uterine contents were equal, these investigators reasoned that the maternal and fetal blood flows to the placenta were roughly of the same magnitude.

Unfortunately, the review of the literature has not contributed appreciably to this study concerning maternal pulmonary function and the maternal-fetal perfusion-perfusion principle. The blood oxygen and carbon dioxide dissociation

curves are each determined separately, with the partial pressure of the other respiratory gas held constant. No blood respiratory gas dissociation curve allowed the partial pressures of the two respiratory gases to vary simultaneously. Generally speaking, the literature review is disconnected and few conclusions can be made with certainty.

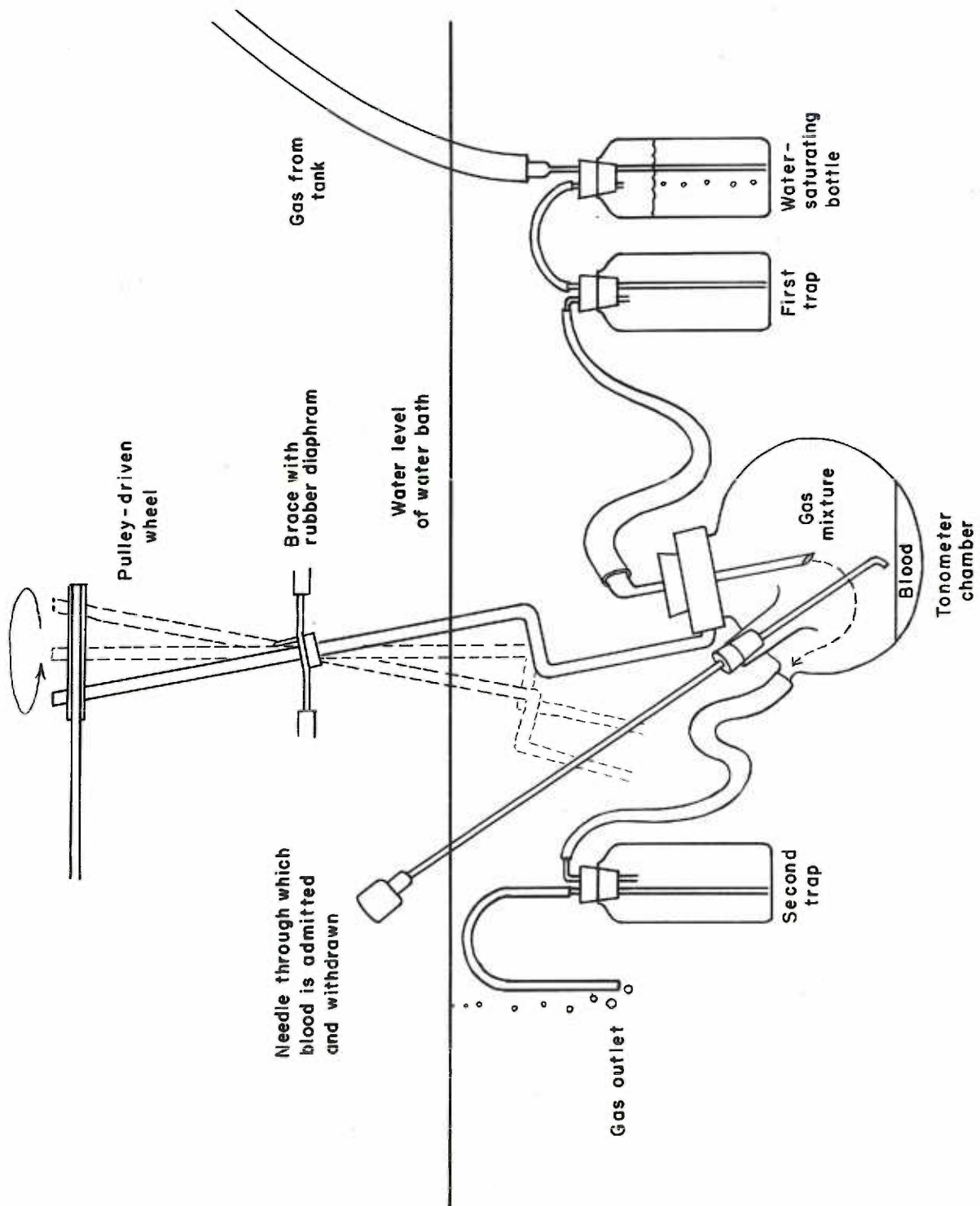
METHOD

Fetal and maternal blood samples were analyzed for oxygen and carbon dioxide contents following equilibration with gas mixtures having various partial pressures of oxygen and carbon dioxide.

Tonometry. Tonometry is the process by which blood is exposed to a gas of known composition until the blood and gas phases are brought to equilibrium. The tonometer system used for this study was designed for operation (51) entirely below the surface of a constant temperature water bath, maintained at 37° C. by thermostatic control. The gas mixtures, containing oxygen and carbon dioxide in nitrogen, were stored in gas cylinders. A connection from the outlet of a gas cylinder was attached to the gas inlet of the tonometer system (figure 1). On entering the tonometer system, the gas was bubbled through a bottle containing water and glass wool, the gas thereby being saturated with water vapor. The gas then passed to a second bottle which served as a trap to prevent water droplets from reaching the tonometer. From the trap, the gas passed to the tonometer chamber itself, where the blood and gas equilibration occurred. To speed equilibration, the contents were agitated by rotating the chamber through an arc of $2 \frac{3}{4}$ inches at a rate of 150 revolutions per minute. Blood was admitted and removed through a long needle, curved near the lower end to enable twisting it in and out of the blood

Figure 1

Tonometer system utilized
for blood gas equilibration.



from above. The upper end of the needle had a syringe adapter extending above the surface of the water bath. This was capped during equilibration. From the tonometer chamber, the gas passed to another trap bottle, from which it was expelled into the water bath at a set recorded depth. The depth of the gas outlet in the water bath created a pressure in the tonometer system greater than atmospheric pressure. The gas was allowed to flow through the system at a rate producing three to six bubbles per second at the outlet.

The gas mixture was allowed to flow through the tonometer for fifteen to twenty minutes. Then 3 cc. of blood was admitted to the chamber. All blood was expelled from the needle into the tonometer with a small syringe filled with air. The needle was then flushed with the gas in the chamber (seen by an absence of bubbling at the outlet), capped, the time recorded, and the agitation begun. After exactly twenty minutes, the blood was withdrawn into a syringe containing sufficient heparin to fill its dead space. The blood was immediately transferred to a 1 cc. VanSlyke pipette and introduced into a VanSlyke-Neill manometric apparatus (30) previously prepared for analysis. The delay (or transfer time) between withdrawal of the blood from the tonometer and its introduction into the analyzer was less than two minutes. While the analysis was being performed, a new gas mixture was introduced to the tonometer

system and allowed to flush out the system preparatory to the next equilibration.

Gas Mixtures. Gas mixtures were prepared with different compositions of carbon dioxide and oxygen and stored in cylinders. These mixtures were analyzed in the Scholander microvolumetric apparatus (52) (Table IV). To obtain the partial pressure of each gas in the tonometer chamber, its fractional concentration in the gas mixture was multiplied by the total pressure (T.P.) of gas in the chamber (expressed in mm. Hg). T.P. was obtained by recording the barometric pressure, adding that pressure due to the depth of the gas outlet to the water bath (converted to mm. Hg), and subtracting 47 mm. Hg (water vapor pressure at 37° C.).

Problem of Glycolysis. It was observed by Christiansen in 1914 that blood kept at 37° C. at a constant partial pressure of carbon dioxide showed a steady decrease in carbon dioxide content (53). The rate of change in whole blood was accelerated by temperature elevation, with little or no change occurring at 0° C. (54,55). The decreasing carbon dioxide contents were found to be due to the quantitative conversion of glucose to lactic or pyruvic acid (54) (glycolysis) occurring in the cells of the blood, particularly the leukocytes. Sodium fluoride and sodium diiodoacetate in 0.1 per cent concentrations prevented acid production (54). For this reason, 0.1 per cent sodium

fluoride has been used in almost all tonometry studies.

It was our observation that blood containing either sodium fluoride or sodium diiodoacetate invariably hemolyzed during the mechanical agitation of tonometry, after four hours storage following collection (from pregnant woman or placenta). The fluoride or diiodoacetate were each mixed with the heparin used as an anti-coagulant. The degree of hemolysis increased with both the duration of agitation and time of storage following collection. Hemolysis occurred in about the same degree in both maternal and fetal blood. Twenty minute equilibrations done within four hours of obtaining the blood were not accompanied by visible hemolysis. No hemolysis occurred at 24 hours storage when not subjected to the agitation of tonometry. Hemolysis under these conditions occurred at all levels of fluoride and diiodoacetate concentrations which would prevent glycolysis. When the use of sodium fluoride and sodium diiodoacetate was discontinued no hemolysis occurred during twenty minutes of agitation in the tonometer even after 24 hours storage. Therefore, the use of fluoride and diiodoacetate was abandoned. No attempt was made to determine the cause of the mechanical fragility of the erythrocytes.

Correction for Blood Acid Production. The change in blood acidity was corrected for as follows. The carbon dioxide content at a given partial pressure of carbon dioxide was found to decrease in approximately linear fashion, the

rate depending upon the temperature (figure 2). When the syringe containing the blood was placed in cracked ice between equilibrations, the acid production was prevented (figure 3). The acid production in the blood occurred only during the twenty minutes of equilibration. The rate of carbon dioxide content decrease was not changed by equilibrating the blood with widely differing partial pressures of carbon dioxide. On some blood samples taken from pregnant women, the sample was divided and a part mixed with 0.1 per cent sodium fluoride. When no fluoride was used, extrapolating the carbon dioxide contents from twenty and forty minute equilibrations (using the same gas mixture) to zero time yielded a value for carbon dioxide content which approximated that obtained from the blood containing fluoride after a twenty minute equilibration. The blood containing fluoride was equilibrated less than four hours after venepuncture, with no hemolysis occurring.

The difference in carbon dioxide contents between the twenty and forty minute equilibrations with one gas mixture was used as a carbon dioxide correction which could be added to the twenty minute equilibration values obtained in each equilibration of that particular blood sample. The gas mixture used for both a twenty and a forty minute equilibration was selected impartially.

Oxygen contents decreased to a much lesser degree as a result of acid production and were related to the

Figure 2

Demonstration of diminishing carbon dioxide combining powers with time and temperature. All equilibrations were performed at constant partial pressures of oxygen and carbon dioxide.

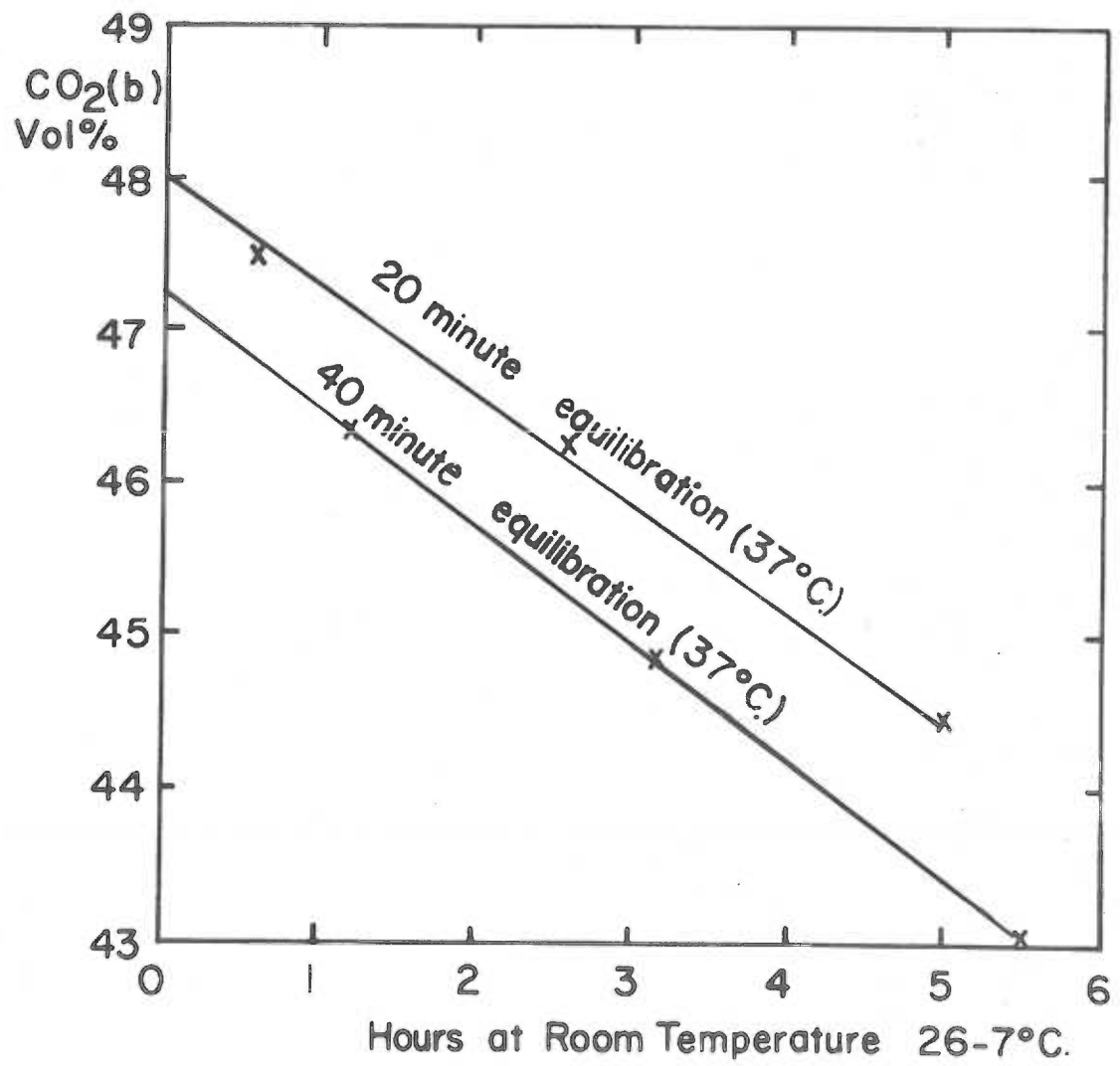
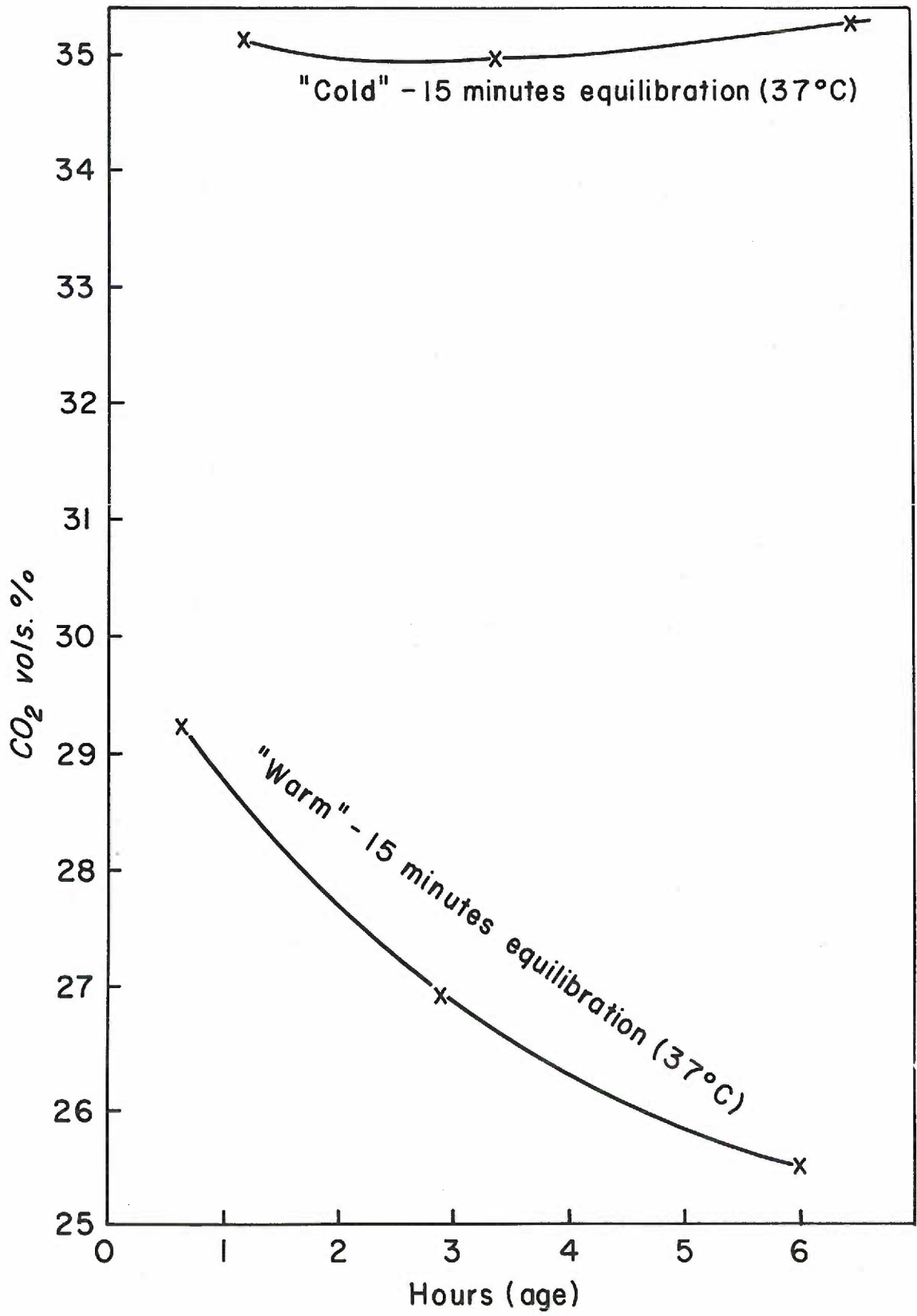


Figure 3

Demonstration of the need for keeping blood cold between equilibrations. "Cold" blood was kept at 0° C. between equilibrations. "Warm" blood was kept at room temperature, 26-27° C., between equilibrations.



partial pressure of oxygen in the gas mixture used for equilibration. The correction for oxygen content is discussed with the results.

Procedure. To enlarge the scope of information on the dissociation curves of fetal blood, it was necessary to analyze two groups of fetal blood samples, equilibrating each with a different set of gas mixtures. These will be referred to as the first and second fetal groups. Duplicate determinations were not done. The first fetal group consisted of blood taken from seventeen placentas. Three cc. aliquots of blood from each sample were equilibrated with each of nine gas mixtures. The second fetal group consisted of blood taken from ten placentas, three cc. aliquots of which were equilibrated with each of seven other gas mixtures. Maternal blood specimens were taken from the arm veins of eight pregnant women within three weeks of term but not in labor. These blood samples were equilibrated with some of the gas mixtures used for the first fetal group.

For fetal blood specimens, blood from the placenta received at delivery was collected in a 30 cc. syringe, containing 1 cc. of 1 per cent heparin. The syringe was capped and placed in a bucket of cracked ice within ten minutes following delivery. For maternal blood specimens, the syringe containing the blood was placed in cracked ice within ten minutes following venepuncture.

The syringe containing blood was kept in ice

throughout the equilibrations, except when briefly removed to admit 3 cc. to the tonometer chamber. The syringe contained a bubble of air and was shaken vigorously just prior to admitting the sample to the tonometer. This attempt to prevent erythrocyte sedimentation was apparently successful, because consecutive determinations of hematocrit following successive tonometries showed no change in hemoconcentration.

Table IV

Scholander Analyses on Tanks

Group	Tank No.	CO ₂ mean per cent	CO ₂ standard deviation per cent	O ₂ mean per cent	O ₂ standard deviation per cent
1. (Used on first group fetal blood and No. 9 on maternal blood)					
	(1)	2.90	0.03	2.16	0.02
	(2)	2.87	0.03	4.35	0.03
	(3)	5.71	0.01	2.20	0.02
	(4)	8.60	0.04	2.16	0.03
	(5)	8.60	0.03	4.32	0.04
	(6)	8.59	0.01	8.56	0.01
	(7)	5.76	0.01	8.60	0.02
	(8)	2.91	0.03	8.61	0.02
	(9)	6.05	0.04	93.30	----
2. (Used on second group fetal blood)					
	(1)	11.10	0.05	13.95	0.02
	(2)	11.36	0.05	11.00	0.04
	(3)	4.47	0.03	6.33	0.03
	(4)	7.71	0.04	3.16	0.04
	(5)	1.51	0.04	3.18	0.04
	(6)	3.57	0.03	0.97	0.04
	(7)	1.47	0.03	0.97	0.02

RESULTS

The First Group of Fetal Blood Determinations.

Tonometry studies were performed on blood samples taken from seventeen placentas. The experimental data are listed in Table V. Also included in Table V are the oxygen and carbon dioxide content corrections, which are content differences in oxygen and carbon dioxide when the forty minute equilibration contents are subtracted from the twenty minute contents, listed under that gas mixture (tank) number in the table. The partial pressures of oxygen and carbon dioxide are determined by multiplying the T.P. (total pressure) by the per cent gas composition of that particular gas mixture. "Original oxygen" is the experimentally determined content of oxygen. Alpha is the solubility coefficient for whole blood, dissolved oxygen in 100 cc. of blood at 760 mm. Hg partial pressure of oxygen, calculated from the hematocrit for that particular blood sample and the solubility coefficients (corrected from 1 cc. to 100 cc.) of plasma and cells taken from the tables of Sendroy et al (56). Alpha for cells is 2.6. Alpha for plasma is 2.09. Then Alpha = $\frac{(2.6 \times \text{hematocrit}) + 2.09 (100 - \text{hematocrit})}{100}$ and dissolved oxygen (vols. %) = Alpha $\times \frac{pO_2}{760}$. The oxygen content associated with hemoglobin was obtained by subtracting the dissolved oxygen content from the experimentally determined oxygen content. The oxygen contents

Table V
Blood Gas Values on First Fetal Group

Fetus Tank No.	pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Vols.%) (Vol.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	% sat. HbO ₂	CO ₂ without corr.	CO ₂ corr., tank #4,				
								(vols. %)	(vols. %)	alpha (sol. coeff.)	T.P. =	
1. (1)	20.35	15.16	7.04	0.05	6.99	32.56	28.98	0.17	0.17	2.34	701.7	49.5
(2)	20.14	30.52	15.22	0.09	15.43	71.67	26.84					
(3)	40.07	15.44	4.63	0.05	4.58	21.27	39.73					
(4)	60.35	15.16	3.67	0.05	3.62	16.81	47.68					
(5)	60.35	30.31	11.14	0.09	11.05	51.32	46.21					
(6)	60.28	60.07	18.65	0.18	18.47	85.79	43.31					
(7)	40.42	60.35	19.16	0.19	18.97	88.11	34.90					
(8)	20.42	60.42	20.43	0.19	20.24	94.01	24.46					
(9)	42.45	654.69	23.55	2.02	21.53	100.00	35.60					
2. (1)	20.47	15.24	5.52	0.05	5.47	30.14	30.26					
(2)	20.25	30.70	12.95	0.09	12.86	70.85	27.49					
(3)	40.30	15.53	4.05	0.05	4.00	22.04	40.02					
(4)	60.69	15.24	2.91	0.05	2.86	15.76	48.86					
(5)	60.69	30.49	9.03	0.09	8.94	49.26	46.41					
(6)	60.62	60.41	15.17	0.18	14.99	82.59	44.56					
(7)	40.65	60.69	16.22	0.18	16.04	88.37	36.06					
(8)	20.54	60.76	17.13	0.18	16.95	93.39	25.69					
(9)	42.69	658.42	20.14	1.99	18.15	100.00	36.31					
3. (1)	20.38	15.19	8.23	0.05	8.18	34.44	28.33					
(2)	20.17	30.57	17.58	0.10	17.48	73.60	25.28					
(3)	40.12	15.46	6.20	0.05	6.15	25.89	40.02					
(4)	60.43	15.19	5.17	0.05	5.12	21.56	47.14					
(5)	60.43	30.36	13.16	0.09	13.07	55.03	45.47					
(6)	60.36	60.15	20.89	0.19	20.70	87.16	43.34					
(7)	40.48	60.43	21.72	0.19	21.53	90.65	35.04					
(8)	20.45	60.50	22.57	0.19	22.38	94.23	24.23					
(9)	42.51	655.62	25.79	2.04	23.75	100.00	35.20					

Retus Tank No.	No.	mm. Hg	pCO ₂ mm. Hg	mm. Hg	Orig. O ₂ (Vols.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	% sat. HbO ₂	CO ₂ without corr. (Vols.%)	CO ₂ corr., tank #
4.	(1)	20.27	15.10	7.99	0.05	7.94	41.27	32.49	CO ₂ corr., tank #8 (vols.%) = 1.68	
	(2)	20.06	30.40	15.53	0.09	15.44	80.25	29.02	O ₂ diff. = -0.50	
	(3)	39.91	15.38	5.35	0.05	5.30	27.55	42.82	alpha (sol. coeff.) = 2.31	
	(4)	60.11	15.10	4.25	0.05	4.20	21.83	51.75	T.P. = 698.9	
	(5)	60.11	30.19	11.49	0.09	11.40	59.25	49.47	Hct. = 43.0	
	(6)	60.04	59.83	17.56	0.18	17.38	90.33	47.27		
	(7)	40.26	60.11	17.94	0.18	17.76	92.31	39.05		
	(8)	20.34	60.18	18.22	0.18	18.04	93.76	28.79		
	(9)	42.28	652.07	21.22	1.98	19.24	100.00	38.67		
5.	(1)	20.68	15.41	8.84	0.05	8.79	41.90	31.51	CO ₂ corr., tank #5, (vols.%) = 0.94	
	(2)	20.47	31.02	16.19	0.10	16.09	76.69	29.14	O ₂ diff. = -0.02	
	(3)	40.72	15.69	6.56	0.05	6.51	31.03	42.55	alpha (sol. coeff.) = 2.33	
	(4)	61.34	15.41	5.25	0.05	5.20	24.79	51.25	T.P. = 713.2	
	(5)	61.34	30.81	12.47	0.09	12.38	59.01	49.26	Hct. = 47.5	
	(6)	61.26	61.05	18.52	0.19	18.33	87.37	46.13		
	(7)	41.08	61.34	19.19	0.19	19.00	90.56	38.41		
	(8)	20.75	61.41	19.91	0.19	19.72	93.99	27.93		
	(9)	43.15	665.42	23.02	2.04	20.98	100.00	38.44		
6.	(1)	20.58	15.33	7.30	0.05	7.25	40.35	32.35	CO ₂ corr., tank #2, (vols.%) = 1.15	
	(2)	20.37	30.87	14.12	0.09	14.03	78.07	30.78	O ₂ diff. = +0.07	
	(3)	40.52	15.61	5.56	0.05	5.51	30.66	44.00	alpha (sol. coeff.) = 2.31	
	(4)	61.03	15.33	4.43	0.05	4.38	24.37	52.36	T.P. = 709.7	
	(5)	61.03	30.66	11.00	0.09	10.91	60.71	49.36	Hct. = 43.0	
	(6)	60.96	60.75	16.06	0.18	15.88	88.37	47.74		
	(7)	40.88	61.03	16.62	0.19	16.43	91.43	39.90		
	(8)	20.65	61.11	17.06	0.19	16.87	93.88	30.01		
	(9)	42.94	662.15	19.98	2.01	17.97	100.00	40.76		

Fetus Tank No.	pcO2 mm. Hg	pO2 mm. Hg	Orig. O2 (Volts.%)	Diss. O2 (Volts.%)	Hb O2 (Volts. %)	% sat. HbO2	CO2 without corr. (Volts. %)
10. (1)	20.53	15.29	7.46	0.05	7.41	35.35	26.20
(2)	20.32	30.80	16.12	0.09	16.03	76.48	25.62
(3)	40.43	15.58	5.53	0.05	5.48	26.15	39.00
(4)	60.89	15.29	4.06	0.05	4.01	19.13	46.84
(5)	60.89	30.59	11.64	0.09	11.55	55.10	45.03
(6)	60.82	60.60	18.74	0.19	18.55	88.50	41.79
(7)	40.78	60.89	19.32	0.19	19.03	91.27	34.51
(8)	20.60	60.96	19.96	0.19	19.77	94.32	24.55
(9)	42.83	660.56	22.99	2.03	20.96	100.00	34.98
CO2 corr., tank #8, (vols. %) = 1.28 O2 diff. (vols. %) = -0.12 alpha (sol. coeff.) = 2.33 T.P. = 708.0 Hct. = 48.0							
11. (1)	20.41	15.20	6.64	0.05	6.59	34.76	29.98
(2)	20.20	30.62	14.36	0.09	14.27	75.26	27.74
(3)	40.19	15.49	4.56	0.05	4.51	23.79	41.79
(4)	60.54	15.20	3.77	0.05	3.72	19.62	49.41
(5)	60.54	30.41	10.32	0.09	10.23	53.96	48.04
(6)	60.47	60.25	16.93	0.18	16.75	88.34	44.57
(7)	40.54	60.54	17.52	0.18	17.34	91.46	36.88
(8)	20.48	60.61	18.57	0.18	18.39	96.99	27.57
(9)	42.59	656.74	20.96	2.00	18.96	100.00	37.50
CO2 corr., tank #3, (vols. %) = 1.94 O2 diff. (vols. %) = -0.47 alpha (sol. coeff.) = 2.31 T.P. = 703.9 Hct. = 44.0							
12. (1)	20.44	15.23	9.51	0.05	9.46	43.98	30.93
(2)	20.23	30.66	18.18	0.09	18.09	84.10	30.18
(3)	40.25	15.51	6.80	0.05	6.75	31.38	42.42
(4)	60.62	15.23	4.82	0.05	4.77	22.18	50.26
(5)	60.62	30.45	13.33	0.09	13.24	61.55	48.85
(6)	60.55	60.34	19.43	0.19	19.24	89.45	45.45
(7)	40.60	60.62	20.54	0.19	20.35	94.61	38.89
(8)	20.51	60.69	20.62	0.19	20.43	94.98	28.20
(9)	42.65	657.67	23.53	2.02	21.51	100.00	39.29
CO2 corr., tank #1, (vols. %) = 1.67 O2 diff. (vols. %) = +0.99 alpha (sol. coeff.) = 2.34 T.P. = 704.9 Hct. = 48.5							

Fetus Tank No.	No.	pCO2 mm. Hg	pO2 mm. Hg	Orig. O2 (Vols.%) (Vols.%)	Diss. O2 (Vols.%)	Hb O2 (Vols. %)	% sat. HbO2	CO2 without corr. (Vols. %)
13.	(1)	20.38	15.19	8.05	0.05	8.00	35.67	23.80
	(2)	20.17	30.57	16.66	0.09	16.57	73.87	22.47
	(3)	40.12	15.46	5.52	0.05	5.47	24.39	34.85
	(4)	60.43	15.19	4.57	0.05	4.52	20.15	43.61
	(5)	60.43	30.36	12.15	0.09	12.06	53.77	40.43
	(6)	60.36	60.15	19.42	0.19	19.23	85.73	37.63
	(7)	40.48	60.43	20.34	0.19	20.15	89.84	30.75
	(8)	20.45	60.50	20.72	0.19	20.53	91.53	20.72
	(9)	42.51	655.62	24.47	2.04	22.43	100.00	31.31
CO2 corr., tank #8 O2 (vols. %) = 1.58 O2 diff. alpha (sol. coeff.) = 40.10 T.P. = 702.7 Hct. = 52.0								
14.	(1)	20.36	15.17	8.26	0.05	8.21	37.73	27.20
	(2)	20.15	30.55	16.49	0.09	16.40	75.37	25.48
	(3)	40.10	15.45	6.72	0.05	6.67	30.65	38.90
	(4)	60.39	15.17	4.89	0.05	4.84	22.24	46.70
	(5)	60.39	30.34	12.69	0.09	12.60	57.90	44.79
	(6)	60.32	60.11	19.26	0.19	19.07	87.64	42.67
	(7)	40.45	60.39	19.84	0.19	19.65	90.30	34.52
	(8)	20.43	60.46	20.47	0.19	20.28	93.20	24.07
	(9)	42.48	655.15	23.79	2.03	21.76	100.00	35.10
CO2 corr., tank #3 O2 (vols. %) = 1.68 O2 diff. alpha (sol. coeff.) = 40.91 T.P. = 702.2 Hct. = 51.0								
15.	(1)	20.74	15.45	8.16	0.05	8.11	36.16	29.24
	(2)	20.52	31.11	16.12	0.10	16.02	77.35	28.00
	(3)	40.83	15.73	5.40	0.05	5.35	25.83	39.88
	(4)	61.50	15.45	3.98	0.05	3.93	18.98	47.26
	(5)	61.50	30.89	11.72	0.10	11.62	56.11	46.29
	(6)	61.43	61.21	18.55	0.19	18.36	88.65	45.36
	(7)	41.19	61.50	19.03	0.19	18.84	90.97	36.96
	(8)	20.81	61.57	19.93	0.19	19.74	95.32	27.07
	(9)	43.26	667.19	22.76	2.05	20.71	100.00	37.87
CO2 corr., tank #2 O2 (vols. %) = 2.44 O2 diff. alpha (sol. coeff.) = 40.24 T.P. = 715.1 Hct. = 48.5								

Petus Tank No.	No.	pCO2 mm. Hg	pO2 mm. Hg	Orig. O2 (Vols.%)	Diss. O2 (Vols.%)	Hb O2 (Vols.%)	% sat. HbO2	CO2 without corr. (Vols. %)
16.	(1)	20.73	15.44	7.34	0.05	7.29	38.76	29.90
	(2)	20.52	31.10	14.96	0.09	14.87	79.05	29.00
	(3)	40.82	15.73	5.53	0.05	5.48	29.13	41.66
	(4)	61.48	15.44	4.52	0.05	4.47	23.76	50.24
	(5)	61.48	30.88	10.65	0.09	10.56	56.14	47.67
	(6)	61.41	61.20	16.68	0.19	16.49	87.67	45.31
	(7)	41.18	61.48	17.59	0.19	17.40	92.50	38.81
	(8)	20.80	61.55	17.85	0.19	17.66	93.89	27.28
	(9)	43.25	667.00	20.85	2.04	18.81	100.00	38.91

CO2 corr., tank #7,
(vols. %) = 1.71
O2 diff.
(vols. %) = +0.23
alpha (sol.
coeff.) = 2.32
T.P. = 714.9
Hot. = 44.5

17.	(1)	20.78	15.48	7.15	0.05	7.10	38.69	30.68
	(2)	20.57	31.18	14.61	0.09	14.52	79.13	28.75
	(3)	40.92	15.77	5.10	0.05	5.05	27.52	41.62
	(4)	61.64	15.48	4.12	0.05	4.07	22.18	50.59
	(5)	61.64	30.96	10.95	0.09	10.86	59.18	48.50
	(6)	61.56	61.35	16.51	0.19	16.32	88.94	46.16
	(7)	41.28	61.64	17.27	0.19	17.08	93.08	38.16
	(8)	20.86	61.71	17.72	0.19	17.53	95.53	28.21
	(9)	43.36	668.68	20.38	2.03	18.35	100.00	38.25

CO2 corr., tank #6,
(vols. %) = 1.42
O2 diff.
(vols. %) = -0.01
alpha (sol.
coeff.) = 2.31
T.P. = 716.7
Hot. = 43.5

associated with hemoglobin (oxyhemoglobin) are expressed as per cent saturation of the oxygen capacity. Carbon dioxide contents are listed, uncorrected for the acid produced during tonometry.

The "uncorrected" carbon dioxide contents are affected by the acid-base status of the blood at the time of collection of the sample with decreasing pH causing a diminished carbon dioxide combining power of the blood. To minimize the variation attributable to the varying carbon dioxide combining powers of the different blood samples, the average carbon dioxide contents of the blood equilibrated with the two gas mixtures having partial pressures of carbon dioxide of approximately 40 mm. Hg (No. 3 and No. 7) was arbitrarily selected as a reference value in volumes per cent for each blood sample. In Table VI, all carbon dioxide contents, still uncorrected for the acid produced during tonometry, are expressed by their deviation from this reference content, as positive or negative volumes per cent. The mean content selected as a reference value for each sample is listed in volumes per cent.

The means of the carbon dioxide content deviations in the blood equilibrated with each gas mixture are listed in Table VII with the standard deviations of each population. The mean of the reference values is also listed in volumes per cent with its standard deviation. The mean carbon dioxide reference content is added to each of the

Table VI
Blood Gas Contents on First Group Fetal Blood

Fetus No.	Ave. #3 and #7 CO ₂ (Vol. %)	Tank No.	CO ₂ (Vol. %)	O ₂ (Vol. %)
1.	37.32	(1)	-8.34	32.56
		(2)	-10.48	71.67
		(3)	+2.41	21.27
		(4)	+10.36	16.81
		(5)	+8.89	51.32
		(6)	+5.99	85.79
		(7)	-2.42	88.11
		(8)	-12.86	94.01
		(9)	-1.72	21.23
2.	38.04	(1)	-7.78	30.14
		(2)	-10.55	70.85
		(3)	+1.98	22.04
		(4)	+10.82	15.76
		(5)	+8.37	49.26
		(6)	+6.52	82.59
		(7)	-1.98	88.37
		(8)	-12.35	93.39
		(9)	-1.73	18.15
3.	37.53	(1)	-9.20	34.44
		(2)	-12.25	73.60
		(3)	+2.49	25.89
		(4)	+9.61	21.56
		(5)	+7.94	55.03
		(6)	+5.81	87.16
		(7)	-2.49	90.65
		(8)	-13.30	94.23
		(9)	-2.33	23.75
4.	40.94	(1)	-8.45	41.27
		(2)	-11.92	80.25
		(3)	+1.88	27.55
		(4)	+10.81	21.83
		(5)	+8.53	59.25
		(6)	+6.33	90.33
		(7)	-1.89	92.31
		(8)	-12.15	93.76
		(9)	-2.27	19.24
5.	40.48	(1)	-8.97	41.90
		(2)	-11.34	76.69
		(3)	+2.07	31.03
		(4)	+10.77	24.79
		(5)	+8.78	59.01
		(6)	+5.65	87.37
		(7)	-2.07	90.56
		(8)	-12.55	93.99
		(9)	-2.04	20.98

Fetus No.	Ave. #3 and #7 CO ₂ (Vol. %)	Tank No.	CO ₂ (Vol. %)	O ₂ (Vol. %)
6.	41.95	(1)	-9.60	40.35
		(2)	-11.17	78.07
		(3)	+2.05	30.66
		(4)	+10.41	24.37
		(5)	+7.41	60.71
		(6)	+5.79	88.37
		(7)	-2.05	91.43
		(8)	-11.94	93.88
		(9)	-1.19	17.97
7.	36.19	(1)	-8.71	41.66
		(2)	-11.58	76.07
		(3)	+2.59	31.45
		(4)	+9.28	23.72
		(5)	+9.17	58.76
		(6)	+5.67	87.34
		(7)	-2.60	89.87
		(8)	-12.79	93.37
		(9)	-1.37	23.69
8.	39.56	(1)	-8.45	39.76
		(2)	-11.74	75.01
		(3)	+1.94	27.18
		(4)	+9.71	19.93
		(5)	+7.65	56.40
		(6)	+4.89	88.36
		(7)	-1.94	92.09
		(8)	-12.25	94.67
		(9)	-2.49	18.21
9.	44.73	(1)	-9.22	41.63
		(2)	-11.04	81.83
		(3)	+2.76	28.63
		(4)	+11.19	22.24
		(5)	+8.84	61.38
		(6)	+5.55	90.49
		(7)	-2.76	91.65
		(8)	-12.34	95.14
		(9)	-1.89	18.93
10.	36.76	(1)	-10.56	35.35
		(2)	-11.14	76.48
		(3)	+2.24	26.15
		(4)	+10.08	19.13
		(5)	+8.27	55.10
		(6)	+5.03	88.50
		(7)	-2.25	91.27
		(8)	-12.21	94.32
		(9)	-1.78	20.96

Fetus No.	Ave. #3 and #7 CO ₂ (Vol. %)	Tank No.	CO ₂ (Vol. %)	O ₂ (Vol. %)
11.	39.34	(1)	-9.36	34.76
		(2)	-11.60	75.26
		(3)	+2.45	23.79
		(4)	+10.07	19.62
		(5)	+8.70	53.96
		(6)	+5.23	88.34
		(7)	-2.46	91.46
		(8)	-11.77	96.99
		(9)	-1.84	18.96
12.	40.66	(1)	-9.73	43.98
		(2)	-10.48	84.10
		(3)	+1.76	31.38
		(4)	+9.60	22.18
		(5)	+8.19	61.55
		(6)	+4.79	89.45
		(7)	-1.77	94.61
		(8)	-12.46	94.98
		(9)	-1.37	21.51
13.	32.80	(1)	-9.00	35.67
		(2)	-10.33	73.87
		(3)	+2.05	24.39
		(4)	+10.81	20.15
		(5)	+7.63	53.77
		(6)	+4.83	85.73
		(7)	-2.05	89.84
		(8)	-12.08	91.53
		(9)	-1.49	22.43
14.	36.71	(1)	-9.51	37.73
		(2)	-11.23	75.37
		(3)	+2.19	30.65
		(4)	+9.99	22.24
		(5)	+8.08	57.90
		(6)	+5.96	87.64
		(7)	-2.19	90.30
		(8)	-12.64	93.20
		(9)	-1.61	21.76
15.	38.42	(1)	-9.18	36.16
		(2)	-10.42	77.35
		(3)	+1.46	25.83
		(4)	+8.84	18.98
		(5)	+7.87	56.11
		(6)	+6.94	88.65
		(7)	-1.46	90.97
		(8)	-11.35	95.32
		(9)	-0.55	20.71

Fetus No.	Ave. #3 and #7 CO ₂ (Vol. %)	Tank No.	CO ₂ (Vol. %)	O ₂ (Vol. %)
16.	40.24	(1)	-10.34	38.76
		(2)	-11.24	79.05
		(3)	+1.42	29.13
		(4)	+10.00	23.76
		(5)	+7.43	56.14
		(6)	+5.07	87.67
		(7)	-1.43	92.50
		(8)	-12.96	93.89
		(9)	-0.98	18.81
17.	39.89	(1)	-9.21	38.69
		(2)	-11.14	79.13
		(3)	+1.73	27.52
		(4)	+10.70	22.18
		(5)	+8.61	59.18
		(6)	+6.27	88.94
		(7)	-1.73	93.08
		(8)	-11.68	95.53
		(9)	-1.64	18.35

Table VII

Blood Gas Contents in the First Group
of Fetal Blood Determinations,
Not Corrected for Acid Produced During Tonometry

I. Carbon Dioxide Contents (Vols. %)

Tank No.	CO ₂ Mean Deviation from Reference Content	Standard Deviation	Mean Carbon Dioxide Content
1	-9.15	0.70	29.77
2	-11.16	0.56	27.76
3	+2.09	0.36	41.01
4	+10.18	0.64	49.10
5	+8.26	0.54	47.18
6	+5.67	0.63	44.59
7	-2.09	0.36	36.83
8	-12.33	0.50	26.59
9	-1.66	0.49	37.26

Mean reference content value = 38.92
Standard deviation = 2.69

II. Oxygen Contents

Tank No.	Oxyhemoglobin (per cent saturation)	Standard Deviation	Oxygen Content (Vols.% at Mean Oxygen Capacity)
1	37.93	3.78	7.71
2	76.74	3.46	15.60
3	27.33	3.22	5.56
4	21.13	2.55	4.30
5	56.75	3.40	11.54
6	87.81	1.87	17.85
7	91.12	1.61	18.52
8	94.25	1.18	19.16
9	100.00	0.00	20.33

Mean oxygen capacity (vols. %) = 20.33
Standard deviation = 1.92

carbon dioxide content deviations from the individual reference values. The sum is the final "uncorrected" carbon dioxide content.

In Table VII, the mean oxyhemoglobin per cent saturations are listed with standard deviations. The mean oxygen capacity is listed with its standard deviation in volumes per cent. Each mean oxygen per cent saturation is multiplied by the over-all mean oxygen capacity. The product is the final "uncorrected" oxygen content.

"Uncorrected" carbon dioxide contents are corrected by adding the mean carbon dioxide correction, the difference in the carbon dioxide contents obtained at twenty and forty minute equilibrations with the same mixture. The mean carbon dioxide correction obtained in this manner is 1.61 volumes per cent, the standard deviation is 0.39. The sum is the corrected carbon dioxide content (Table VIII). This procedure compensated for the additional acid production occurring during tonometry.

The oxygen content corrections, the decrease in oxygen content resulting from acid production, are greatly influenced by the partial pressure of oxygen in the gas mixture used for equilibration. The oxygen content mean corrections are therefore separately determined for each group of gas mixtures with like partial pressures of oxygen. The oxygen corrections are listed in Table V and are the difference between the oxygen content obtained for the

Table VIII

Corrected Mean Blood Gas Contents and Partial Pressures
for First Group of Fetal Blood Determinations

Tank No.	CO ₂ Content (Vols. %)	O ₂ Content (Vols. %)	Mean pCO ₂ (mm. Hg)	Standard Deviation	Mean pO ₂ (mm. Hg)	Standard Deviation
1	31.38	8.04	20.51	0.16	15.28	0.12
2	29.37	15.96	20.30	0.16	30.77	0.24
3	42.62	5.89	40.39	0.31	15.56	0.12
4	50.71	4.63	60.84	0.48	15.28	0.12
5	48.79	11.90	60.84	0.48	30.56	0.24
6	46.20	18.08	60.77	0.48	60.55	0.47
7	38.44	18.75	40.75	0.32	60.84	0.48
8	28.20	19.39	20.59	0.16	60.91	0.48
9	38.87	20.70	42.80	0.34	660.00	5.17

twenty minute equilibration and the oxygen content obtained for the forty minute equilibration on the same gas mixture. The mean oxygen content correction for gas mixtures having approximately 15 mm. Hg oxygen partial pressure is 0.28 volumes per cent. The mean correction for mixtures having approximately 30 mm. Hg oxygen partial pressure is 0.27 volumes per cent. For mixtures having approximately 60 mm. Hg oxygen partial pressure the same correction is 0.04 volumes per cent.

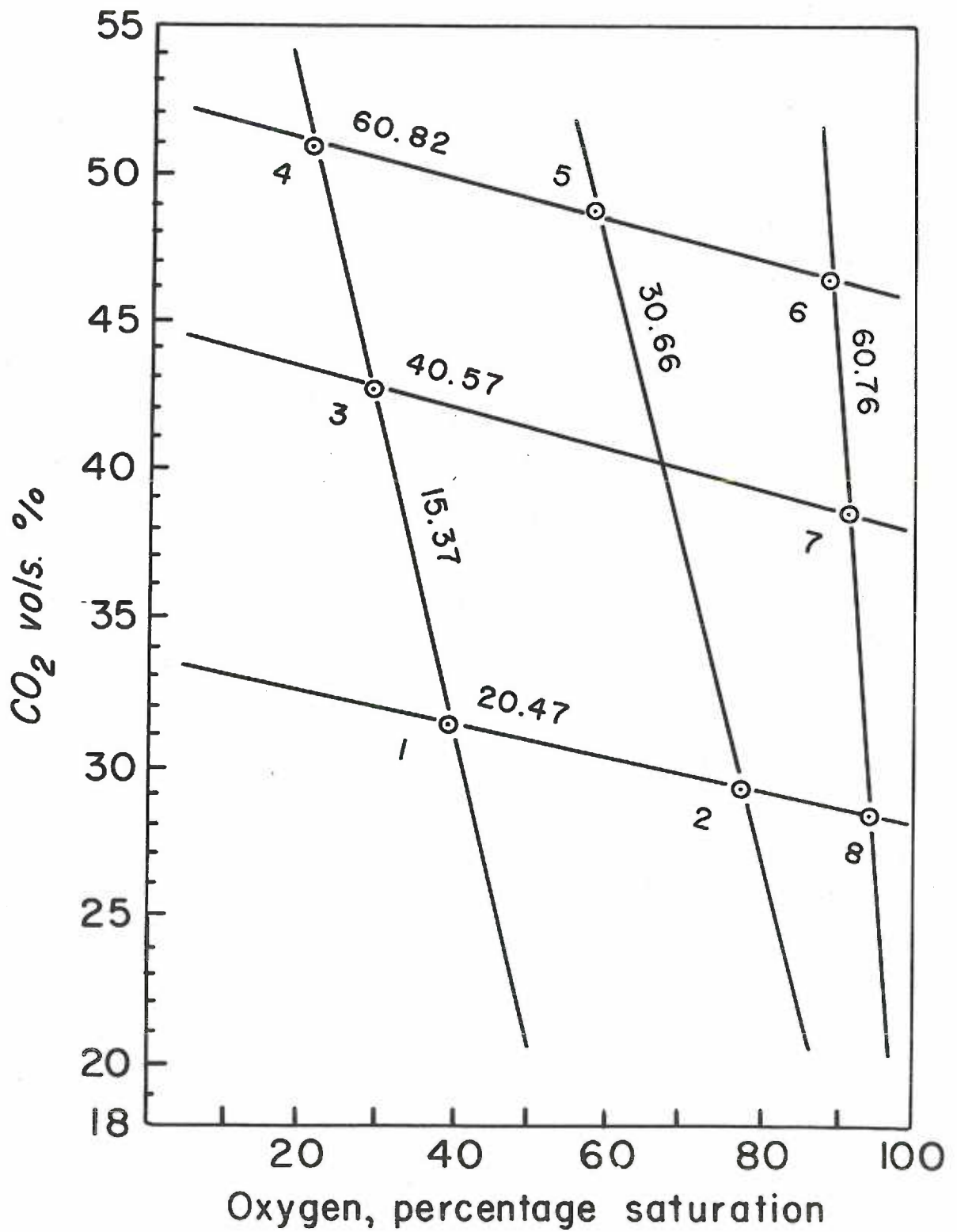
The corrected oxygen contents (Table VIII) are obtained by adding the mean dissolved oxygen and the mean oxygen content correction to the uncorrected mean oxygen content. The partial pressure of oxygen at oxygen capacity was arbitrarily designated to be 120 mm. Hg. The amount of dissolved oxygen was calculated for 120 mm. Hg and added as the dissolved oxygen content for oxygen capacity.

A definite relationship exists between oxygen capacity and hematocrit (57). The mean oxygen capacity (volumes per cent)/hematocrit ratio was 0.4311, with a standard deviation of 0.0088.

The mean partial pressures of carbon dioxide and oxygen with standard deviations are listed in Table VIII. The mean oxygen contents (per cent saturation) and the mean carbon dioxide contents (volumes per cent) at the mean oxygen and carbon dioxide partial pressures (mm. Hg) are shown graphically in figure 4. In figure 4, the nearly horizontal lines are the carbon dioxide partial pressure

Figure 4

Oxygen and carbon dioxide dissociation curves established for the first fetal group of blood determinations. The nearly horizontal lines are carbon dioxide partial pressure isopleths. The nearly vertical lines are oxygen partial pressure isopleths. The mean partial pressure representing the isopleth is listed along with that isopleth. The tank (gas mixture) number is listed with the blood gas contents obtained from equilibration.



isopleths and the nearly vertical lines are the oxygen partial pressure isopleths.

The Second Group of Fetal Blood Determinations.

Tonometry studies were performed on blood samples taken from ten placentas. The experimental data are listed in Table IX. Alpha, T.P., hematocrit, partial pressure of oxygen, partial pressure of carbon dioxide, experimentally determined oxygen content, dissolved oxygen content, oxyhemoglobin, and uncorrected experimentally determined carbon dioxide contents of the second group of fetal blood determinations are shown in Table IX in the same manner as the corresponding measurements were shown for the first group of fetal blood determinations in Table V.

The oxygen capacity of each sample was calculated by multiplying the mean oxygen capacity/hematocrit ratio, established for the first group of fetal blood determinations, 0.4311, by the hematocrit obtained with that blood sample. The oxygen contents associated with hemoglobin (oxyhemoglobin) are expressed as per cent of the predicted oxygen capacity.

The mean values for carbon dioxide content, oxygen saturation, and partial pressures of carbon dioxide and oxygen are listed in Table X with their respective standard deviations.

Peters (58) established that a linear relationship exists between the logarithm of the partial pressures of

Table IX
Blood Gas Values on Second Fetal Group

Fetus Tank No.	No.	pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Volts.%)	Diss. O ₂ (Volts.%)	Hb O ₂ (Volts.%)	% sat. HbO ₂	CO ₂ without corr. (Volts. %)
1.	(1)	79.69	100.15	20.78	0.31	20.47	94.03	47.29
	(2)	81.55	78.97	20.05	0.24	19.81	91.00	48.42
	(3)	32.09	45.44	17.90	0.14	17.76	81.58	31.13
	(4)	55.35	22.69	7.47	0.07	7.40	33.99	44.19
	(5)	10.84	22.83	14.12	0.07	14.05	64.54	18.13
	(6)	25.63	6.96	1.57	0.02	1.55	7.12	32.26
	(7)	10.55	6.96	2.30	0.02	2.28	10.47	20.31
<p>alpha = 2.35 T.P. = 717.9 Hct. = 50.5 Therefore O₂ capacity = 21.77</p>								
2.	(1)	79.42	99.81	16.97	0.30	16.67	92.10	46.71
	(2)	81.28	78.71	16.45	0.24	16.21	89.56	47.56
	(3)	31.98	45.29	15.18	0.14	15.04	83.09	32.12
	(4)	55.17	22.61	6.13	0.07	6.06	33.48	42.45
	(5)	10.80	22.75	11.51	0.07	11.44	63.20	18.75
	(6)	25.54	6.94	1.27	0.02	1.25	6.91	32.57
	(7)	10.52	6.94	2.27	0.02	2.25	12.43	21.04
<p>alpha = 2.30 T.P. = 715.5 Hct. = 42.0 Therefore O₂ capacity = 18.10</p>								
3.	(1)	79.54	99.97	22.66	0.31	22.35	94.26	43.10
	(2)	81.41	78.83	21.27	0.25	21.02	88.65	43.86
	(3)	32.03	45.36	19.02	0.14	18.88	79.63	26.97
	(4)	55.25	22.64	8.18	0.07	8.11	34.20	39.56
	(5)	10.82	22.79	13.92	0.07	13.85	58.41	14.62
	(6)	25.58	6.95	2.20	0.02	2.18	9.19	28.29
	(7)	10.53	6.95	2.62	0.02	2.60	10.97	16.31
<p>alpha = 2.37 T.P. = 716.6 Hct. = 55.0 Therefore O₂ capacity = 23.71</p>								

Fetus Tank No.	No.	pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Vols.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	% sat. HbO ₂	CO ₂ without corr. (Vols. %)
4.	(1)	79.38	99.76	21.78	0.31	21.47	94.87	51.26
	(2)	81.24	78.66	21.08	0.24	20.84	92.09	51.24
	(3)	31.96	45.27	19.60	0.14	19.46	85.99	34.39
	(4)	55.13	22.60	9.73	0.07	9.66	42.69	48.31
	(5)	10.80	22.74	15.99	0.07	15.92	70.35	20.46
	(6)	25.53	6.94	2.17	0.02	2.15	9.50	36.01
	(7)	10.51	6.94	3.35	0.02	3.33	14.71	23.51
5.	(1)	79.02	99.31	15.46	0.30	15.16	93.75	50.47
	(2)	80.87	78.31	14.77	0.23	14.54	89.92	52.56
	(3)	31.82	45.06	13.61	0.14	13.47	83.30	36.27
	(4)	54.89	22.50	5.73	0.07	5.66	35.00	47.90
	(5)	10.75	22.64	10.76	0.07	10.69	66.11	23.24
	(6)	25.41	6.91	1.45	0.02	1.43	8.84	37.75
	(7)	10.46	6.91	2.21	0.02	2.19	13.54	24.79
6.	(1)	78.09	98.14	19.30	0.30	19.00	96.84	50.10
	(2)	79.92	77.39	17.99	0.24	17.75	90.47	50.90
	(3)	31.45	44.53	17.08	0.14	16.94	86.34	34.54
	(4)	54.24	22.23	8.19	0.07	8.12	41.39	48.36
	(5)	10.62	22.37	14.42	0.07	14.35	73.14	21.76
	(6)	25.11	6.82	2.05	0.02	2.03	10.35	35.50
	(7)	10.34	6.82	2.76	0.02	2.74	13.97	23.70

alpha = 2.36
T.P. = 715.1
Hct. = 52.5
Therefore O₂ capacity = 22.63

alpha = 2.28
T.P. = 711.9
Hct. = 37.5
Therefore O₂ capacity = 16.17

alpha = 2.32
T.P. = 703.5
Hct. = 45.5
Therefore O₂ capacity = 19.62

Fetus Tank No.	No.	pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Vols.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	% sat. HbO ₂	CO ₂ without corr. (Vols. %)	
7.	(1)	79.29	99.64	20.36	0.31	20.05	93.96	50.73	alpha = 2.34 T.P. = 714.3 Hct. = 49.5 Therefore O ₂ capacity = 21.34
	(2)	81.14	78.57	19.69	0.24	19.45	91.14	50.45	
	(3)	31.93	45.22	18.13	0.14	17.99	84.30	33.78	
	(4)	55.07	22.57	9.40	0.07	9.33	43.72	46.21	
	(5)	10.79	22.71	15.45	0.07	15.38	72.07	21.02	
	(6)	25.50	6.93	2.17	0.02	2.15	10.07	34.91	
	(7)	10.50	6.93	4.18	0.02	4.16	19.49	22.63	
8.	(1)	79.35	99.73	21.25	0.31	20.94	91.48	41.00	alpha = 2.36 T.P. = 714.9 Hct. = 53.1 Therefore O ₂ capacity = 22.89
	(2)	81.21	78.64	20.39	0.24	20.15	88.03	42.08	
	(3)	31.96	45.25	18.26	0.14	18.12	79.16	25.66	
	(4)	55.12	22.59	8.09	0.07	8.02	35.04	36.86	
	(5)	10.79	22.73	13.10	0.07	13.03	56.92	14.50	
	(6)	25.52	6.93	2.22	0.02	2.20	9.61	26.14	
	(7)	10.51	6.93	2.53	0.02	2.51	10.97	15.81	
9.	(1)	79.29	99.64	19.43	0.31	19.12	94.37	51.78	alpha = 2.33 T.P. = 714.3 Hct. = 47.0 Therefore O ₂ capacity = 20.26
	(2)	81.14	78.57	18.37	0.24	18.13	89.49	52.37	
	(3)	31.93	45.22	17.13	0.14	16.99	83.86	34.63	
	(4)	55.07	22.57	8.02	0.07	7.95	39.24	46.92	
	(5)	10.79	22.71	13.43	0.07	13.36	65.94	21.52	
	(6)	25.50	6.93	1.73	0.02	1.71	8.44	35.67	
	(7)	10.50	6.93	2.55	0.02	2.53	12.49	23.14	

Fetus Tank No.	No. pCO2 mm. Hg	pO2 mm. Hg	Orig. O2 (Vols.%)	Diss. O2 (Vols.%)	Hb O2 (Vols. %)	% sat. HbO2	CO2 without corr. (Vols. %)
10.	(1) 79.09	99.39	23.30	0.31	22.99	94.38	44.02
	(2) 80.94	78.38	22.22	0.25	21.97	90.19	46.19
	(3) 31.85	45.10	19.49	0.14	19.35	79.43	28.18
	(4) 54.93	22.52	8.36	0.07	8.29	34.03	40.23
	(5) 10.76	22.66	14.78	0.07	14.71	60.39	16.15
	(6) 25.44	6.91	2.17	0.02	2.15	8.83	28.57
	(7) 10.47	6.91	2.43	0.02	2.41	9.89	17.25

alpha = 2.38
T.P. = 712.5
Hct. = 56.5
Therefore O2 capacity = 21.36

Table X

Final Values--Second Group Fetal Blood

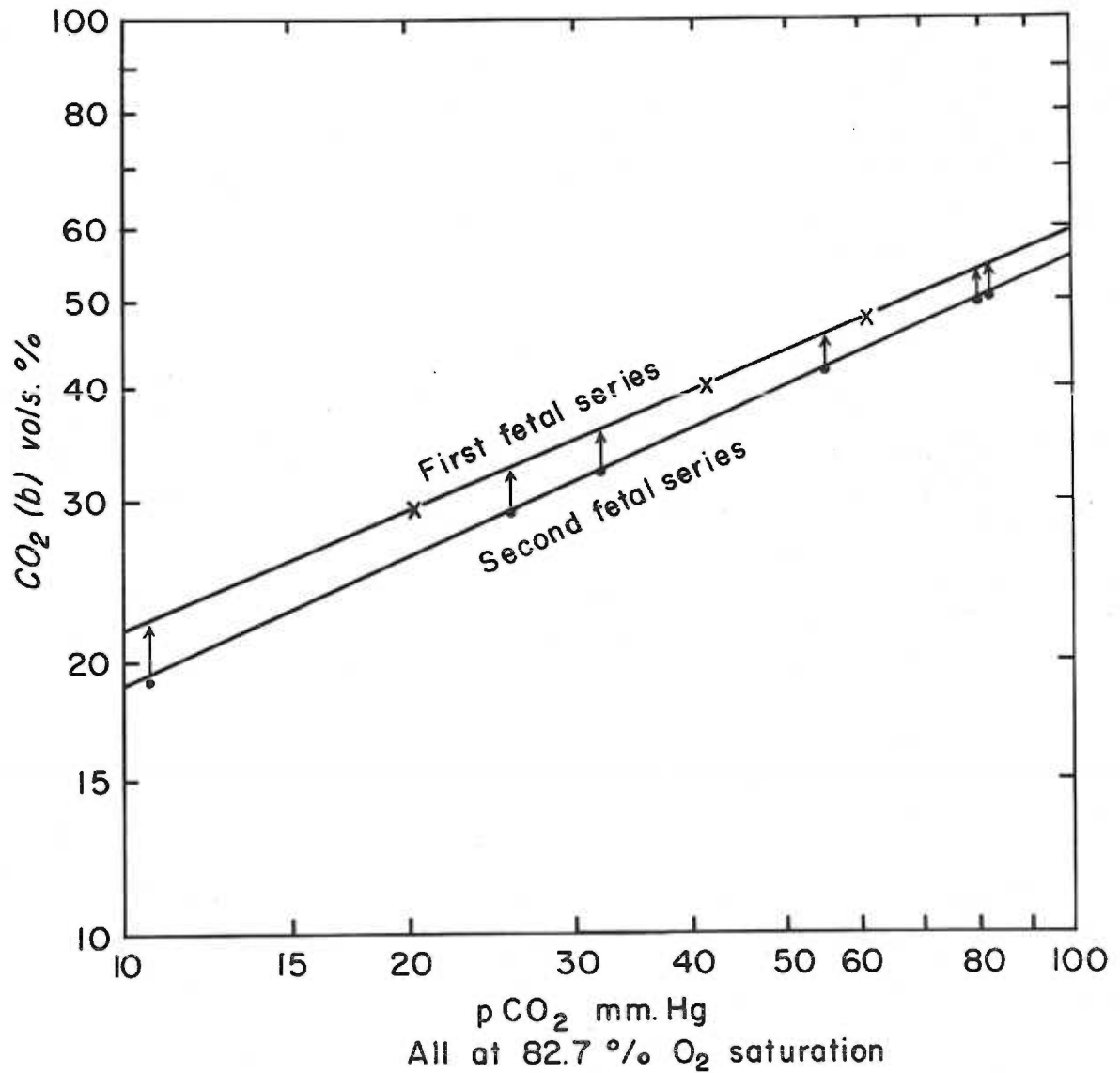
Tank No.	Mean CO ₂ vols. %	Mean O ₂ (% sat.)	Standard Deviation	Standard Deviation	mm. Hg pCO ₂	mm. Hg pO ₂	Standard Deviation	Standard Deviation	by	bx	r	sx · y
(1)	47.65	94.00	3.84	1.53	79.22	99.55	0.44	0.55	0.202	1.395	0.531	1.31
(2)	48.56	90.05	3.61	1.20	81.07	78.50	0.45	0.44	0.218	1.96	0.652	0.97
(3)	31.77	82.67	3.66	2.63	31.90	45.17	0.18	0.25	0.637	1.233	0.886	1.30
(4)	44.10	37.28	4.13	4.04	55.02	22.55	0.31	0.13	0.648	0.677	0.662	3.21
(5)	19.02	65.11	3.10	5.58	10.78	22.69	0.06	0.13	1.776	0.467	0.910	0.97
(6)	32.77	08.89	3.91	1.14	25.48	6.92	0.14	0.04	0.017	0.201	0.058	1.21
(7)	20.85	12.89	3.31	2.81	10.49	6.92	0.06	0.04	0.407	1.385	0.618	2.34

carbon dioxide and the logarithm of carbon dioxide contents in blood at constant oxygen saturation. Unfortunately, the line established on a double logarithm graph of carbon dioxide partial pressure and carbon dioxide content for the second group of fetal blood determinations lay below the line established for the first group of fetal blood determinations at a constant arbitrarily chosen 82.7 per cent oxygen saturation (figure 5). This indicated that the blood population of the second fetal group contained greater concentrations of non-volatile acids than did the blood population of the first fetal group. It was, therefore, impossible to construct a unified series of dissociation curves from the two different populations of fetal blood. Several of the blood samples used in the second fetal group were taken from the placentas of infants following deliveries involving long and difficult labors, which could result in increased blood non-volatile acid. The two blood samples in the second group that were taken from placentas following elective caesarean section had much higher carbon dioxide combining powers than did most of the others in the second fetal group of bloods and closely approximated those carbon dioxide combining powers obtained in the first group of fetal bloods. For this reason, it was assumed that the first fetal group was representative of the normal population of fetal bloods.

It was necessary, therefore, to correct the oxygen

Figure 5

Graphical correction of the carbon dioxide contents obtained in the second group of fetal blood determinations to those anticipated for the first group of fetal blood determinations equilibrated at same partial pressures of carbon dioxide and are constant 82.7% oxygen saturation.



and carbon dioxide contents obtained in the second group of fetal blood determinations to those anticipated for the first group of fetal blood determinations at the same partial pressures of oxygen and carbon dioxide.

The carbon dioxide dissociation curve, at one arbitrarily chosen oxygen saturation (82.7 per cent oxygen saturation), was corrected graphically as illustrated by arrows drawn along constant carbon dioxide partial pressures in figure 5, originating at the carbon dioxide contents obtained for the second fetal group of blood samples and extending to the anticipated carbon dioxide contents for the first fetal group of blood samples. However, this established the carbon dioxide dissociation curve for only one level of oxygen saturation.

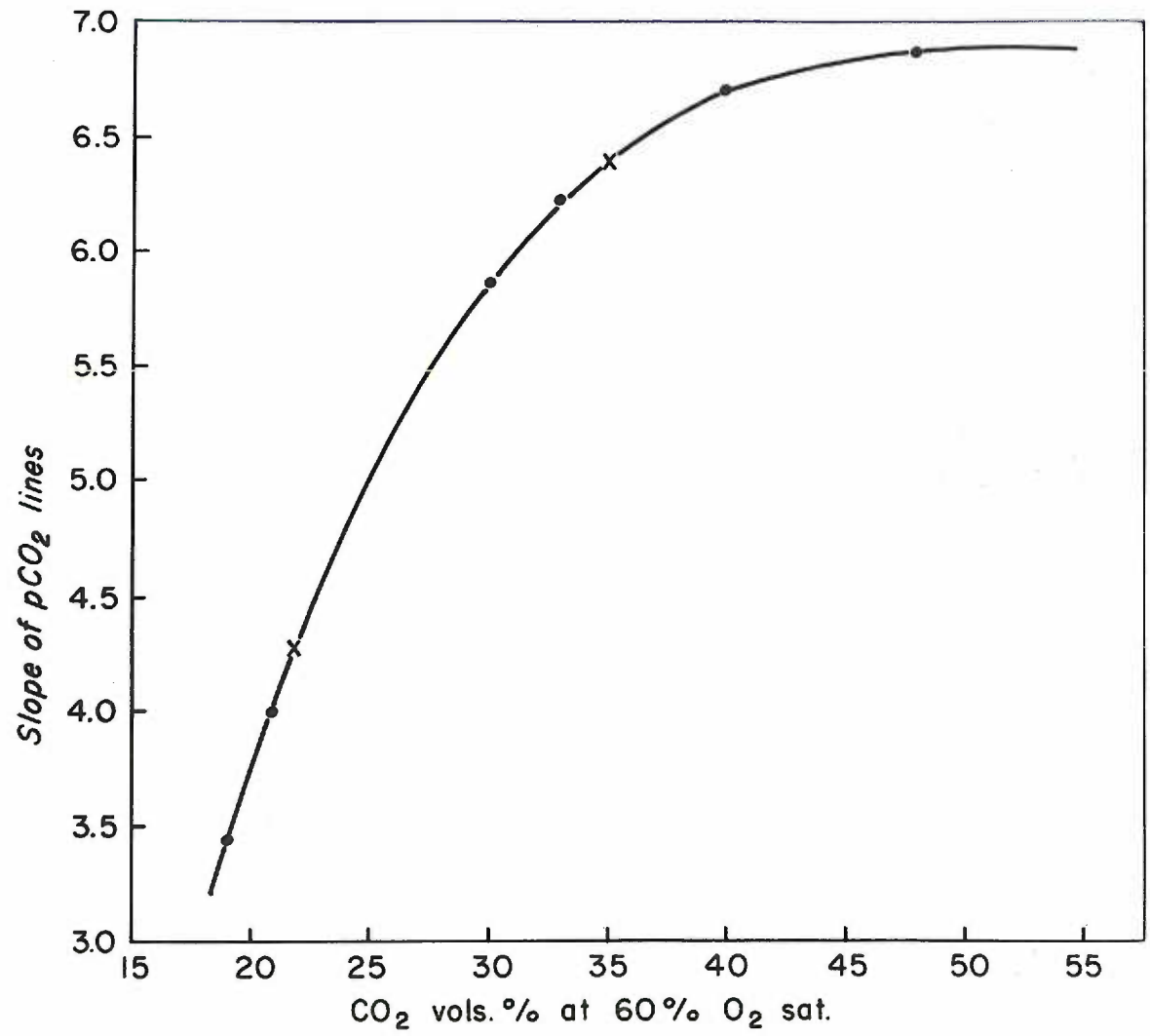
The carbon dioxide dissociation curve was needed for all levels of oxygen saturation. The Haldane effect, the decrease in carbon dioxide combining power due to the oxygenation of hemoglobin, may be noted in figures 4 and 7 by the fact that at a constant carbon dioxide partial pressure, the carbon dioxide content decreases with increasing oxygenation in virtually a linear fashion. At low carbon dioxide partial pressures the slopes of the carbon dioxide partial pressure isopleths (the nearly horizontal lines in figures 4 and 7) decreases slightly indicating a decrease in magnitude of the Haldane effect. The determination of this slope due to the Haldane effect is necessary for each carbon dioxide partial pressure and carbon dioxide content

established at one constant oxygen saturation (as in figure 5). In figure 6, the carbon dioxide partial pressure slopes due to the Haldane effect are plotted against the carbon dioxide content obtained from both fetal groups of blood determinations at a constant 60 per cent oxygen saturation. Using figure 6, the slope due to the Haldane effect was obtained for each carbon dioxide content indicated by an arrow in figure 5. A line with the appropriate slope for each of these carbon dioxide contents was constructed so as to extend through the corresponding carbon dioxide content (indicated by the arrows in figure 5) at 82.7 per cent saturation. This established the complete carbon dioxide dissociation curve for the population of blood samples in the first fetal group with the gas mixtures equilibrated with the blood samples of both fetal groups.

Increased non-volatile acid also decreases the oxygen content at a constant oxygen partial pressure. A positive correlation between carbon dioxide contents and oxygen per cent saturations was demonstrated for blood samples in the second fetal group equilibrated with certain gas mixtures (Table X). In Table X, r is the correlation coefficient, b_y is the slope of oxygen saturation on carbon dioxide content, b_x is the slope of carbon dioxide content on oxygen saturation, $s_{x \cdot y}$ is the standard error of estimate from a line extending through the point representing the mean carbon dioxide and oxygen contents and having a slope b_y .

Figure 6

The carbon dioxide content decrease in volumes per cent for each per cent oxygen saturation increase at constant partial pressure of carbon dioxide (expressed as slopes of pCO_2 lines) is plotted against carbon dioxide content. The purpose is to establish intervening slopes of pCO_2 lines.



From the mean carbon dioxide and oxygen contents for blood equilibrated with each gas mixture in the second fetal group (an x in figure 7), an arrow with the slope b_y was drawn to intersect the same carbon dioxide partial pressure line predicted for the first fetal group of blood samples. The point of intersection (a dot in figure 7) of the arrow and the predicted partial pressure isopleth of carbon dioxide represents the oxygen and carbon dioxide contents expected for the population of "normal" bloods of the first fetal group if the second set of gas mixtures actually had been used for equilibration. The mean oxygen capacity obtained for the first group of fetal blood determinations was assigned to the entire population of fetal blood determinations. The oxygen contents were established by multiplying the oxygen per cent saturations by the oxygen capacity.

Fetal Dissociation Curves Expressed as A Nomogram.

The d'Ocagne nomogram (59-61) permits the simultaneous graphical representation of numerous variables. The nomogram for a "normal" adult blood (60) is shown in figure 8. The use of a nomogram is possible because of the virtually linear relationship (figure 4) of partial pressures isopleths of either carbon dioxide or oxygen in terms of carbon dioxide and oxygen contents. With the knowledge of any two variables, a straight edge ruler placed through these known variables will intersect the values of the unknown variables.

The fetal oxygen and carbon dioxide dissociation

Figure 7

Method by which the carbon dioxide and oxygen contents are predicted for the population of the first group of fetal blood determinations from those contents actually obtained from the second group of fetal blood determinations. Circles with dots in the center are located at points representing the contents obtained in the first group of fetal blood determinations (figure 4). Xs are located at points representing the contents obtained in the second group of fetal blood determinations. The dotted lines with (2) designate the carbon dioxide partial pressure isopleths actually obtained with the second group of fetal blood determinations. The arrow follows the path of correction. The almost horizontal solid lines with (1) designate the carbon dioxide partial pressure isopleths anticipated for the first fetal group of blood determinations. The dots at the end of the arrows represent the oxygen and carbon dioxide contents anticipated for the first fetal group with the gas tensions actually used in equilibration with the second fetal group.

THE MATCHING OF FETAL GROUPS NOS. 1 AND 2

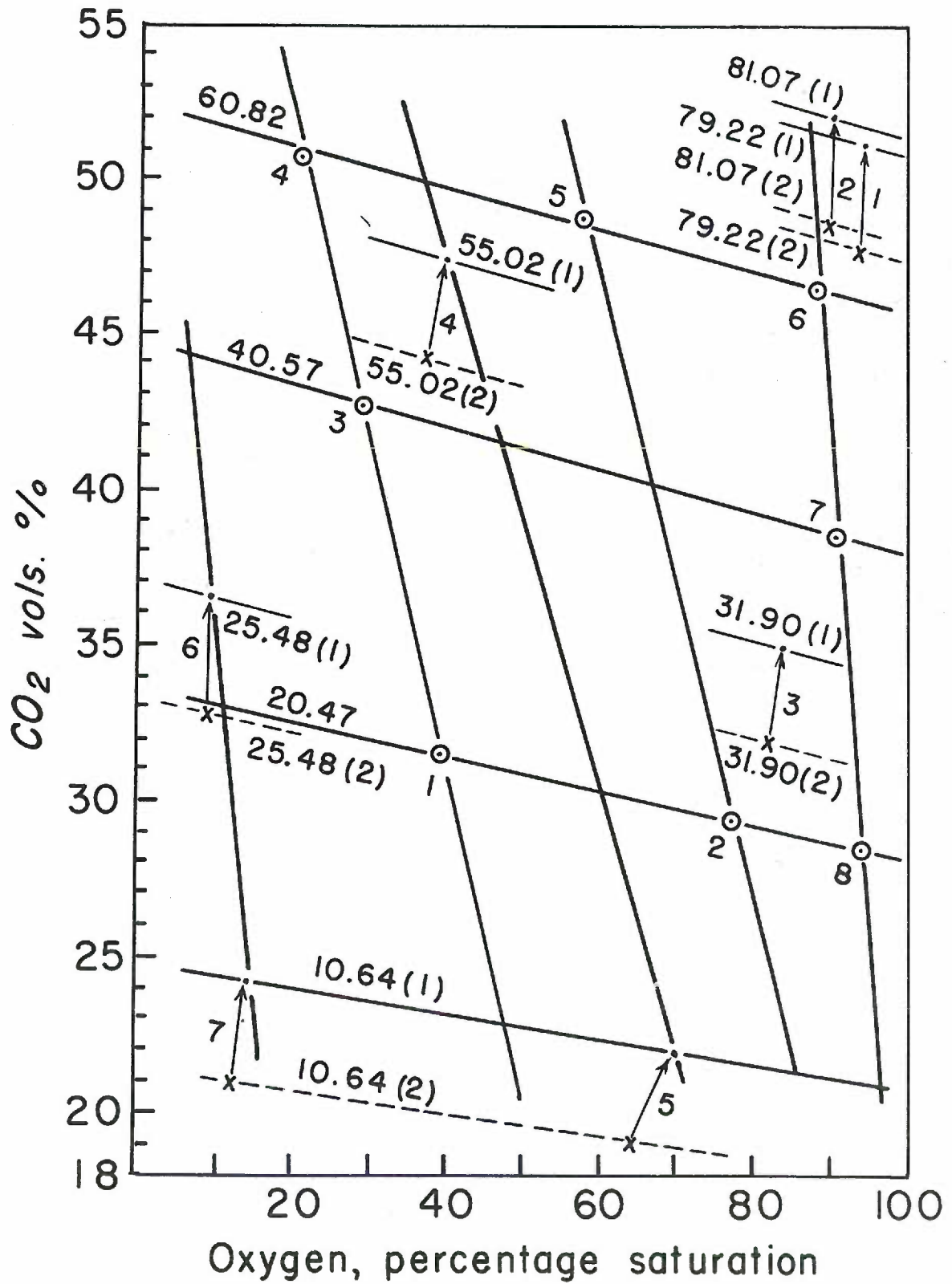
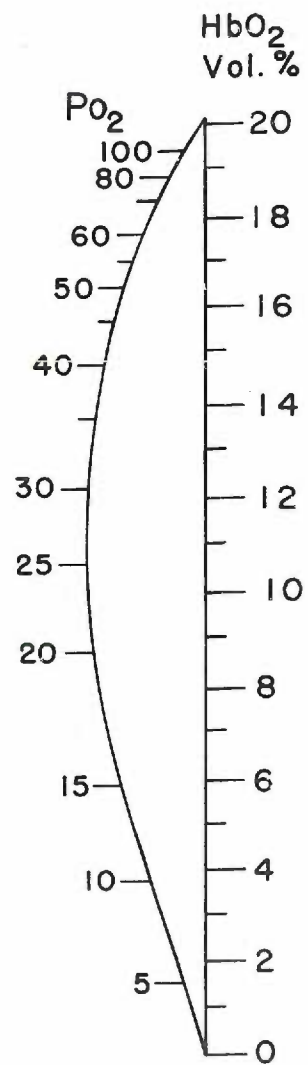
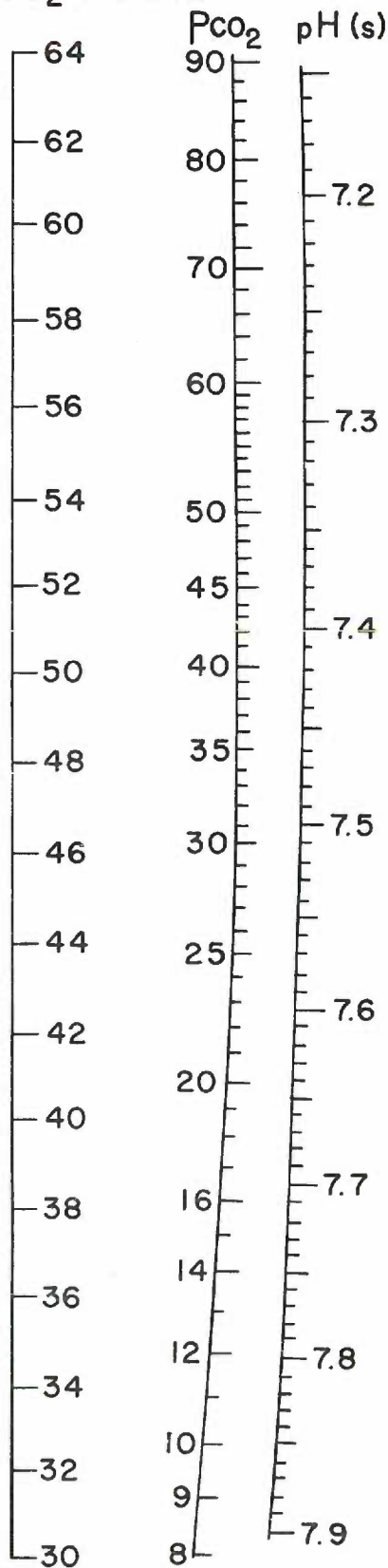


Figure 8

Normal adult nomogram (60)

total CO₂ Vol. % (b)



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

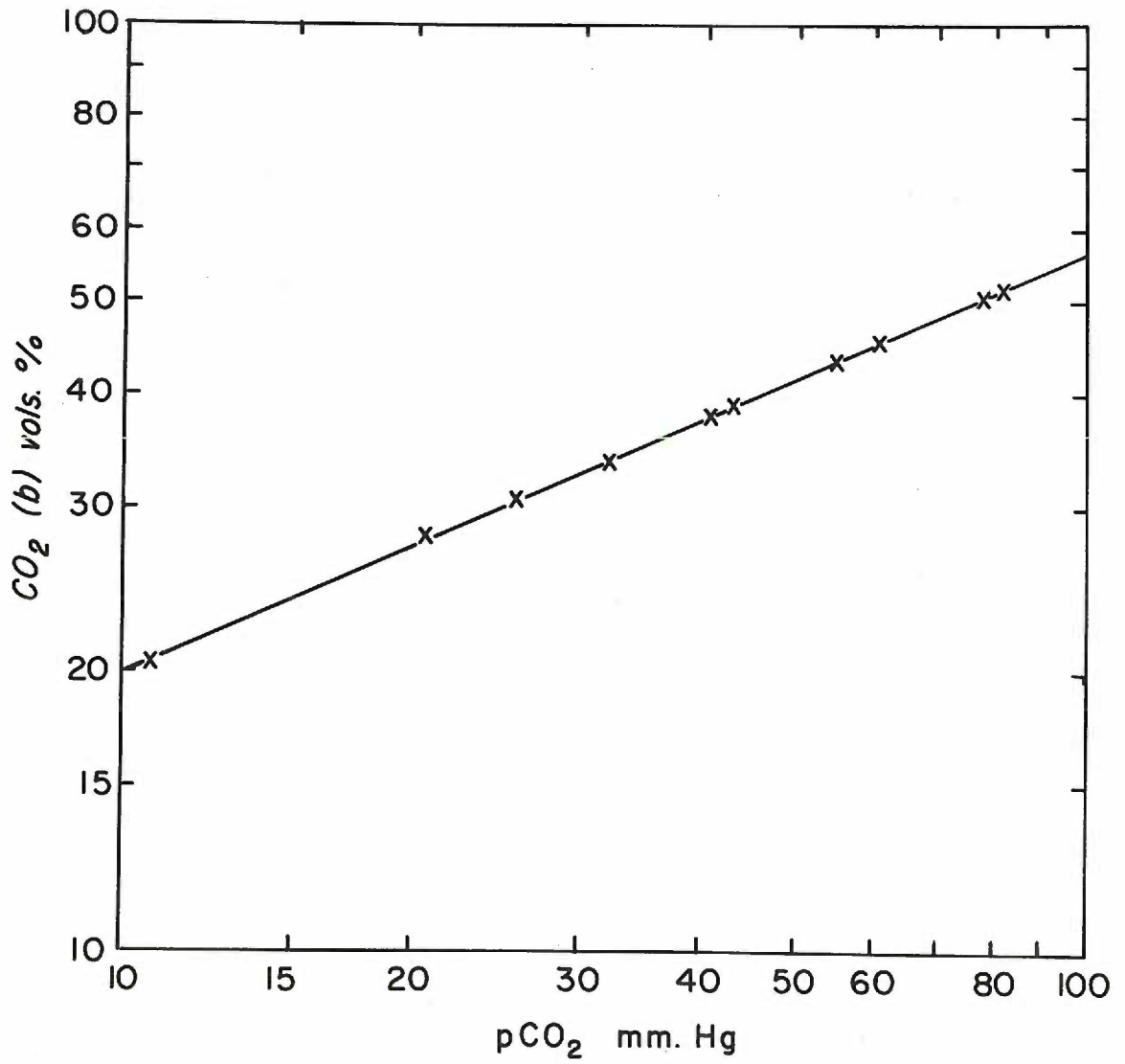
curves were transferred to the d'Ocagne nomogram. The curvature of the partial pressure of oxygen and carbon dioxide lines on the nomogram were established by locating those partial pressures of each gas which were used in two or more gas mixtures by placing a ruler through the carbon dioxide and oxygen contents obtained with each gas mixture and locating the intersection. The curve was then drawn through these points.

The intervening partial pressures of carbon dioxide were established graphically at 100 per cent oxygen saturation on Peters' (58) double log graph of partial pressure of carbon dioxide and carbon dioxide content (figure 9). The intervening partial pressures of oxygen were established graphically at a constant 34 volumes per cent carbon dioxide by describing oxygen contents in volumes per cent at various partial pressures of oxygen (figure 10). Figure 11 shows the completed nomogram for fetal blood.

Maternal Blood. Blood samples were drawn from arm veins of eight pregnant women, less than eighteen days before labor. The women were considered clinically normal, as were the infants at birth. Their blood samples were equilibrated with the gas mixture in tank No. 9, which consisted of 93.3 per cent oxygen and 6.05 per cent carbon dioxide. There was no consistent difference in oxygen and carbon dioxide contents obtained after equilibration of blood containing sodium fluoride and the oxygen and carbon dioxide contents, corrected for changes in acidity, obtained

Figure 9

Graphical estimation of the intervening carbon dioxide contents and partial pressures in fetal blood.



All at 100 % O₂ saturation

Figure 10

Graphical estimation of the intervening oxygen contents and partial pressures in fetal blood.

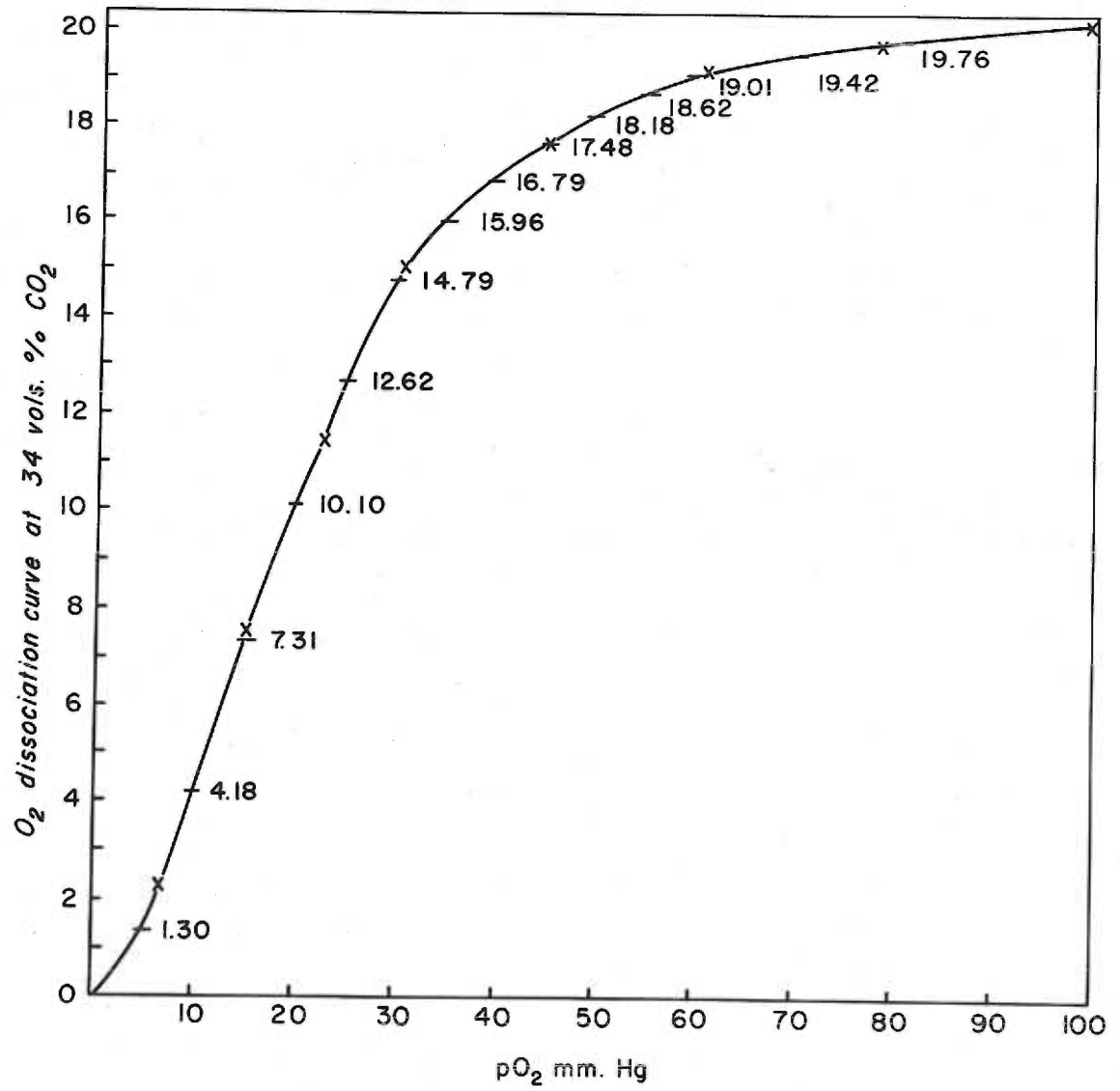
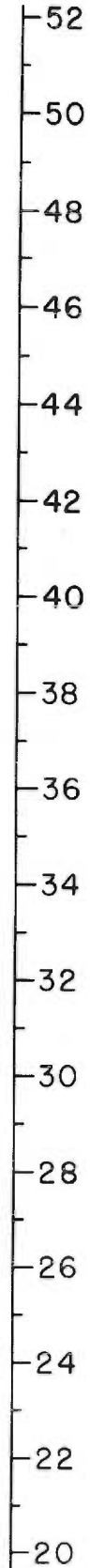


Figure 11

Completed nomogram for fetal blood.

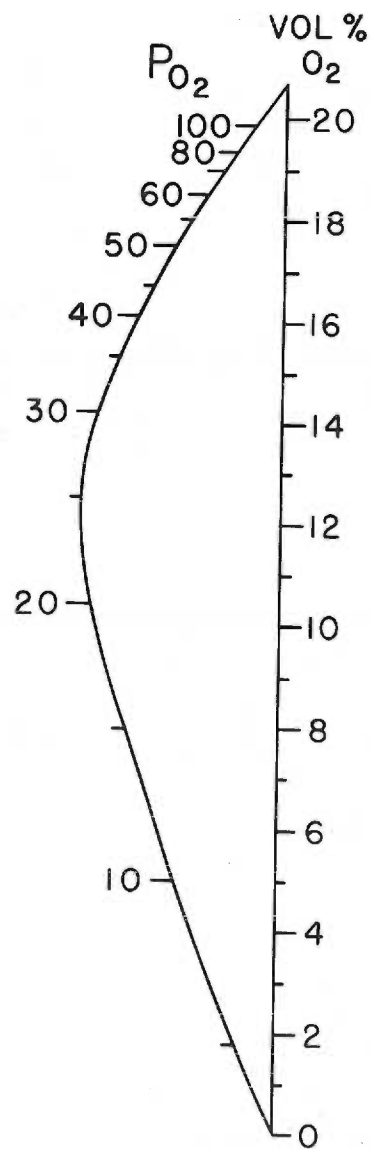
VOL % CO₂



P_{CO2}



FETAL WHOLE BLOOD



from equilibrating blood without fluoride. Equilibrations with two other gas mixtures were performed on three of the blood samples. Experimental data are listed in Table XI, as previous data on fetal blood determinations were listed in Tables V and IX. The number of days that blood was drawn prior to delivery is listed in Table XI. Carbon dioxide content correction for acid produced during equilibration are listed. When the blood contained no fluoride, the carbon dioxide content correction was determined in the same manner as was done with the first group of fetal blood determinations. An asterisk with "non-fluoride" carbon dioxide content corrections marks those cases in which this scheme was used. The carbon dioxide correction listed for blood containing fluoride merely represents the difference between the carbon dioxide contents obtained on twenty minutes' equilibrations both on blood with and without fluoride, on the blood from the same patient. An asterisk with "fluoride" carbon dioxide content corrections merely indicates that the carbon dioxide content obtained on blood containing fluoride was used, actually without correction. The means and standard deviations for oxygen capacity and carbon dioxide contents are listed in Table XII.

Peters (57,62) established that the slope of the straight line on the double log graph of carbon dioxide partial pressure and carbon dioxide content is a function of the oxygen capacity or hemoglobin content. The difference in carbon dioxide contents in volumes per cent between

Mother Tank
No. No.

		pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Vols.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	CO ₂ without corr. (Vols.%)	CO ₂ with corr. (Vols.%)
4.	(1) 20 min.	---	---	---	---	---	---	---
	(2) 20 min.	---	---	---	---	---	---	---
	(1) or (2) 40 min.	---	---	---	---	---	---	---
	(9) 20 min.	42.57	656.46	17.13	1.96	15.17	41.64	42.81
	(9) 40 min.	---	---	16.97	1.96	15.01	40.47	---
	(9) fluoride	---	---	---	---	---	---	---
alpha = 2.27 T.P. = 703.6 Hct. = 35.0 18 days bef. delivery CO ₂ corr. (non-fl.) = *1.17								
5.	(1) 20 min.	---	---	---	---	---	---	---
	(2) 20 min.	---	---	---	---	---	---	---
	(1) or (2) 40 min.	---	---	---	---	---	---	---
	(9) 20 min.	42.45	654.89	18.42	1.96	16.46	43.06	---
	(9) 40 min.	---	---	18.49	1.96	16.53	42.02	---
	(9) fluoride	---	---	18.10	1.96	16.14	44.27	44.27
alpha = 2.28 T.P. = 701.7 Hct. = 36.0 6 days bef. delivery CO ₂ corr. (non-fl.) = 1.04 CO ₂ corr. (fl.) = *1.21								
6.	(1) 20 min.	---	---	---	---	---	---	---
	(2) 20 min.	---	---	---	---	---	---	---
	(1) or (2) 40 min.	---	---	---	---	---	---	---
	(9) 20 min.	42.93	662.06	18.78	1.99	16.79	44.79	---
	(9) 40 min.	---	---	18.83	1.99	16.84	42.96	---
	(9) fluoride	---	---	18.89	1.99	16.90	45.99	45.99
alpha = 2.28 T.P. = 709.6 Hct. = 37.5 18 days bef. delivery CO ₂ corr. (non-fl.) = 1.84 CO ₂ corr. (fl.) = *1.20								

Mother Tank No.	No.	Time	pCO ₂ mm. Hg	pO ₂ mm. Hg	Orig. O ₂ (Vols.%)	Diss. O ₂ (Vols.%)	Hb O ₂ (Vols.%)	CO ₂ without corr. (Vols.%)	CO ₂ with corr. (Vols.%)
7.	(1)	20 min.	-----	-----	-----	-----	-----	-----	-----
	(2)	20 min.	-----	-----	-----	-----	-----	-----	-----
	(1)	or (2) 40 min.	-----	-----	-----	-----	-----	-----	-----
	(9)	20 min.	42.91	661.78	18.00	1.98	16.02	43.81	-----
	(9)	40 min.	-----	-----	18.36	1.98	16.38	41.62	-----
	(9)	fluoride	-----	-----	17.72	1.98	15.74	44.10	44.10
			alpha = 2.27						
			T.P. = 709.3						
			Hct. = 36.0						
			9 days bef. delivery						
			CO ₂ corr. (non-fl.) = 2.19						
			CO ₂ corr. (fl.) = *0.29						
8.	(1)	20 min.	-----	-----	-----	-----	-----	-----	-----
	(2)	20 min.	-----	-----	-----	-----	-----	-----	-----
	(1)	or (2) 40 min.	-----	-----	-----	-----	-----	-----	-----
	(9)	20 min.	42.86	660.94	18.52	1.99	16.53	43.39	-----
	(9)	40 min.	-----	-----	18.56	1.99	16.57	43.84	-----
	(9)	fluoride	-----	-----	-----	-----	-----	-----	43.84
			alpha = 2.29						
			T.P. = 708.4						
			Hct. = 35.0						
			17 days bef. delivery						
			CO ₂ corr. (fl.) = *0.45						

Table XII

Final Maternal Blood Gas Contents

Part I
Equilibrated with Tank No. 9

Mother No.	CO ₂ (Vols. %)	O ₂ (Vols. %)
1	42.37	14.85
2	43.26	17.10
3	42.55	17.92
4	42.81	15.17
5	44.27	16.14
6	45.99	16.90
7	44.10	15.74
8	43.84	16.57
Mean	43.65	16.30
Standard Deviation	1.18	1.03

Dissolved oxygen at 120 mm. Hg $pO_2 = 0.36$ vols. %

Oxygen capacity = $16.30 + 0.36 = 16.66$ vols. %

Part II
Equilibrated with Tanks No. 1 and No. 2

Tank No. 1

Mother No.	CO ₂ (Vols. %)	O ₂ (Vols. %)	O ₂ (% sat.)
1	34.80	4.13	27.81
2	35.65	4.38	25.61
3	33.93	4.45	24.83
Mean	34.79	-----	26.08

Tank No. 2

Mother No.	CO ₂ (Vols. %)	O ₂ (Vols. %)	O ₂ (% sat.)
1	33.56	10.20	68.69
2	32.78	11.08	64.80
3	32.56	11.01	61.44
Mean	32.97	-----	64.98

The contents of oxygen and carbon dioxide given below have the same relationship to the mean contents obtained with bloods equilibrated with tank No. 9 as do the obtained oxygen and carbon dioxide contents given above have to the contents in maternal blood samples No. 1, No. 2, and No. 3 equilibrated with tank No. 9.

	Tank No. 1	Tank No. 2
CO ₂	35.71	33.89
O ₂	4.30	10.68

those obtained at 60 mm. and 30 mm. Hg partial pressures of carbon dioxide at a constant oxygen per cent saturation is equal to a constant multiplied by the oxygen capacity plus another constant (62).

$$\Delta[\text{CO}_2]_{60 - 30} = 0.334 (\text{Oxygen capacity, vols. \%}) + 6.3$$

The two constants are 0.334 and 6.3. The mean oxygen capacity of the maternal blood is 16.66 volumes per cent.

$$\Delta[\text{CO}_2]_{60 - 30} = 0.334 (16.66) + 6.3$$

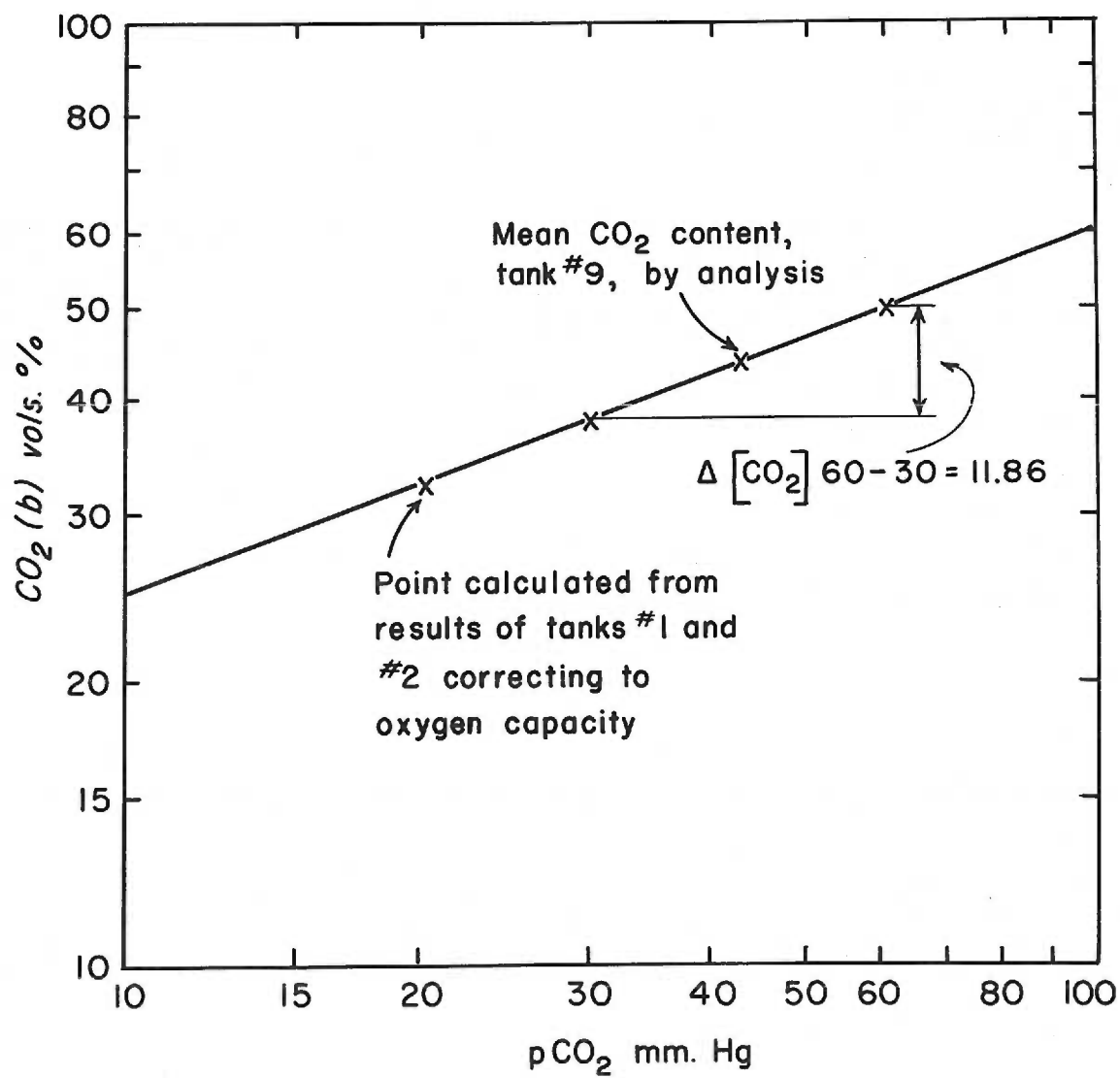
$$\Delta[\text{CO}_2]_{60 - 30} = 11.86 \text{ volumes per cent}$$

The difference in carbon dioxide contents between those obtained at 60 mm. Hg and 30 mm. Hg partial pressure of carbon dioxide is 11.86 volumes per cent. The mean carbon dioxide content experimentally determined for gas mixture No. 9 is 42.73 volumes per cent at a mean carbon dioxide partial pressure of 43.65 mm. Hg and oxygen saturation. With a point and a slope, the major portion of the entire carbon dioxide curve is plotted on double log paper in figure 12.

The three oxygen and carbon dioxide contents obtained at equilibration with the gas mixtures No. 1 and No. 2 (from those used for the first fetal group) were used to locate the 20 mm. Hg carbon dioxide partial pressure point on the nomogram. A straight line from the oxygen capacity through the 20 mm. Hg carbon dioxide point on the nomogram intersected the carbon dioxide content line at 32 volumes per cent. In figure 12, this content of carbon dioxide obtained at a partial pressure of 20 mm. Hg carbon

Figure 12

Means of estimating the carbon dioxide dissociation curves knowing one carbon dioxide content at one carbon dioxide partial pressure and the oxygen capacity. A carbon dioxide content experimentally determined and corrected to oxygen capacity at 20 mm. Hg $p\text{CO}_2$ verified the method.



dioxide at oxygen saturation lies on the line established by Peters' oxygen capacity method. This was used as a check of Peters' method of determining the carbon dissociation curve slope by oxygen capacity.

The pH of the serum was established as follows. Blood carbon dioxide content in volumes per cent was converted to plasma carbon dioxide content in millimoles per liter (63). The pH of the serum was then calculated by the Henderson-Hasselbalch equation.

$$\text{pH}_s = 6.10 + \log \frac{[\text{total CO}_2]_p - 0.0301 \text{ pCO}_2}{0.0301 \text{ pCO}_2}$$

The plasma carbon dioxide contents and pH_s values determined are listed in Table XIII. The pH_s line was drawn on the maternal nomogram along a line in the same position that it appears on the "normal" adult nomogram (60) (figure 8). The pH_s values on this line, however, do not coincide.

To establish the maternal oxygen dissociation curve, the nomogram of "normal" adult blood (60) (figure 8) was used, altered in regard to maternal oxygen capacity and pH_s . The partial pressure of oxygen was obtained for each value of oxygen saturation and pH_s on the "normal" adult blood nomogram using a straight edge ruler. The ruler was then placed through the same value of oxygen saturation and pH_s on the maternal nomogram. The point representing the partial pressure of oxygen was placed on this line at a distance from the oxygen content line equal to the corresponding distance on the "normal" adult nomogram. The

Table XIII

Serum pH Values Determined from Carbon Dioxide Contents
and Partial Pressures on Maternal Blood

mm.Hg pCO ₂	Vols. % Blood CO ₂	Vols. % Plasma CO ₂	mM./l.	pHs
15	29.1	30.35	13.63	7.565
16.25	30	31.57	14.18	7.547
20	32.5	35.00	15.72	7.500
24.25	35	38.47	17.28	7.456
25	35.4	39.03	17.53	7.448
30	38	42.67	19.17	7.406
34.1	40	45.49	20.44	7.377
35	40.3	45.92	20.63	7.369
40	42.6	49.20	22.10	7.339
42.73	43.65	50.73	22.79	7.323
45	44.5	51.96	23.34	7.310
46.1	45	52.67	23.66	7.306
50	46.3	54.60	24.53	7.285
55	48.2	57.36	25.77	7.263
60	49.9	59.86	26.89	7.243
60.5	50	60.02	26.96	7.238
65	51.3	61.99	27.85	7.222
70	52.9	64.37	28.92	7.205
75	54.2	66.37	29.82	7.187
77.5	55	67.56	30.85	7.180
80	55.8	68.75	30.88	7.173

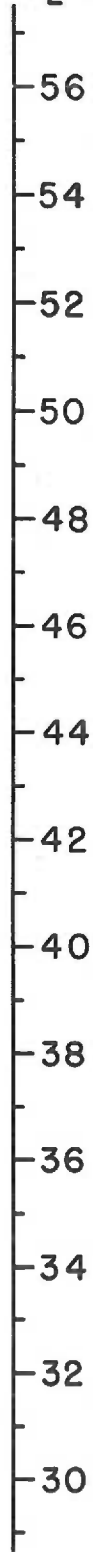
complete maternal blood nomogram is shown in figure 13.

Construction of Carbon Dioxide and Oxygen Iso-
pleths on the pO_2 - pCO_2 Diagram. Using the maternal and fetal nomograms, the carbon dioxide and oxygen content isopleths were drawn on separate pO_2 - pCO_2 diagrams (1). The fetal blood pO_2 - pCO_2 diagram is shown in figure 14. The maternal blood pO_2 - pCO_2 diagram is shown in figure 15.

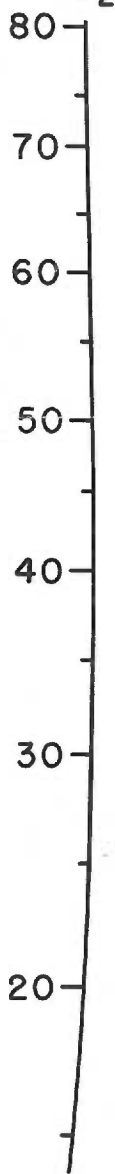
Figure 13

Completed nomogram for maternal blood.

VOL. %
CO₂ (b)



P_{CO₂}



pH (s)



MATERNAL BLOOD

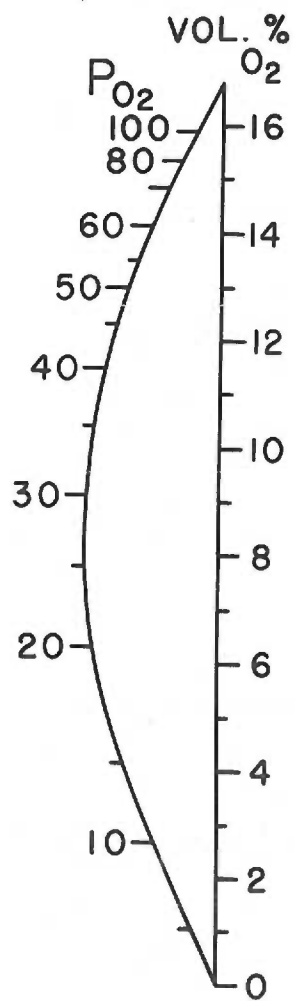


Figure 14

Fetal blood dissociation curves on O_2 - CO_2 diagram.

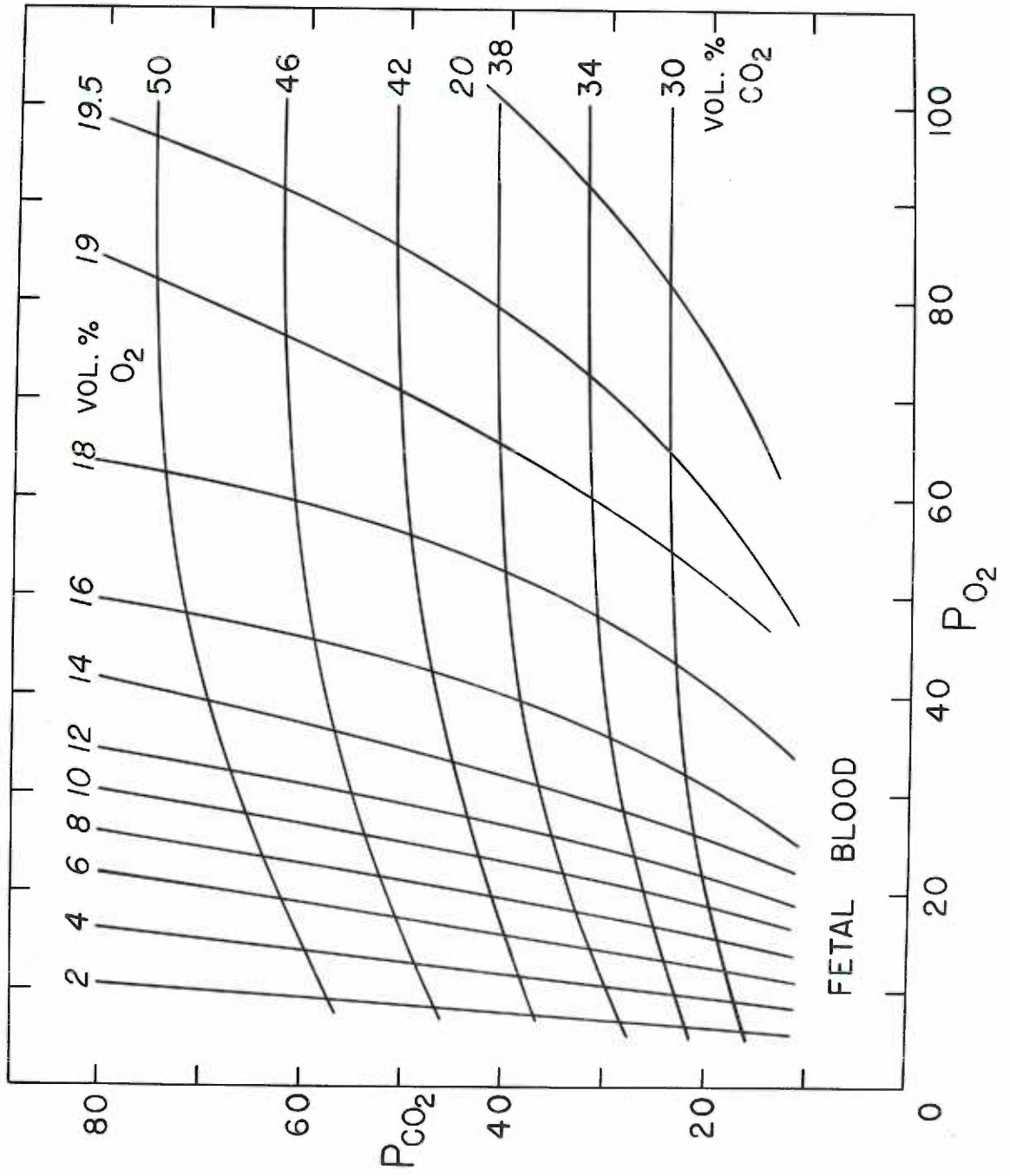
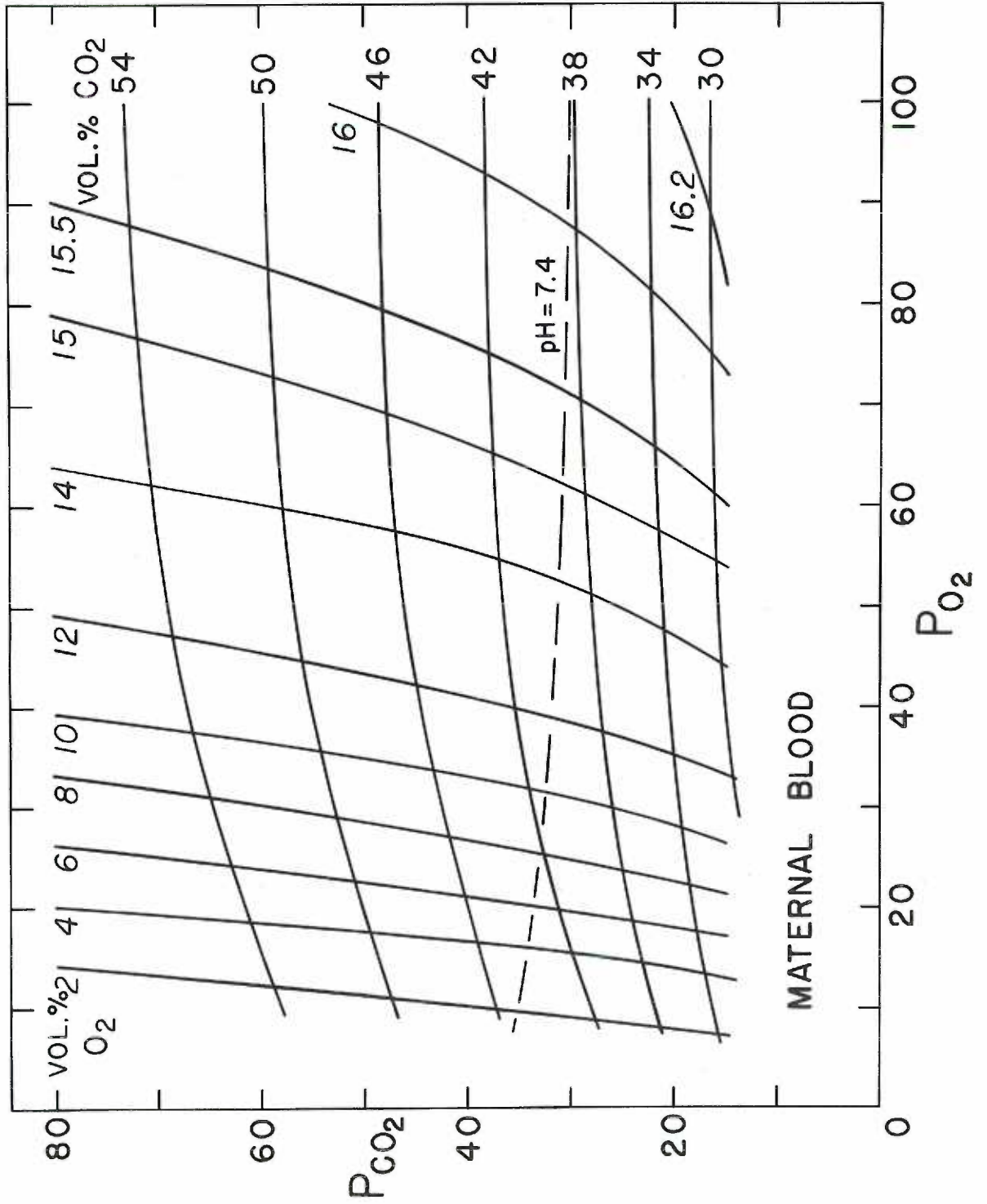


Figure 15

Maternal blood dissociation curves on O_2 - CO_2 diagram.



DISCUSSION AND CONCLUSIONS

The carbon dioxide and oxygen dissociation curves obtained in this study are those of the mother and the fetus at or within three weeks of delivery. They, therefore, do not necessarily represent the carbon dioxide and oxygen dissociation curves of either mother or fetus earlier in pregnancy.

With the corrections used for carbon dioxide and oxygen contents, the population of fetal blood dissociation curves corresponds with those of each group of fetal blood samples that were determined on blood taken from the placentas at elective routine caesarean sections. The caesarean sections were performed because of the obstetrical routine of doing an operative delivery on all pregnant women who have previously been delivered by this method. There was no clinical evidence of fetal hypoxic distress or maternal disease that required the operation. The fetal dissociation curves are therefore taken to represent those of fetal blood when the fetus is in the uterus, at term but before labor.

The fetal dissociation curves, when compared to those of the blood of the normal adult (60) (figure 8), demonstrated a much more pronounced Bohr effect, the influence of increasing carbon dioxide upon inhibiting the oxygenation of hemoglobin. This may be observed by noting the displacement of the oxygen partial pressure line to the left on the

nomogram of the fetus (figure 11) compared to that displacement in the nomogram of the normal adult (figure 8). This may be an important mechanism by which the fetal blood can unload oxygen in the fetal tissues where the partial pressure of oxygen is low and the partial pressure of carbon dioxide is elevated. No appreciable difference in the magnitude of the Haldane Effect was noted.

Both the fetal and maternal carbon dioxide combining powers were less than those established as normal for the non-pregnant adult (60) (figure 8). This confirms all previous investigations. The fetal blood carbon dioxide combining power was less than that of the maternal blood, agreeing closely with the observations of Eastman, Geiling, and DeLawder (13). This indicates that the pregnant woman at term has a metabolic acidosis, either primary or secondary to hyperventilation causing respiratory alkalosis. In either case, hyperventilation must be occurring. Using the maternal curves obtained in this study, the alveolar and arterial partial pressure of carbon dioxide must be about 30-32mm. Hg in order that the blood possess a normal pH of 7.4. The partial pressure of carbon dioxide corresponding to pH of 7.4 at a partial pressure of 100-110 mm. Hg in normal blood (figure 8) is about 40 mm. Hg. The partial pressure of carbon dioxide in the maternal blood at the placenta must therefore be lower than it would be if the changes in carbon dioxide combining power and ventilation had not occurred. The

hyperventilation would elevate the partial pressure of oxygen of the maternal alveolar and arterial blood about 10 mm. Hg (at normal respiratory exchange ratios) but the resulting alveolar partial pressure of oxygen of 100-110 mm. Hg would not appreciably elevate the oxygen content of the maternal arterial blood.

It is hoped that the dynamic aspects of maternal-fetal blood gas transport can be illustrated by the utilization of this information, using the recently developed O₂-CO₂ diagram (1). It may be possible to draw a maternal-fetal perfusion-perfusion curve to demonstrate the quantitative aspects of changes in partial pressures of the respiratory gases resulting from changes in the maternal-fetal perfusion-perfusion ratio, the individual placental perfusions of maternal and fetal blood and maternal pulmonary function. The location of this maternal-fetal perfusion-perfusion curve would be established by the respiratory exchange ratio for each blood stream, the partial pressures of the respiratory gases in the maternal alveoli and arterial blood, and the partial pressures of the respiratory gases in the fetal mixed venous blood (the umbilical artery). If the fetus is considered to be a maternal tissue supplied by the maternal blood stream, it might be postulated that the fetal R (respiratory exchange ratio) determines the maternal R for that maternal blood perfusing the placenta.

Preliminary establishment of R lines between

arbitrarily chosen maternal arterial and fetal mixed venous points, using the appropriate blood dissociation curves, indicates that equal R values for each superimpose almost perfectly, in spite of the reported differences between maternal and fetal blood dissociation curves. This, however, awaits further study for confirmation.

The foregoing discussion serves to illustrate the utility of the dissociation curves derived in this study and it is hoped that future research will be directed toward the resolution of problems in fetal respiration using these nomograms as a basic tool.

SUMMARY

1. Blood samples from twenty-seven placentas and eight pregnant women at term were equilibrated with various gas mixtures containing various partial pressures of oxygen and carbon dioxide. These were then analyzed for blood gas content.
2. The oxygen and carbon dioxide dissociation curves were obtained and expressed on both the d'Ocagne nomogram and the O_2 - CO_2 diagram.
3. The carbon dioxide combining powers of both maternal and fetal blood were low, compared to blood of the normal adult.
4. The fetal blood studies indicate that a more marked Bohr effect is present in fetal than in normal adult blood.
5. Oxygen capacities for both maternal and fetal blood were obtained.
6. A maternal-fetal perfusion-perfusion ratio concept was discussed.

BIBLIOGRAPHY

1. Rahn, Hermann, and Wallace O. Fenn. A Graphical Analysis of the Respiratory Gas Exchange, the O_2 - CO_2 Diagram. The American Physiologic Society, Washington D. C., 38 pages, 1955.
2. Barcroft, J., R. H. E. Elliott, L. B. Flexner, F. G. Hall, W. Herkel, E. F. McCarthy, T. McClurkin, and M. Talaat. Conditions of Fetal Respiration in the Goat. *Journal of Physiology* 83, pp. 192-214, 1934-5.
3. McCarthy, E. F. The Oxygen Affinity of Human Maternal and Fetal Haemoglobin. *Journal of Physiology* 102, pp. 55-61, 1943.
4. Jonxis, J. H. P. Foetal Haemoglobin and Rh Antagonisms. Haemoglobin, a Symposium, New York, pp. 261-7, 1949.
5. Wyman, Jeffries Jr., J. A. Rafferty, and Elizabeth N. Ingalls. Solubility of Adult and Fetal Carboxyhemoglobin of the Cow. *Journal of Biological Chemistry* 153, pp. 275-284, 1944.
6. Jope, H. M., and J. R. P. O'Brien. Crystallization and Solubility Studies on Human Adult and Fetal Hemoglobins. Haemoglobin, a Symposium, New York, pp. 269-278, 1949.
7. Allen, David W., Jeffries Wyman, Jr., and Clement A. Smith. The Oxygen Equilibrium of Fetal and Adult Hemoglobin. *The Journal of Biological Chemistry* 203, pp. 81-87, 1953.
8. Hall, F. G. A Spectroscopic Comparison of Foetal and Maternal Blood in the Rabbit and Goat. *Journal of Physiology* 82, pp. 33-37, 1934.
9. Hall, F. G. Haemoglobin Function in the Developing Chick. *Journal of Physiology* 83, pp. 222-228, 1934-5.
10. McCutcheon, F. H. Hemoglobin Function During the Life History of the Bullfrog. *Journal of Cellular and Comparative Physiology* 8, pp. 63-81, 1936.
11. Barron, D. H. Some Aspects of the Placental Transfer of Oxygen across the Syndesmochorial Placenta of the Sheep. *Yale Journal of Biology and Medicine* 24, pp. 169-190, 1951.

12. Leibson, R. G., I. I. Likhnitzky, and M. G. Sax. Oxygen Transport of the Foetal and Maternal Blood during Pregnancy. *Journal of Physiology* 87, pp. 97-111, 1936.
13. Eastman, W. J., E. M. K. Geiling, and A. M. DeLawder. Fetal Blood Studies. IV. The Oxygen and Carbon Dioxide Dissociation Curves of Fetal Blood. *Bulletin of the Johns Hopkins Hospital* 53, pp. 246-254, 1933.
14. Darling, Robert C., Clement A. Smith, Erling Assmussen, and Felix M. Cohen. Some Properties of Human Fetal and Maternal Blood. *Journal of Clinical Investigation* 20, pp. 739-747, 1941.
15. Bohr, Chr., K. Hasselbalch, und August Krogh. Ueber einen in biologischer Beziehung Wichtigen Einfluss, den die Kohlensäurespannung des Blutes auf dessen Sauerstoffbindung übt. *Skandinavisches Archiv für Physiologie* 16, pp. 402-412, 1904.
16. Barcroft, Joseph. *The Respiratory Function of the Blood*. Cambridge, 317 pages, 1914.
17. Ylppö, A. Neugeborenen, Hunger, und Intoxikationsacidosis in ihren Beziehungen Zueinander. *Zeitschrift für Kinder Heilkunde* 14, pp. 268-448, 1916.
18. Keys, Ancel B. The Carbon Dioxide Balance Between the Maternal and Foetal Bloods in the Goat. *Journal of Physiology* 80, pp. 491-501, 1933-4.
19. Williamson, A. C. Acid-Base Equilibrium in Pregnancy and the Newborn. *American Journal of Obstetrics and Gynecology* 6, pp. 263-275, 1923.
20. Döring, Gerd K., und Hans H. Loescheke. Atmung and Säure-Basengleichgewicht in der Schwangerschaft. *Pflüger's Archiv für die Gesamte Physiologie* 249, pp. 437-450, 1947-8.
21. Kaiser, Irwin H. The Hydrogen Ion Concentration of Human Fetal Blood in Utero at Term. *Science* 118, pp. 29-30, 1953.
22. Bell, W. Blair, L. Cunningham, M. Jowett, H. Millet, and J. Brooks. The Metabolism and Acidity of the Foetal Tissues and Fluids. *British Medical Journal* 1, pp. 126-130, 1928.
23. Barron, Donald H. A Comparative Study of the Alkali Reserve of Normal, Pregnant, and Fetal Sheep. *Yale Journal of Biology and Medicine* 26, pp. 119-125, 1953.

24. Rähkä, C. E. Ueber Einege Neugeborenenprobleme. *Acta Paediatrica* 28, pp. 390-406, 1941.
25. Wilson, James L., Helen S. Reardon, Makio Murayama, Bruce Graham, M. U. Tsao, and M. L. Baumann. Anaerobic Metabolism in the Newborn Infant. I. On the Resistance of the Fetus and Newborn to Oxygen Lack. *Pediatrics* 1, pp. 581-591, 1948.
26. Branning, W. S. Acid-Base Balance of Premature Infants. *Journal of Clinical Investigation* 21, pp. 101-105, 1942.
27. Eastman, N. J., and C. M. McLane. Fetal Blood Studies. II. The Lactic Acid Content of Umbilical Cord Blood Under Various Conditions. *Bulletin of the Johns Hopkins Hospital* 48, pp. 261-268, 1931.
28. Marples, E., and V. W. Lippard. Acid-Base Balance of Newborn Infants. *American Journal of Diseases of Children* 44, pp. 31-39, 1932.
29. Barcroft, J., J. A. Kennedy, and M. F. Mason. Oxygen in the Blood of the Umbilical Vessels of Sheep. *Journal of Physiology* 97, pp. 347-356, 1940.
30. VanSlyke, Donald D., and James M. Neill. The Determinations of Gases in Blood and Other Solutions by Vacuum Extractions and Manometric Measurement. *Journal of Biological Chemistry* 61, pp. 523-573, 1924.
31. Riley, R. L., D. D. Proemmel, and R. E. Franke. A Direct Method for Determination of Oxygen and Carbon Dioxide Tensions in Blood. *Journal of Biological Chemistry* 161, pp. 621-633, 1945.
32. Walker, James, and Elizabeth P. W. Turnbull. Haemoglobin and Red Cells in the Human Foetus and Their Relation to the Oxygen Content of the Blood in the Vessels of the Umbilical Cord. *The Lancet* 2, pp. 312-318, 1953.
33. Walker, James. Foetal Anoxia. *The Journal of Obstetrics and Gynaecology of the British Empire* LXI, pp. 162-180, 1954.
34. Eastman, N. J. Foetal Blood Studies. I. The Oxygen Relationship of Umbilical Cord Blood at Birth. *Bulletin of the Johns Hopkins Hospital* XLVII, pp. 221-230, 1930.

35. Goldbloom, Alton, and Rudolf Gottlieb. Icterus Neonatorum. III. The Oxygen Capacity and Saturation of the Mother and Foetus. *Journal of Clinical Investigation* 9, pp. 139-142, 1930-1.
36. Dieckmann, W. J., and Sylvia Kramer. Serial Studies of Oxygen and Carbon Dioxide Content of Human Cord Blood. *Proceedings of the Society for Experimental Biology and Medicine* 55, pp. 242-243, 1944.
37. Eastman, N. J. Foetal Blood Studies. III. The Chemical Nature of Asphyxia Neonatorum and its Bearing on Certain Practical Problems. *Bulletin of the Johns Hopkins Hospital* 50, pp. 39-50, 1932.
38. Haselhorst, G., und K. Stromberger. Über den Gasgehalt des Nabelschnurblutes vor und nach der Geburt des Kindes und über den Gasaustausch in der Plazenta. *Zeitschrift für Geburtshilfe und Gynäkologie* 98, pp. 49-78, 1930.
39. Haselhorst, G., und K. Stromberger. Über den Gasgehalt des Nabelschnurblutes vor und nach der Geburt des Kindes und über den Gasaustausch in der Plazenta. *Zeitschrift für Geburtshilfe und Gynäkologie* 100, pp. 48-70, 1931.
40. Haselhorst, G., und K. Stromberger. Über den Gasgehalt des Nabelschnurblutes vor und nach der Geburt des Kindes und über den Gasaustausch in der Plazenta. *Zeitschrift für Geburtshilfe und Gynäkologie* 102, pp. 16-36, 1932.
41. Clemetson, C. A. B. Oxygen and Carbon Dioxide Content of Umbilical Artery and Vein Blood in Toxaemic and Normal Pregnancy. *The Journal of Obstetrics and Gynaecology of the British Empire* 60, pp. 335-344, 1953.
42. Watts, Joseph, Harold Henderson, D. H. Kaump, and R. M. Davis. Oxygen Studies of the Arterial Blood in Newborn Infants. *American Journal of Obstetrics and Gynecology* 61, pp. 1025-1033, 1951.
43. Lund, Curtis J. Studies on the Iron Deficiency Anemia of Pregnancy. *American Journal of Obstetrics and Gynecology* 62, pp. 947-961, 1951.
44. Huggett, A. StG. Foetal Blood-Gas Tensions and Gas Transfusion through the Placenta of the Goat. *Journal of Physiology* 62, pp. 373-384, 1926-7.

45. Mossman, Harland W. The Rabbit Placenta and the Problem of Placental Transmission. *The American Journal of Anatomy* 37, pp. 433-497, 1926.
46. Wilkin, P. Contribution a l'étude de la Circulation Placentaire d'origine Foetale. *Gynecologie et Obstetrique* 53, pp. 239-263, 1954.
47. Assali, N. S. Measurement of Uterine Blood Flow and Uterine Metabolism. *American Journal of Obstetrics and Gynecology* 66, pp. 3-10, 1953.
48. Metcalfe, James, Seymour L. Romney, Lloyd H. Ramsay, and Duncan E. Reid. Measurement of Uterine Blood Flow in Pregnancy. *Journal of Clinical Investigation* 32, pp. 589-590, 1953.
49. Assali, N. S., Roy A. Douglass, Jr., William W. Baird, D. B. Nicholson, and Roy Suyemoto. Measurement of Uterine Blood Flow and Uterine Metabolism. IV. Results in Normal Pregnancy. *American Journal of Obstetrics and Gynecology* 66, pp. 248-253, 1953.
50. Romney, Seymour L., Duncan E. Reid, James Metcalfe, and C. Sidney Burwell. Oxygen Utilization by the Human Fetus in Utero. *American Journal of Obstetrics and Gynecology* 70, pp. 791-799, 1955.
51. Bjork, V. O., and H. J. Hilty. Microvolumetric Determination of CO_2 and O_2 Tensions in Arterial Blood. *Journal of Applied Physiology* 6, pp. 800-808, 1954.
52. Scholander, P. F. Analyzer for Accurate Estimation of Respiratory Gases in One-half Cubic Centimeter Samples. *Journal of Biological Chemistry* 167, pp. 235-250, 1947.
53. Christiansen, Johanne, C. G. Douglas, and J. S. Haldane. The Absorption and Dissociation of Carbon Dioxide by Human Blood. *Journal of Physiology* xlviii, pp. 244-271, 1914.
54. Evans, C. Lovatt. Acid Production in Shed Blood. *Journal of Physiology* 56, pp. 146-156, 1922.
55. Austin, J. H., G. E. Cullen, A. B. Hastings, F. C. McLean, J. P. Peters, and D. D. VanSlyke. Studies of Gas and Electrolyte Equilibria in Blood. I. Technique for Collection and Analysis of Blood, and for its Saturation with Gas Mixtures of Known Composition. *Journal of Biological Chemistry* 54, pp. 121-146, 1922.

56. Sendroy, Julius Jr., Robert T. Dillon, and Donald D. VanSlyke. Studies of Gas and Electrolyte Equilibria in Blood. XIX. The Solubility and Physical State of Uncombined Oxygen in Blood. *Journal of Biological Chemistry* 105, pp. 597-632, 1934.
57. Peters, John P., Harold A. Bulger, and Anna J. Eisenman. Studies of the Carbon Dioxide Absorption Curve of Human Blood. IV. The Relation of the Hemoglobin Content of Blood to the Form of the Carbon Dioxide Absorption Curve. *Journal of Biological Chemistry* 58, pp. 747-768, 1923-4.
58. Peters, John P., Anna J. Eisenman, and Harold A. Bulger. Studies of the Carbon Dioxide Absorption Curve of Human Blood. II. The Nature of the Curve Representing the Relation of pH to BHCO_3 . *Journal of Biological Chemistry* 55, pp. 709-716, 1923.
59. Henderson, Lawrence J. *Blood, A Study in General Physiology*. Yale University Press, New Haven, 389 pages, 1928.
60. Dill, D. B., H. T. Edwards, and W. V. Consolazio. Blood as a Physicochemical System. XI. Man at Rest. *Journal of Biological Chemistry* 118, pp. 635-648, 1937.
61. Dill, D. B., John H. Talbott, and W. V. Consolazio. Blood as a Physicochemical System. XII. Man at High Altitudes. *Journal of Biological Chemistry* 118, pp. 649-666, 1937.
62. Peters, John P., Harold A. Bulger, and Anna J. Eisenman. Studies of the Carbon Dioxide Absorption Curve of Human Blood. V. The Construction of the CO_2 Absorption Curve from one Observed Point. *Journal of Biological Chemistry* 58, pp. 769-771, 1923-4.
63. Peters, John P., Harold A. Bulger, and Anna J. Eisenman. Studies of the Carbon Dioxide Absorption Curve of Human Blood. VI. The Relationship of the CO_2 of Blood to that of Plasma. *Journal of Biological Chemistry* 58, pp. 773-791, 1923-4.