

## Effect of Normal and Preeclamptic Pregnancies on the Oxyhemoglobin Dissociation Curve

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Hemoglobin affinity for oxygen in whole blood of ten normal nonpregnant women, ten normal pregnant women at first trimester, ten normal pregnant women at second trimester, 24 normal pregnant women at or near term, and 14 pregnant women with preeclampsia at or near term was studied. The mean P-50 values for normal nonpregnant women, normal pregnant women in first trimester, second trimester, and at or near term were  $26.7 \pm 0.11$  mmHg,  $27.8 \pm 0.08$  mmHg,  $28.8 \pm 0.17$  mmHg, and  $30.4 \pm 0.20$  mmHg, respectively. The mean P-50 of pregnant women with preeclampsia at or near term was  $25.1 \pm 0.38$  mmHg. It is concluded that in normal pregnant women there was a significant shift of P-50 to the right compared with the normal nonpregnant women ( $P < 0.01$ ), and the extent of this shift to the right is directly related to the duration of the pregnancy. In addition, preeclamptic parturients showed a significant shift of P-50 to the left when compared with normal pregnant women at or near term ( $P < 0.001$ ). (Key words: Measurement techniques: oxygen saturation. Oxygen: oxyhemoglobin dissociation; P-50; transport. Pregnancy: normal; preeclampsia.)

HEMOGLOBIN AFFINITY FOR OXYGEN is one of the factors controlling delivery of oxygen to tissues, including the placenta and, concomitantly, the fetus. Data on hemoglobin affinity for oxygen in normal pregnant women at or near term have been conflicting,<sup>1-4</sup> and data from pregnant women in the first and second trimesters are not reported. We studied hemoglobin affinity for oxygen in whole blood from a group of normal nonpregnant women and normal pregnant women in the first trimester, in the second trimester, and at or near term.

Preeclampsia (pregnancy-induced hypertension with proteinuria, edema, or both after 20-weeks gestation) is a disease of pregnancy resulting in diminished perfusion and oxygen supply to various tissues, including the fetus.<sup>5-7</sup> The effect of preeclampsia on the oxyhemoglobin dissociation curve is not reported. Hemoglobin affinity for oxygen may be important when there is an alteration in perfusion, as in the case of preeclampsia. Therefore, we also studied hemoglobin affinity for oxygen in preeclamptic parturients at or near term.

### Methods

This study was approved by the Committee for the Protection of Human Subjects, and informed permission was obtained from each patient. Five ml of venous blood was drawn into a heparinized syringe from each volunteer. The blood was immediately equilibrated in an Instrumentation Laboratories 237 Tonometer<sup>®</sup> with gas mixtures containing 3.5% and 4.5% oxygen, 5.6% carbon dioxide and the balance nitrogen at 37° C for 15 min. Total hemoglobin, per cent oxyhemoglobin saturation, and per cent carboxyhemoglobin saturation were measured in a Radiometer, OSM2 Hemoximeter<sup>®</sup>. The blood gases were measured in a Corning<sup>®</sup> 168 pH/blood gas analyzer. Barometric pressure adjustments were made in the blood gas machine.

The Radiometer, OSM2 Hemoximeter<sup>®</sup>, and the pH, P<sub>CO<sub>2</sub></sub>, and P<sub>O<sub>2</sub></sub> electrodes of Corning<sup>®</sup> 168 pH/blood gas analyzer were calibrated before and after each determination. The measured P<sub>O<sub>2</sub></sub> data were corrected to pH 7.40. Because the uniform carbon dioxide in the gas mixtures gave a normal P<sub>CO<sub>2</sub></sub> of 40 mmHg and the blood gas measurements were made at 37° C, no P<sub>CO<sub>2</sub></sub> or temperature corrections were needed. A two-point saturation curve was plotted in the linear portion of the oxyhemoglobin dissociation curve, and P-50 (see "Discussion") was obtained from the saturation curve for normal pregnant women, normal nonpregnant women, and preeclamptic women.

Analysis with one-way analysis of variance (ANOVA) and testing by the Newman-Keul's test was used to compare nonpregnant and normal pregnant groups. A difference was considered significant if  $P < 0.05$ . Student's *t* test was used to determine the significance of difference between the preeclamptic group and the normal pregnant group at term.

### Results

Table 1 contains the values of P-50 of normal nonpregnant, pregnant, and preeclamptic women. The shift of P-50 to the right was significant at all three trimesters of pregnancy when compared with the normal nonpregnant women ( $P < 0.01$ ). The mean P-50 value for pregnant women with preeclampsia at or near term was  $25.1 \pm 0.38$  mmHg. There was a  $5.2 \pm 0.82$  mmHg shift of P-50 to the left in preeclamptic women at or near term

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when compared with normal pregnant women at or near term, and this shift was statistically significant ( $P < 0.001$ ).

All of the women had hemoglobin values between 10.5 and 14.0 g/dl (mean 12 g/dl), and carboxyhemoglobin values of less than 1%.

### Discussion

The release of oxygen to tissues is influenced by the affinity of hemoglobin for oxygen. This affinity of hemoglobin for oxygen is commonly expressed as P-50, which is the partial pressure of oxygen at which 50% of hemoglobin is saturated at a pH of 7.40,  $P_{CO_2}$  of 40 mmHg, and temperature of 37° C. The volume of oxygen that can be unloaded to the tissues at a given  $P_{O_2}$  is increased with a higher P-50 (shift to the right) and decreased with a lower P-50 (shift to the left).

In pregnancy, oxygen demand of various tissues, including placenta and fetus, is increased.<sup>8</sup> Therefore, compensation must occur or a corresponding deficit in oxygen delivery to the tissues will occur. This compensation takes the form of increased blood flow (cardiac output), increased red blood cell volume,<sup>9</sup> and increased P-50. A shift to the right of P-50 is advantageous in patients with borderline cardiac reserve and in situations where further increase in cardiac output is not possible. In addition, a shift of P-50 to the right is beneficial in situations such as aorto-caval compression syndrome and antepartum hemorrhage where there is an acute decrease in cardiac output.

Our P-50 values in pregnant women at term agree with the results of Bauer *et al.*,<sup>4</sup> Liebson *et al.*,<sup>1</sup> and Darling *et al.*,<sup>2</sup> who also showed a rightward shift of P-50 in normal pregnancy. On the other hand, Prystowski *et al.* reported no significant change in P-50 in normal pregnancy.<sup>3</sup> Prystowski *et al.* used a methodology in which they did not maintain a standard  $P_{CO_2}$  of 40 mmHg and a temperature of 37° C in the determination of P-50 values. We believe their method may account for the difference in results.

In summary, our data demonstrated a significant shift of the oxyhemoglobin dissociation curve to the right in normal pregnant women compared with normal non-

TABLE I. P-50 Values of Nonpregnant, Pregnant, and Preeclamptic Subjects

Subjects		P-50 (mmHg)	
Status	n	Mean	SEM
Nonpregnant*	10	26.7	0.11
Pregnant			
1st trimester*	10	27.8	0.08
2nd trimester*	10	28.8	0.17
At or near term*	24	30.4	0.20
Preeclamptic†	14	25.1	0.38

\* All means significantly different from one another ( $P < 0.01$ ), Newman-Keul's test.

† Significance level of difference between pregnant at term and preeclamptic at term ( $P < 0.001$ ).

pregnant women ( $P < 0.01$ ), and the extent of this shift to the right appears to be directly related to the duration of the pregnancy. Our data also show a significant shift of P-50 to the left in preeclamptic parturients when compared with normal parturients ( $P < 0.001$ ) at term.

### References

1. Leibson RG, Likhnitzki II, Sax MG: Oxygen transport of the fetal and maternal blood during pregnancy. *J Physiol (Lond)* 87: 97-112, 1936
2. Darling RC, Smith CA, Asmussen E: Some properties of human fetal and maternal blood. *J Clin Invest* 20:739-747, 1941
3. Prystowski H, Hellegers A, Bruns P: A comparative study of the oxygen dissociation curve. *Am J Obstet Gynecol* 78:489-493, 1959
4. Bauer C, Ludwig M, Ludwig I, Bartels H: Factors governing the oxygen affinity of human adult and foetal blood. *Respir Physiol* 7:271-276, 1969
5. Dixon HG, Brown JCM, Davey DA: Choroiddecidual and myometrial blood flow. *Lancet* 2:369, 1963
6. Johnson T, Clayton CG: Diffusion of radioactive sodium in normotensive and pre-eclamptic pregnancies. *Br Med J* 1:312, 1957
7. Chesley LC: *Hypertensive Disorders in Pregnancy*. New York, Appleton-Century-Crofts, 1978, pp 445-476
8. Pernoll ML, Metcalf J, Schlenker TL, Matsumoto JA: Oxygen consumption at rest and during exercise in pregnancy. *Respir Physiol* 25:285, 1975
9. Peck TM, Arias F: Hematologic changes associated with pregnancy. *Clin Obstet Gynecol* 22:785-798, 1979