HYDROGEN ION CONCENTRATION AND ACID-BASE EQUILIBRIUM IN NORMAL PREGNANCY

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INTRODUCTION

In 1912 Hasselbalch, with Lundsgaard and Gammeltoft (6, 7), described a lowering of the alveolar carbon dioxide and of the carbon dioxide-combining power of the blood in the later months of normal pregnancy. These changes have been abundantly confirmed by others and found to appear early in the course of pregnancy. These findings together with an increased ammonia to total nitrogen ratio in the urine described by Hasselbalch and Gammeltoft (6) have long been considered as an expression of an increased acid production in pregnancy.

This conception has arisen partly from the impression that Hasselbalch and his associates detected a reduction in the pH of the blood in pregnancy. In actual point of fact they did not determine the pH of the blood directly, but only after exposure to a known concentration of CO₂ in air. This is equivalent, of course, to measuring the bicarbonate content or alkaline reserve and yields no information concerning the actual reaction of the blood in the body. The distinction was clearly recognized by Hasselbalch who concluded that the hydrion concentration of the blood in pregnancy remained normal.

Hasselbalch did, however, interpret the increased ammonia to nitrogen ratio as an indication of an abnormally great acid production. It is now recognized that acid production is proportional not to the urinary ammonia to nitrogen ratio, but to the ab-

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solute quantity of ammonia in the urine. The latter does not appear to be unusually large during pregnancy (13).

The conception that the reduced alkali reserve might be due not to increased acid products, but to a base deficit, was advanced by Marrack and Boone (8) in 1923, because of their failure to find increased cations which they believed should be present if there were a demonstrable increase in the anions. Oard and Peters (9) described the total acid-base equilibrium of the blood serum in pregnancy. They found that the reduced carbon dioxide content and lowered serum proteins were accompanied by a comparable reduction of total base and that there was no increase in the undetermined acids of the blood.

These studies indicate that the reduced alkali reserve is due to a reduction of the cations and that there is no "acidosis of pregnancy." Williamson (16) in 1923 reports the pH normal in five cases, although he does not state the method. Marrack and Boone (8) determined the pH colorimetrically and found a shift from the normal toward alkalinity (normal 7.30 to 7.45 pH, pregnant 7.25 to 7.55 pH).

Because of the unsatisfactory status of the value of pH in pregnancy, it was thought desirable to extend the investigation of the total acid-base equilibrium to include determination of pH. While these investigations were in progress Stander, Eastman, Harrison, and Cadden (14) reported three electrometric pH determinations which lie within their determined normal range.

Methods

The blood for these studies was withdrawn from the antecubital vein anaerobically and without stasis (or with only a minimal preliminary amount of stasis in those cases in which the veins were not otherwise apparent) because of the inspissating effect of stasis (10, 12). The blood was handled and the serum separated according to the anaerobic technique of Austin et al. (1).

The hydrogen ion concentration was determined according to the gasometric method of Eisenman (5). However, by utilizing Van Slyke and Neill's micro method for the CO₂ analyses (15) the procedure was carried out with less than 5 cc. of serum. 2 cc. of serum were introduced into each of two tonometers, one having a CO₂ partial pressure of 30 mm. and the other of 60 mm.
These were saturated for 20 minutes and each serum was then analyzed in duplicate for CO₂ content, as was the original serum. The value $pK'_1 = 6.12$ was used in our calculations.

The total proteins and protein fractions were determined by the modification of Howe's technique described by Bruckman, D'Esopo, and Peters (3). In order to conserve serum a few of the total proteins were determined by a micro modification. 0.2 cc. of serum was diluted with 2.5 cc. of physiological saline solution. 1 cc. aliquots were digested by the micro-Kjeldahl technique and distilled into 0.02 N acid. The non-protein nitrogen was determined in a trichloroacetic acid filtrate by the method of Bock and Benedict (2). The remaining electrolytes were determined by methods described by Oard and Peters (9).

Results

Summarized in Table I are the results of Oard and Peters (9) to which have been added the data collected in the present study. Chloride, phosphorus, and undetermined acid values have been

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Serum Electrolytes and pH in Pregnant and Non-Pregnant Women</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Protein</td>
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<td>---------</td>
<td>---------</td>
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<tr>
<td>Pregnant individuals</td>
<td></td>
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<tr>
<td>No. of patients</td>
<td>22</td>
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<tr>
<td>Maximum</td>
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<tr>
<td>Minimum</td>
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<tr>
<td>Average</td>
<td>6.21</td>
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<tr>
<td>Non-pregnant individuals</td>
<td></td>
</tr>
<tr>
<td>No. of observations</td>
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<tr>
<td>Maximum</td>
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<tr>
<td>Minimum</td>
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<tr>
<td>Average</td>
<td>6.93</td>
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</tbody>
</table>

* Bruckman, D'Esopo, and Peters (3).
† Oard and Peters (9).
omitted as they do not differ materially from normal non-pregnant values. In order to establish a comparable normal standard, hydrogen ion determinations were carried out on eight normal non-pregnant individuals by a technique as nearly similar as possible to that used on gravid individuals. These results are summarized in Table I. The remaining determinations on non-pregnant individuals were performed by techniques comparable to those used in the present study and have been previously reported.

Chart 1. The CO₂ content and pH of the serum in normal and pregnant women. Values obtained in pregnancy are represented by crosses, in the non-pregnant by dots. The broken lines delimit the non-pregnant values and the solid lines the values in pregnancy.

The results indicate that in normal pregnant individuals the carbon dioxide content of the serum is reduced from the normal by about 9 volumes per cent, but the partial pressure of CO₂ is about 4 mm. lower than normal. By virtue of the reduced CO₂ tension the pH in gravid individuals coincides with that in the non-pregnant. This is shown graphically in Chart 1. The results of one
determination that fall outside this range were from serum obtained from an individual who, although normal according to our criteria, had, during a previous pregnancy, developed a severe unexplained anemia.

The lowering of the serum total proteins has long been recognized and it is also well established that fibrinogen is increased during the course of normal pregnancy. Concerning the fractions, albumin and globulin, however, Plass and Mathews (11) in reviewing the literature found considerable confusion. These authors found a definite decrease in the albumin fraction and a relative increase in the globulin fraction when compared to their normal figures. This has been confirmed by Eastman (4) and the present study.

Seven further observations on total base in pregnancy are added. These are in full agreement with the values previously reported (9, 14).

SUMMARY

In normal pregnancy the bicarbonate of serum falls without change in the hydrogen ion concentration. The serum proteins are reduced at the expense of the albumin fraction, the globulin being at the normal level or relatively slightly increased. The values for serum chloride, phosphorus, and undetermined acids are the same as in normal non-pregnant individuals. The reduction in the anions is balanced by a reduction of total base.

BIBLIOGRAPHY

Acid-Base Equilibrium in Pregnancy

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