THE ACID-BASE EQUILIBRIUM IN ABNORMAL PREGNANCY

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In previous papers (9, 14) we have discussed the changes that occur in the acid-base equilibrium of serum of normal women during pregnancy. In brief, these changes are reduction of the serum carbon dioxide content and serum proteins, accompanied by a comparable reduction of total base. These findings have been confirmed by Stander, Eastman, Harrison, and Cadden (21). The reduction of serum proteins appeared to be at the expense of the albumin fraction (5, 9, 17). Stander et al. (21) reported a normal hydrogen ion concentration and this has been confirmed by us (9). Thus the reduction of the carbon dioxide content of the serum, which has long been known to occur during the course of normal pregnancy, is associated with a diminished total base and not an accumulation of other "acids."

The explanation of these abnormal findings remains obscure and it was felt that a study of abnormal pregnancy might contribute not only to the solution of the pathogenesis of the toxemias themselves but also to the explanation of the acid-base disturbances in normal pregnancy.

During the course of pregnancy there may occur one of a group of disorders, loosely termed the toxemias of pregnancy. Because of their obscure etiology as well as clinical diversity, the classification of the toxemias has been difficult and confused. The numer-

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ous investigations of these disorders have been confined mainly
to determinations of blood carbon dioxide and nitrogenous con-
stituents. These investigations have been reviewed by Stander
(19). Because they have consisted of more or less isolated obser-
vations discussed without proper relation to the changes found in
normal pregnancy they have not aided in the solution of the
general problem. Stander et al. (20, 21) and Muntwyler, Lim-
bach, Bill, and Myers (13) have described complete acid-base
studies in abnormal pregnancy. These will be discussed below.
In this paper are reported studies of the complete acid-base equi-
librium of the serum of patients with abnormal pregnancy during
the acute phase and, in so far as was possible, after recovery.

Methods

The methods for withdrawal of blood and the analytical pro-
cedures and calculations utilized in these investigations have been
described in previous papers from this laboratory (9, 14). The
pH was determined gasometrically, with the value for pK_1 of
6.12. The vomitus was analyzed by techniques similar to those
used for serum. In the less acute cases the blood was withdrawn
in the morning before the patient's breakfast. In cases with
convulsions or severe vomiting the first blood sample was with-
drawn as soon as possible after the patient entered the hospital,
before treatment was instituted.

Results

Results of the analyses are presented diagrammatically in Charts
I to III. The acid anions actually determined by analysis were
bicarbonate, chloride, phosphate, and protein. The sum of these
subtracted from the total base, the undetermined acids, is pre-
sumably composed of sulfates and organic acids. In the absence
of evidence that sulfates accumulate in excess in the serum in
pregnancy, it may be assumed that changes of the undetermined
acid fraction are referable entirely to organic acids. The total
height of each column on Charts I to III represents the amount of
total base found. This determination, for brevity, is not separ-
ately indicated. For comparison there have been included with
each chart columns representing the normal non-pregnant and
normal pregnant states. The chief clinical symptoms of each
The patient are shown on Charts I to III. The clinical classification of Stander (19) has been employed.

CHART I. The acid-base balance in eclampsia. Alb. = albumin expressed in gm. per cent; glob. = globulin expressed in gm. per cent; und. = undetermined acids. When the clinical manifestations noted on the left occur, there is a plus sign (+); when absent, a minus sign (−). The columns representing the acid-base balance in normal individuals and normal pregnant individuals were constructed from figures previously published (9, 14, 15). The figures given above the columns represent the respective case numbers.
Chart I represents the findings in six cases of eclampsia, three of which proved fatal. In brief, the deviations from the normal pregnant acid-base balance in the acute stage of the condition are: a considerable lowering of the carbon dioxide content, accompanied by an elevation of the total base, chlorides, and undetermined acids of the serum. The proteins appear to be reduced at the time of the convulsive seizure. There are, unfortunately, but two observations of pH, which was definitely lowered on both occasions. Stander (21) has reported five cases of eclampsia with results quite similar to ours except that the pH values are much lower, due probably to the fact that he withdrew the blood practically during convulsions. Even in his cases the changes are no greater than those found by Barr (2) during severe muscular activity. It is to be noted that in Case 80,989 there is practically no reduction of CO₂. This case, having received large doses of morphine, had been without convulsions for several hours. Henderson and Haggard (8) and also Cobet (4) found, after large doses of morphine, high CO₂ and low pH, which they ascribed to reduction of the respiratory rate. It is our belief that the disturbances described are the effect rather than the cause of the convulsions. In one case, Case 62,482, blood was obtained the day before any convulsions had occurred. Although the patient exhibited all the premonitory symptoms of eclampsia, the serum acid-base equilibrium was that of normal pregnancy.

In their last report Stander et al. (20) suggest that the acidosis associated with eclampsia may be a cause of the fatalities. In two of our fatal cases (Cases 62,482 and 2933), samples of blood were obtained shortly before death, but after the convulsions had ceased. In these two instances the acid-base equilibrium no longer had acidic characteristics but had become more like that of normal pregnancy. The third fatal case (Case 61,702) survived 10 days after delivery and the last convulsions. In this case also the deviations of the acid-base balance found during the convulsive period disappeared after recovery from this phase. These observations strongly indicate that the acidosis is referable to the symptoms, convulsions, rather than to the underlying pregnancy toxemia.

The reduction of serum proteins during the convulsive stages of
eclampsia is not so simply explained. Analysis of the protein fractions in Case 80,989 indicate that both albumin and globulin are affected. This would suggest that the reductions were due to temporary hemodilution. Blood cell volumes, determined in Cases 61,702, 80,989, and 2933 indicate hemodilution, despite the increase in total base and other ions noted above. The phenomenon deserves more careful analysis, perhaps with direct
determinations of blood volume. Comparison with other convulsive states would also be desirable. That the protein reductions are connected with the convulsive phase of the condition seems to follow from the fact that proteins were lower during, than either before or after, this phase (compare Case 62,482 with Cases 61,702, 80,989, and 2933).

Vomiting of Pregnancy

The findings in six cases of vomiting of pregnancy are represented in Chart II. In these cases of severe and protracted vomiting, blood cell volume and serum protein are elevated, evidencing dehydration. The carbon dioxide content is depressed and the undetermined acids are increased. This condition is usually accompanied by the presence of acetonuria and other evidences of starvation. The serum chloride is either normal or low. If low, it appears to be accompanied by a low total base. The pH is in the normal range in all cases. Because these results differ very markedly from those found in cases of protracted vomiting caused, for example, by pyloric obstruction, the vomitus in these cases was examined (Table I). In all instances the amount of chloride found in the vomitus was equaled or exceeded by the amount of total base. In none of the specimens was there any free hydrochloric acid. Arzt (1), in studying the gastric secretion, found free hydrochloric acid absent in twenty-nine out of 50 cases of early pregnancy and diminished in all the remaining cases. This finding of an equivalent amount or an excess of total base in relation to the amount of chloride lost in the vomitus accounts

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Total chloride</th>
<th>Total base</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mM</td>
<td>mM</td>
</tr>
<tr>
<td>41,580</td>
<td>49.8</td>
<td>73.5</td>
</tr>
<tr>
<td>81,870</td>
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<td>52.0</td>
</tr>
<tr>
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</tr>
<tr>
<td>97,261</td>
<td>79.0</td>
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</tr>
<tr>
<td>97,261</td>
<td>15.2</td>
<td>15.3</td>
</tr>
</tbody>
</table>

In none of the specimens was there any free hydrochloric acid.
for the electrolytic picture observed. Following treatment and relief of vomiting, the serum assumes the characteristics found in normal pregnancy.

**Chart III.** The acid-base balance in "low kidney reserve." Alb. = albumin expressed in gm. per cent; glob. = globulin expressed in gm. per cent; und. = undetermined acids. When the clinical manifestations noted on the left occur, there is a plus sign (+); when absent, a minus (−). The columns representing the acid-base balance in normal individuals and normal pregnant individuals were constructed from figures previously published (9, 14, 15). The last column represents a case of nephritis complicated by pregnancy. The figures given above the columns represent the respective case numbers.
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Low Kidney Reserve

In Chart III are presented the data from cases with "low kidney reserve." In order to conform to the classification given by Stander (19) all but one of the cases not already considered have been placed in this group. This we found somewhat unsatisfactory as there are actually two types of cases, namely those with edema and those without. Because of the overlapping, it is difficult completely to separate the two. The cases without edema show no deviation of the electrolyte picture from that of normal pregnancy and the pH is also normal. In edematous patients the serum proteins are reduced below the level found in normal pregnancy, but the electrolyte picture is otherwise undisturbed. These findings agree with those of Stander (20, 21).

The case represented by the last column on Chart III is a case of chronic nephritis complicated by pregnancy. Here the deviations from the normal are well marked but simulate very closely the changes described as occurring in nephritis of the same degree in the absence of pregnancy.

Discussion

The observations reported give no indication that any type of toxemia per se is associated with a characteristic electrolyte disturbance. Deviation of the acid-base and electrolyte patterns from those of normal pregnancy appear to be related to symptoms which the patients exhibit rather than to the underlying disease. With relief of these symptoms the deviations become negligible.

During eclamptic convulsions there is an acidosis similar to that of severe exercise.

In vomiting of pregnancy the electrolyte picture differs from that usually encountered in vomiting states only because the vomitus is deficient in hydrochloric acid. Base is lost in amounts equaling or exceeding those of chloride. This, together with the accession of ketone acids resulting from starvation, causes a carbon dioxide deficit instead of the carbon dioxide excess found in patients who vomit an excess of hydrochloric acid.

The excessive reduction of proteins found in patients with edema may be attributable to the drain of proteinuria added to the unknown factors which are responsible for the slight protein deficiency of normal pregnancy. The protein deficits are not,
however, comparable in degree to those which are necessary for the production of edema in nephritis (12, 16), malnutrition (3, 11, 22), or after phasmapheresis (10); and would seem, therefore, to act merely as a contributory factor in the pathogenesis of edema during pregnancy.

The results of these studies are in general agreement with those of comparable investigations made by Stander (20, 21), however conclusions concerning their cause and significance may differ. Muntwyler, Limbach, Bill, and Myers (13) have recently reported similar analyses from twenty-six cases of abnormal pregnancy. Their results are in accord with ours, with one exception: They found the average serum pH in their cases distinctly elevated. They conclude that the acid-base disturbances are due to hyperventilation. This, they believe, lowers the CO₂, the base falling secondarily as a compensatory reaction. Not content with confining these conclusions to pathological cases, they extend them to cover the changes of normal pregnancy, without presenting any data from uncomplicated cases.

These conclusions are open to serious objections on several grounds. In the first place the discovery of high pH is at variance with the results of observations by the gasometric method reported in this paper and a preceding paper from this laboratory (9), dealing with pathological and normal pregnant subjects respectively, and with the electrometric determinations on normal and pathological pregnant subjects published by Stander et al. (20, 21), Rolly (18), and others. In the second place Muntwyler's paper deals with heterogeneous material of great variability. His pH values are not consistent, but there are no clinical records to facilitate analysis of the results. Averages from such data can have little significance.

Finally, Muntwyler finds by a similar treatment of averages, that the elevation of pH persists for some days after the termination of pregnancy, although base and CO₂ have returned to the normal level. This would in any case invalidate his theory concerning the cause of the CO₂ and base deficits, because the high pH is evidence that the hyperventilation persists after the CO₂ deficit, to which it is supposed to have given rise, has disappeared. It may not be amiss to point out in this connection, also, that no one has yet demonstrated that the CO₂ deficit of hyperventilation
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is compensated by base reduction. Some experiments on the subject by Peters, Bulger, Eisenman, and Lee (15) and others (6, 7) indicate that compensation for such CO₂ deficit is established by increase of chloride without change of base.

SUMMARY

1. In pregnancy toxemias disturbances of the electrolyte and acid-base equilibria in the serum appear to be referable to symptoms of the conditions rather than to the fundamental character of the toxemias.

2. During the convulsions of eclampsia the changes in serum electrolytes are similar to those found in severe exercise: reduction of CO₂ and pH, with increase in base, Cl, and organic acids. Protein is also slightly diminished.

3. In severe vomiting CO₂ falls. The explanation for this is found in the low acidity of the vomitus.

4. Serum proteins are lower in edematous cases than in non-edematous cases or normal pregnancy.

For the opportunity to study these cases and cooperation in securing the data we are indebted to the Department of Obstetrics and Gynecology and especially to Professor Arthur H. Morse.

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