Evaluation of Antenatal and Perinatal Vitamin C Status in Pregnancies Threatened with Prematurity

S. C. Sharma

Department of Pharmacology and Therapeutics, Trinity College, Dublin 2, Republic of Ireland

Although the cause of prematurity is often difficult to ascertain, many conditions can predispose the pregnant woman to preterm labor. Abruptio placentae, placenta praevia, and preeclampsia are some of the conditions that cause (or necessitate) an early termination of pregnancy. Although placenta praevia is generally regarded as an anatomical abnormality (1), hematological changes characteristic of folic acid deficiency are a common feature in women suffering from abruptio placentae (2,3); however, the administration of folic acid supplements to pregnant women (4) or the determination of maternal blood folate activity (5-7) has failed to show conclusively that the condition is related to folic acid deficiency. Its cause has remained unknown, and the condition is a major threat to the successful outcome of human pregnancy.

Preeclampsia is another condition that can cause fetal and maternal morbidity, but its etiology is equally obscure. Numerous theories have been put forward to explain its cause(s), but none has so far been proven (8). We have investigated whether levels of ascorbic acid in abruptio placentae, placenta praevia, unexplained prematurity, and preeclampsia are different from those in the normal pregnancy. In addition, we have assessed the fetal supply of ascorbic acid in these conditions by measuring its concentrations in the fetal umbilical vein immediately following delivery.

SUBJECTS AND METHODS

Levels of total ascorbic acid (TAA) in antecubital vein blood were measured in 80 samples from 45 women with abruptio placentae and in 85 samples from 45 women with placenta praevia. In addition, blood samples from ma-
ternal antecubital vein and fetal umbilical vein were obtained from eight women with placenta praevia and seven women with abruptio placentae immediately following their vaginal deliveries. [Full details of subjects with placenta praevia and 42 subjects with abruptio placentae can be found in an earlier publication (9).] Three additional women in the group with abruptio placentae were between 30 and 34 years, and two of them had one previous pregnancy. The third had two previous pregnancies. Two of the three women were delivered at 38 weeks, and the third at 39 weeks of gestation. All three were delivered by the vaginal route, but signs of fetal distress were found in one of the babies. All the subjects in the abruptio placentae group had bleeding from the normally situated placenta, whereas those with placenta praevia had shown some degree of placental displacement. On admission, the diagnosis was based on history, physical examination, and ultrasonic placentography. Cases of abruptio placentae were further confirmed by close examination of the placenta at the time of delivery. The presence of depression with retroplacental clot and/or evidence of infarction on the placenta established the diagnosis. Patients in whom the diagnosis could not be made with certainty and those with twin pregnancies were excluded from the study.

Levels of TAA were also estimated in 25 cases of unexplained prematurity. Only those subjects in whom the threat of premature labor had revealed itself by the onset of labor pains, with or without the rupture of membranes, were selected. At the time of delivery the gestation in these patients varied from 28 to 36 weeks. Only one blood sample per subject was collected from the antecubital vein, after admission to hospital but before the start of any treatment. A second sample from maternal antecubital vein was collected from eight women immediately following their deliveries. Corresponding numbers of fetal umbilical vein blood samples were also simultaneously collected.

In addition, peripheral blood levels of TAA were measured in 53 women with preeclampsia. Preeclampsia was defined where a blood pressure of at least 140/90 mm Hg in association with edema and proteinuria was present in patients with a history of normal blood pressure in early pregnancy. Forty-one of these subjects had urinary protein values of over 1 g/24 hr and were classified as severe preeclampsia patients. The other 12 had lower protein values and were grouped as moderate preeclampsia subjects. One blood sample per patient from the antecubital vein was collected at admission and before treatment. A second antecubital blood sample from ten subjects with severe preeclampsia and eight with moderate preeclampsia was collected immediately following their vaginal deliveries. Equal numbers of fetal umbilical vein blood samples were also simultaneously obtained from these subjects. [Further details on these patients may be found in an earlier publication (10).]

For ascorbic acid values, samples of antecubital vein blood were obtained
from 86 women attending the antenatal clinic. A single sample was taken from each woman at different times of their gestational periods. All the subjects were nonfasting, aged 16 to 37 years, and had no history of medical or gynecological abnormalities. Their present pregnancies were normal, and none of the women were taking supplemental vitamin C. On the basis of their dietary intake they consumed 90 to 150 mg ascorbic acid/day.

All the patients in the above studies and the women with normal pregnancies had volunteered to participate in the study. Methods for blood collection and TAA estimations were the same as described earlier (11).

RESULTS AND DISCUSSION

Placental Bleeding

The results shown in Table 1 indicate that mean blood levels of TAA in abruptio placentae vary from 0.67 to 0.80 mg/100 ml. In each group they are significantly lower than the values found either in placenta praevia or normal pregnancy. These comparisons are based on the length of gestation at which the blood samples were collected. Single blood samples were obtained from 19 women in the abruptio placentae and 17 in the placenta praevia group. From all others, serial blood samples were obtained at weekly intervals. This compares with one sample per person collected in the normal pregnancy.

<table>
<thead>
<tr>
<th>Gestation (weeks)</th>
<th>Abruptio placentae</th>
<th>Placenta praevia</th>
<th>Normal pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>28–31</td>
<td>0.78 ± 0.070</td>
<td>1.06 ± 0.075</td>
<td>1.06 ± 0.090</td>
</tr>
<tr>
<td>(n = 23)</td>
<td>(n = 26)</td>
<td>(n = 25)</td>
<td></td>
</tr>
<tr>
<td>32–34</td>
<td>0.80 ± 0.081</td>
<td>1.24 ± 0.086</td>
<td>1.18 ± 0.136</td>
</tr>
<tr>
<td>(n = 19)</td>
<td>(n = 21)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td>35–37</td>
<td>0.72 ± 0.079</td>
<td>1.14 ± 0.062</td>
<td>1.07 ± 0.109</td>
</tr>
<tr>
<td>(n = 20)</td>
<td>(n = 22)</td>
<td>(n = 20)</td>
<td></td>
</tr>
<tr>
<td>38–40</td>
<td>0.67 ± 0.061</td>
<td>1.16 ± 0.094</td>
<td>0.99 ± 0.114</td>
</tr>
<tr>
<td>(n = 18)</td>
<td>(n = 16)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td>28–40</td>
<td>0.74 ± 0.035</td>
<td>1.14 ± 0.039</td>
<td>1.07 ± 0.055</td>
</tr>
<tr>
<td>(n = 80)</td>
<td>(n = 85)</td>
<td>(n = 86)</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 1. Comparison of blood levels of TAA in abruptio placentae with those in placenta praevia and the third trimester of normal pregnancy at different gestational periods (mean ± SEM)*

* Adapted from Sharma et al. (9).

b p < 0.05, compared with values in the placenta praevia group and the normal group.

c p < 0.01, compared with values in the placenta praevia group and the normal group.
Although the total number of blood samples collected per person in the abruptio placentae and the placenta praevia groups did not exceed four, the possibility remains that subjects with low (or high) blood TAA values and multiple samples may have influenced the level of significance shown in Table 1. In order to exclude this possibility the results displayed in Fig. 1 are based on one sample per person collected on the first day of admission of subjects with abruptio placentae or placenta praevia.

The results shown in Fig. 1 show that approximately 71% of the women with abruptio placentae have TAA values below 0.8 mg/100 ml, compared with 14% with placenta praevia and 30.2% with normal pregnancy. Furthermore, 13.3% of the subjects with abruptio placentae have TAA values between 0.8 and 1.2 mg/100 ml, compared with 33% with placenta praevia and 23.2% with normal pregnancy. It is also interesting that only 4.4% of the abruptio placentae patients have values over 1.6 mg/100 ml blood, compared with 15.5% in placenta praevia and 21% in normal pregnancy.

Table 2 shows that fetal umbilical vein blood in abruptio placentae has a mean TAA value of 1.17 mg/100 ml. This compares with a mean value of 1.70 mg/100 ml in placenta praevia and 1.62 mg/100 ml in normal pregnancy. Furthermore, maternal (antecubital vein) to fetal (umbilical vein) blood ratio of ascorbic acid in abruptio placentae is lower than the ratio found in either placenta praevia or in normal pregnancy.
TABLE 2. Fetal umbilical vein blood levels and maternal:fetal ratios of TAA in abruptio placentae, placenta praevia, and normal pregnancy (mean ± SEM)

<table>
<thead>
<tr>
<th>Subject</th>
<th>n</th>
<th>TAA (mg/100 ml)</th>
<th>Maternal:fetal ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abruptio placentae</td>
<td>7</td>
<td>1.17* ± 0.094</td>
<td>1.71* ± 0.145</td>
</tr>
<tr>
<td>Placenta praevia</td>
<td>8</td>
<td>1.70 ± 0.215</td>
<td>2.11 ± 0.096</td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>12</td>
<td>1.62 ± 0.158</td>
<td>2.00 ± 0.101</td>
</tr>
</tbody>
</table>

* \( p > 0.05, \) but < 0.1, compared with values in the normal pregnancy group.

The present investigation has demonstrated that maternal and fetal levels of ascorbic acid in abruptio placentae are considerably below normal. The fetus in this condition seems to receive low ascorbic acid mainly due to low maternal levels, although the maternal:fetal blood TAA ratio is also somewhat reduced; however, this does not seem to be the case in placenta praevia. Maternal or fetal levels of ascorbic acid in placenta praevia, or the fetal blood in abruptio placentae, have not been previously estimated, but Clemetson and Cafaro (12) have similarly found low maternal plasma ascorbic acid levels in abruptio placentae.

Whether low TAA can play an important role in the genesis of abruptio placentae is not known, but ascorbic acid is essential in a number of biochemical processes in the body. It is required in the synthesis of collagen (13) and in the maintenance of various vascular structures (14). In addition, it is essential in the formation and maintenance of intercellular material in the human body (15). Thus, its deficiency could result in the development of placental lesions, such as necrosis of the marginal basal decidua and infarction of placenta commonly observed in abruptio placentae (16).

From earlier studies, it has been suggested that folic acid deficiency is closely related to the occurrence of abruptio placentae (17–19); however, the administration of folic acid supplements from an early stage of pregnancy has not produced rewarding results (4). It is possible that folic acid utilization (rather than folic acid deficiency) or, indeed, the deficiency of other nutritional factors in the body is important in reducing the incidence of abruptio placentae and the associated megaloblastic anemia reported in earlier studies (17,20). May et al. (21,22) have demonstrated that prolonged feeding of ascorbic-acid-deficient diets to immature infants and monkeys produces megaloblastic anemia, which responds to folic acid but can also be cured by ascorbic acid.

Low blood ascorbic acid in abruptio placentae could have been the result of inadequate supply, decreased absorption from the gastrointestinal tract, and/or enhanced degradation and elimination from the body. Ascorbic acid is mainly absorbed by a specialized carrier-mediated process (23,24); however, there is no evidence that this process in abruptio placentae is in any
way impaired. Mucosal cell abnormality is associated with poor absorption of vitamin E from the gastrointestinal tract (25), but there is no evidence that such an abnormality does exist in abruptio placentae and indeed can affect ascorbic acid absorption. There is also no evidence for the enhanced degradation and elimination of ascorbic acid in these subjects.

We have recently shown that plasma levels of certain fat-soluble vitamins and carotenoids are low in abruptio placentae (26), and others have found a common occurrence of this condition in populations with poor socioeconomic conditions (18,27). Because foods rich in carotenoids and vitamin A are also rich in vitamin C, low intake of these foods in patients with abruptio placentae could have been the reason for low ascorbic acid levels in these patients; however, the social backgrounds of our subjects with abruptio placentae and placenta praevia were about the same, but levels of ascorbic acid in placenta praevia were not below normal.

Prematurity

Ten patients delivered between 28 and 34 weeks, and the other 15 delivered during 35 to 37 weeks of gestation. In Table 3 the blood ascorbic acid levels in these groups are compared with values at similar periods of gestation in normal pregnancy. Two types of comparisons have been made, and in one the total number of subjects in prematurity has been combined.

The results show that mean blood TAA levels in prematurity, although lower, are not significantly different from the values in normal pregnancy ($p > 0.05$ for both comparisons); however, combined TAA blood values from the total population of prematurity show a significant difference at 90% confidence limits ($p < 0.1$) from values in the normal pregnancy, suggesting that the level of significance may be real and may depend on the number of

<table>
<thead>
<tr>
<th>Gestation (weeks)</th>
<th>TAA (mg/100 ml)</th>
<th>Level of significance ($p$ value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prematurity</td>
<td>Normal pregnancy</td>
</tr>
<tr>
<td></td>
<td>$n = 10$</td>
<td>$n = 44$</td>
</tr>
<tr>
<td>28–34</td>
<td>0.86 ± 0.117</td>
<td>1.11 ± 0.078</td>
</tr>
<tr>
<td>35–37</td>
<td>0.93 ± 0.131</td>
<td>1.13 ± 0.098</td>
</tr>
<tr>
<td>28–37</td>
<td>0.90 ± 0.090</td>
<td>1.12 ± 0.060</td>
</tr>
</tbody>
</table>

TABLE 3. Comparison of maternal blood ascorbic acid levels in prematurity with those in normal pregnancy at different gestational periods (mean ± SEM)
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FIG. 2. Comparison of distribution pattern of maternal blood TAA values in prematurity (PM) with normal pregnancy (NP) of 28–37 weeks gestation.

populations in each group. This view is further supported by our observation that a larger proportion of women delivering prematurely have low blood ascorbic acid. These results are shown in Fig. 2. In prematurity, 56% of subjects have blood TAA values below 0.8 mg/100 ml, compared with 26.6% in normal pregnancy. (For this comparison, subjects of 28–37 weeks of gestation only are considered.) As a result, the percentage of subjects with TAA values over 0.8 mg/100 ml blood in prematurity is considerably reduced.

Fetal umbilical vein blood in prematurity has a mean TAA value of 1.18 mg/100 ml, in comparison with a mean value of 1.62 mg/100 ml in normal pregnancy. Maternal (antecubital vein) to fetal (umbilical vein) blood ratio of ascorbic acid is only slightly reduced in prematurity. These results are shown in Table 4.

Wideman and Baird (28) have found that the incidence of premature rup-

<table>
<thead>
<tr>
<th>Subject</th>
<th>n</th>
<th>TAA (mg/100 ml)</th>
<th>Maternal:fetal ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>8</td>
<td>1.18 ± 0.99</td>
<td>1.89 ± 0.208</td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>12</td>
<td>1.62 ± 0.158</td>
<td>2.00 ± 0.101</td>
</tr>
</tbody>
</table>

*p > 0.05, but < 0.1, compared with values in the normal pregnancy.
ture of membranes and of premature labor is high in women who have below-normal plasma levels of ascorbic acid. We have measured levels of TAA in the blood of women threatened with premature labor, but our results would seem to support the view of these workers. In addition, however, we have found that fetal supply of ascorbic acid in these subjects is also below normal. Although this could be explained on the basis of low maternal levels, it is not yet clear if the values in the maternal circulation reflect inadequate supply, inefficient absorption, and/or quick metabolism of ascorbic acid.

Women threatened with premature labor of unknown etiology have a higher estrogen/progesterone ratio than women with normal pregnancies. This may be due to increased blood levels of estrogen (29) or decreased levels of progesterone (30), but the overall effect would be increased estrogenic activity. Estrogen treatment in the human can raise plasma ceruloplasmin levels (31), and this is known to have ascorbate oxidase properties (32). An increased activity of this enzyme could cause increased ascorbic acid breakdown in these patients.

Whatever the reason, low ascorbic acid values in these subjects could predispose them to untimely rupture of their fetal membranes. Ascorbic acid is required for the synthesis of collagen (13) and for the maintenance of various vascular structures (14). Its deficiency could therefore reduce the tensile strength of these membranes and lead to their premature rupture.

Preeclampsia

Thirty-two subjects in our study were primigravidas, and others had one or more previous pregnancies. Twenty-five of the primigravidas were under the age of 29 years and had severe preeclampsia. Their mean blood TAA value of 1.29 mg/100 ml was, however, not significantly different \((p > 0.05)\) from the corresponding value of 1.18 mg/100 ml found in 10 parous women with severe preeclampsia in a similar age group.

In Table 5, TAA values from the two populations of severe and moderate preeclampsia have been combined and compared on the basis of gestational lengths with TAA values in normal pregnancy. The results show that mean ascorbic acid levels in preeclampsia vary from 1.05 to 1.44 mg/100 ml blood. Although in each group they are higher than the values in the corresponding weeks of normal gestation, it is only during the period of 28 to 31 weeks that they are significantly different from those in the normal pregnancy group. Combined results from the two populations also indicate that the distribution pattern of ascorbic acid values in preeclampsia is not different from that of normal pregnancy. The results are shown in Fig. 3.

In about half of the subjects with preeclampsia, the TAA values are similar to those of normal pregnancy, and they lie between 0.8 and 1.6 mg/100 ml blood. In preeclampsia the percentage of subjects with low TAA values \((<0.8\)
TABLE 5. Comparison of maternal blood ascorbic acid in preeclampsia with normal pregnancy at different gestational periods* (mean ± SEM)

<table>
<thead>
<tr>
<th>Gestation (weeks)</th>
<th>TAA (mg/100 ml)</th>
<th>Preeclampsia</th>
<th>Normal pregnancy</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28–31</td>
<td>1.44 ± 0.086</td>
<td>1.06 ± 0.090</td>
<td>(n = 10)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>32–34</td>
<td>1.30 ± 0.149</td>
<td>1.18 ± 0.136</td>
<td>(n = 12)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>35–37</td>
<td>1.25 ± 0.163</td>
<td>1.07 ± 0.109</td>
<td>(n = 15)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>38–40</td>
<td>1.05 ± 0.076</td>
<td>0.99 ± 0.114</td>
<td>(n = 16)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

* From Sharma et al. (10).

mg/100 ml) is only 6% lower, whereas that with high TAA values (>1.6 mg/100 ml) is 11% higher than for normal pregnancy.

When blood TAA values in severe preeclampsia and in moderate preeclampsia are compared separately with those in the normal pregnancy, however, a significant difference is found for the first comparison but not for the second. These results are shown in Table 6. Fetal umbilical vein blood has a mean TAA value of 1.35 mg/100 ml in severe preeclampsia and 1.64 mg/100 ml in moderate preeclampsia. Neither of the two values are signif-

![FIG. 3. Comparison of distribution pattern of maternal blood TAA values in preeclampsia (PE) (moderate and severe combined) with normal pregnancy (NP).](image-url)
TABLE 6. Comparison of maternal blood ascorbic acid in preeclampsia with normal pregnancy*

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>TAA (mg/100 ml) (mean ± SEM)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe and moderate preeclampsia</td>
<td>53</td>
<td>1.24 ± 0.065</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>41</td>
<td>1.29 ± 0.076</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Moderate preeclampsia</td>
<td>12</td>
<td>1.09 ± 0.113</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>86</td>
<td>1.07 ± 0.055</td>
<td>—</td>
</tr>
</tbody>
</table>

* Adapted from Sharma et al. (10).

significantly different (p > 0.05 for both comparisons) from the mean TAA value of 1.62 mg/100 ml found in normal pregnancy, although the value in severe preeclampsia seems to be considerably reduced. Maternal (antecubital vein) to fetal (umbilical vein) blood ratio of ascorbic acid in severe preeclampsia is, however, significantly reduced (p < 0.05). The results are shown in Table 7. Chesley (33) has suggested that preeclampsia is a disease restricted to primigravidas. He has further proposed that the presence of this condition in multiparous pregnancy must have a precedent of some vascular or endocrine abnormality. In the present study the levels of TAA in primigravidas were not significantly different from those in multiparous women. This is interesting, since Sheppard and Bonnar (34) have also demonstrated that the placental morphology in the two groups of patients is not different.

In severe preeclampsia the maternal blood ascorbic acid was raised, whereas that of fetal blood was somewhat reduced. This was not, however, the case in moderate preeclampsia, where values near normal were found both in the fetal and maternal circulation. A restricted placental perfusion is known to occur in preeclampsia (35,36), and increased maternal TAA values in severe preeclampsia may simply reflect a decreased perfusion of ascorbic acid from maternal to fetal circulation.

Plasma levels of ascorbic acid do not bear any relationship to the actual values in blood or to the prevailing clinical picture in patients (37). Neither

TABLE 7. Fetal umbilical vein blood levels and maternal:fetal ratios of TAA in preeclampsia and in normal pregnancy (mean ± SEM)

<table>
<thead>
<tr>
<th>Subject</th>
<th>n</th>
<th>TAA (mg/100 ml)</th>
<th>Maternal:fetal ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe preeclampsia</td>
<td>10</td>
<td>1.35 ± 0.120</td>
<td>1.59* ± 0.128</td>
</tr>
<tr>
<td>Moderate preeclampsia</td>
<td>8</td>
<td>1.64 ± 0.155</td>
<td>1.89 ± 0.123</td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>12</td>
<td>1.62 ± 0.158</td>
<td>2.00 ± 0.101</td>
</tr>
</tbody>
</table>

* p < 0.05, compared with values in normal pregnancy.
do they reflect levels in body tissues and may even lead to fallacious conclusions (38,39). We have therefore measured ascorbic acid levels in blood and not in plasma. Nevertheless, our results are not mutually exclusive from those obtained by earlier workers (40,41). Both teams found low plasma levels of L-ascorbic acid (LAA) in preeclampsia. They have independently suggested that in preeclampsia, the ascorbic acid metabolism is altered and that this leads to a fall in LAA and consequently to a decline in the LAA to dehydroascorbic acid (DHAA) ratio. According to earlier published work, however, it is the DHAA form of ascorbic acid that can readily penetrate blood cells (42). Here it is converted back to LAA (43), which is not readily soluble in the lipoidal membrane (42), and is thus retained within the blood cells. An increased passage of DHAA into blood cells, followed by its conversion into LAA and subsequent retention by the blood cell in preeclampsia, could be the reason for high blood TAA levels found in the present study. Levels of circulating Cu$^{2+}$ in preeclampsia are high (44,45), and Cu$^{2+}$ can increase the oxidation of LAA to DHAA (41,46,47); however, fetal blood ascorbic acid in severe preeclampsia was decreased, not increased.

There was also a significant reduction in maternal (antecubital vein) to fetal (umbilical vein) blood ascorbic acid ratio. The most likely explanation of the altered blood ascorbic acid value in preeclampsia is therefore its retention by the maternal blood cells. Such a shift of ascorbic acid from plasma to blood cells would reduce its plasma levels (as found by the above workers) and decrease its availability for transfusion into fetal circulation. The fetal supply of ascorbic acid may be further curtailed by the restricted placental perfusion present in these patients.

**SUMMARY AND CONCLUSIONS**

1. In abruptio placentae and prematurity, maternal blood total ascorbic acid (TAA) is reduced. The maternal to fetal blood TAA ratio is, however, not significantly reduced. The results suggest that the fetal supply of ascorbic acid in these patients is curtailed because of low maternal levels.

2. In placenta praevia, maternal blood TAA is not significantly reduced. Neither is the maternal to fetal blood TAA ratio. The results indicate that in placenta praevia, the fetal supply of ascorbic acid is not significantly altered.

3. In preeclampsia, maternal blood TAA is increased, and this seems to depend on the severity of the condition. Fetal blood TAA is reduced, as is the maternal to fetal blood TAA ratio. The results suggest that ascorbic acid is retained by the maternal blood cells. This leads to its low plasma levels and low availability to the fetus.
ACKNOWLEDGMENTS

The financial help of F. Hoffmann-La Roche & Co. Ltd., Basle, and the technical help of Ken Scott are gratefully acknowledged. Professor J. Bonnar kindly provided facilities in his department; Dr. M. Walzmann and Dr. A. Sabra obtained blood samples.

REFERENCES