Within the last 5 years Widmark and his collaborators have put forward an interesting aspect of carbohydrate metabolism. Observing from their figures a difference between the level of blood sugar of lactating and non-lactating cows, Widmark and Carlens (1) advanced the view that the lower level found in the former was brought about by the removal of glucose from the blood stream through the activity of the mammary gland in its formation of lactose. Moreover, averaging the blood sugar determinations on a number of individual cows, producing differing amounts of milk, they found a progressively lower blood sugar with an increasing degree of lactation. "In diesen Bestimmungen kann man einen gewissen Zusammenhang zwischen Milchmenge und Blutzuckergehalt bemerken: je intensiver die Lactation desto niedriger ist der Blutzuckergehalt." They calculate that a cow yielding 28 kilos of milk daily uses 60 gm. of glucose an hour, and is under the necessity of renewing the circulating blood glucose every 15 minutes. Carlens and Krestownikoff (2) observed a lowering of the blood sugar during the process of milking in the cow, though they did not find an analogous phenomenon in goats. An extension of the above views led Widmark and Carlens (3) to conclude that in heavy milking cows the blood sugar might be lowered to such an extent that hypoglycemic symptoms would supervene. This condition they found in "milk fever" or "parturient paresis in cattle." Such cows showed a blood sugar of around 30 to 40 mg. per 100 cc. and recovered from their symptoms on intravenous administration of glucose solutions. The similarity between the symptoms of milk fever in cattle and the hypoglycemic symptoms following insulin injection in rabbits had been previously noted by an unknown Canadian veterinarian (4). Widmark and Carlens (5) produced insulin hypoglycemia in cows and found a great similarity of symptoms with those of milk fever. Auger (6), by slightly different methods confirmed the results of Widmark, both in the lowering of blood sugar brought about by lactation, and in the effectiveness of glucose injections in milk fever. He claimed a similar lowering of blood sugar in lactation in goats. Maguire (7), apparently not knowing of
Widmark's work, found low blood sugar values of 30 to 40 mg. in cows with milk fever. He apparently assumed a blood sugar level in normal cows of 80 to 120 mg. per 100 cc. of blood, and attributed the lowering found in milk fever to a disturbance of endocrine function.

Neither the views nor the facts alleged by Widmark and Carlens, have escaped challenge. All recent investigators find a low blood sugar in milking cows. Their averages range from 48 to 77 mg. per 100 cc. A general average from all the figures we have collected is 59 mg. on 215 determinations, ranging from 33 to 95 mg. in individual estimations (1) (7-14). The average of Widmark and Carlens is 57 mg. They state 85 mg. as the average blood sugar in heifers and dry cows. Scheunert and Pelehrzim (8), Moussu and Moussu (11), Andejewa, Prowatorowa, Sawitsch, and Thal (12), and Hayden and Fish (13) find no difference in the blood sugar level between the dry and milking states. The much more comprehensive figures of Schwarz and Schwarz and Mezler-Andelburg (14) show a difference between the lactating cow and non-milking cattle. The former show an average blood sugar of 63 mg. in contrast with 82 mg. in the latter. While this confirms the figures of Widmark and Carlens, the authors were unable to find any correlation between the amount of milk production and the lowering of the blood sugar. Hayden and Sholl (15) and Hayden (16) claim a hyperglycemia rather than a hypoglycemia in milk fever. Nor is clinical opinion unanimous on the efficacy of intravenous glucose solutions in the treatment of milk fever (17).

Amino acid N is reported as low in milking cows. Cary (18) found it rarely to exceed 3.0 mg. per 100 cc. of plasma. For whole blood the figures of Cary average 4.5 mg. per 100 cc. Meigs (19) suggests that owing to the big demand for glucose for the formation of lactose, and the paucity of carbohydrate reserves, there is no lack of glucose is compensated by an extra deamination of amino acids, leaving a smaller supply circulating in the plasma. Compared with man the figures for amino acid N in milking cows are low. For plasma Berglund (20) gives the range in normal man as 4.3 to 6.2 mg., with an average of 5.3 mg. For whole blood, the average is 6.4 mg. Compared with the non-milking cow, it is by no means certain that the range of, and average, amino acid N in lactation are significantly lowered. For beef blood Blau's (21) figures range from 3.76 to 5.54 mg. on fourteen determinations, with an average of 4.81 mg. The one example of amino acid N in whole blood in the dry cow given by Cary is 3.99 mg., while the cow yielding 25 liters of milk daily was shown to have an amino acid N of 5.34 mg. We have come across no figures for plasma amino acid N in the dry animal. The suggestion of Meigs seems to require further data, before it can be accepted, as it seems unquestioned that plasma amino acids bear the same relation to milk proteins that blood glucose bears to lactose.

Despite the criticisms which have been made of the views of Widmark, the principle, that the amount of lactose produced by the mammary gland can affect the level of the blood glucose, is,
in our opinion, of sufficient import to make it worth while to see if an analogous phenomenon can be found in other animals. Similarly, attention should be paid to the level of amino acid N in lactation. We have consequently examined a series of women, relating the amount of milk production with the sugar, and amino acid N of the blood or plasma. The production of milk by women is, of course, on a much lower level than that of the cow. Nevertheless it should be possible to find some evidence of correlation if the views of Widmark represent a true physiological principle. Moreover we have been fortunate enough to obtain data on two women whose lactose production per unit weight is comparable with that of a high class dairy animal.

EXPERIMENTAL.

We have made determinations of blood sugar and amino acid N on the blood of puerperal women in the early stage of lactation. The blood specimens were taken on the morning of the 10th day after labor. By this time the involution of the uterus is rapidly nearing completion and milk flow is well established. The subjects remained in bed and on uniform hospital diet. All cases studied gave a history of normal pregnancy, labor, and puerperium. We used the method of Shaffer and Hartmann (22) for blood sugar determination and of Folin (23) for amino acid N; both determinations being carried out on plasma.

The milk production of our subjects was determined from the average result of the "2 hour lactation test" taken on the morning of the 10th, 11th, and 12th days post partum. The description of this test and its relation to the 24 hour output of milk has been described elsewhere (24). The results show that there is a rather wide range of normal milk production in women, varying from 10 to 40 cc. of milk per sq. m. of body surface per 2 hours. Amounts of milk below 10 cc. are definitely low, and amounts of milk over 40 cc. per sq. m. of body surface per 2 hours are definitely high. Women in the latter category could be classed as heavy milkers in the comparative sense. Such women are few and constitute only about 15 per cent of public ward cases. We examined in this way 130 cases. We have arranged our analytical results according to the lactation class. Our group of average lactating women contains over 90 subjects, making our
average values in this class reliable. The numbers in the low and high lactating classes are small. The results are shown in Table I.

Glucose.—The amount of plasma sugar varies within normal limits. The extreme variations found are 56 to 146 mg. per 100 cc. of plasma. 80 per cent of our cases, however, fall in the usual normal range of 80 to 120 mg. The general average is 95 mg. Morriss (25) gives 100 mg. and Bergsma (26) 94 mg. of sugar per 100 cc. of blood for women 7 days post partum. Only eight of our subjects showed 75 mg. or less plasma sugar and only one of these would fall into the high lactation group. There is no significant difference between the three groups of lactating women.

### Table I

Relation between Blood Sugar and Amino Acid N, Lipoid and Inorganic P with the Amount of Lactation in Women.

<table>
<thead>
<tr>
<th>Lactation group</th>
<th>Low.</th>
<th>Average</th>
<th>High.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk in 2 hr. lactation test per sq.m.</td>
<td>0–10</td>
<td>10–40</td>
<td>40+</td>
</tr>
<tr>
<td>surface, cc.</td>
<td>16</td>
<td>89</td>
<td>20</td>
</tr>
<tr>
<td>No. of observations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mg. per 100 cc. plasma</td>
<td>95</td>
<td>95</td>
<td>93</td>
</tr>
<tr>
<td>Average glucose</td>
<td>5.3</td>
<td>5.2</td>
<td>5.1</td>
</tr>
<tr>
<td>&quot; amino acid N</td>
<td>11.1</td>
<td>10.8</td>
<td>10.7</td>
</tr>
<tr>
<td>&quot; lipoid P</td>
<td>4.0</td>
<td>3.9</td>
<td>4.0</td>
</tr>
<tr>
<td>&quot; inorganic P</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Amino Acid N.—The figures fall within a normal range set by Folin and Berglund for adult man. Our range is from 4.44 to 7.00 mg. amino acid N per 100 cc. of plasma. 87 per cent of our figures lie within the extremely narrow range of 4.70 to 5.70 mg. of amino acid N. Of the eight subjects showing amino acid N below this range only one would be classed in the high lactation group. It is true our average results show a slightly decreasing amino acid N as the average lactation increases. The decrease, however, is so slight that at present, we do not consider it significant, especially when the small number of subjects in the low and high lactating groups, is considered.

In order to make certain that our figures for blood sugar repre-
sented the usual proportion of glucose and non-fermentable sub-
stances, and did not, by any chance, represent a low glucose
value, with a proportion of lactose in the non-fermentable fraction
sufficiently high to give a total sugar of normal range, we deter-
mined on a further series of women the fermentable and non-
fermentable sugar in whole blood. The presence of lactose is
common in the urine of lactating women and cows. It is generally

<table>
<thead>
<tr>
<th>Subject</th>
<th>Post partum.</th>
<th>24 hr. milk output.</th>
<th>Sugar (as glucose).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>days</td>
<td>cc.</td>
<td>mg. per 100 cc.</td>
</tr>
<tr>
<td>S-g-s</td>
<td>12</td>
<td>135</td>
<td>112</td>
</tr>
<tr>
<td>Y-r-k</td>
<td>10</td>
<td>187</td>
<td>101</td>
</tr>
<tr>
<td>H-p-r</td>
<td>10</td>
<td>210</td>
<td>112</td>
</tr>
<tr>
<td>C-k-r</td>
<td>10</td>
<td>240</td>
<td>101</td>
</tr>
<tr>
<td>R-t-e</td>
<td>10</td>
<td>277</td>
<td>105</td>
</tr>
<tr>
<td>G-n-g</td>
<td>10</td>
<td>280</td>
<td>99</td>
</tr>
<tr>
<td>H-d-n</td>
<td>10</td>
<td>285</td>
<td>92</td>
</tr>
<tr>
<td>Me-y</td>
<td>10</td>
<td>330</td>
<td>106</td>
</tr>
<tr>
<td>T-e-s</td>
<td>13</td>
<td>387</td>
<td>112</td>
</tr>
<tr>
<td>H-m-n</td>
<td>10</td>
<td>411</td>
<td>76</td>
</tr>
<tr>
<td>G-r-e</td>
<td>10</td>
<td>430</td>
<td>110</td>
</tr>
<tr>
<td>C-f-d</td>
<td>10</td>
<td>483</td>
<td>87</td>
</tr>
<tr>
<td>J-r-s</td>
<td>10</td>
<td>1130</td>
<td>102</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td>102</td>
</tr>
</tbody>
</table>

accepted as a non-threshold substance in human blood. Hayden
(16) has examined the blood of five normal milking cows for
lactose and reported its absence, though it is easily demonstrable
after the suppression of lactation by air inflation of the udder in
milk fever cows. The sugar determinations in our series were
made by a modification of the Shaffer-Hartmann method. This
modification was given to the Insulin Committee of the Uni-
versity of Toronto by Professor Shaffer, and has been in use in
their laboratories for over 2 years. It is very satisfactory for the
determination of sugar in hypoglycemic conditions. Duggan and
Scott (27) and DeLong (28) have pointed out the inhibiting effect
of iodide on the reducing power of sugar towards the Shaffer-
Hartmann reagent. The new reagent is made up as described in
the original paper of Shaffer and Hartmann with the omission of
the iodide. This is made separately as a 1 per cent solution.
The sugar solution, or Folin-Wu filtrate, and the copper reagent
are mixed and heated in a boiling water bath exactly as described
by the original authors. The solution is then cooled at 30°, 2.0
cc. of iodide solution added, followed by 2.0 cc. of N H₂SO₄.
The titration by 0.005 N sodium thiosulfate is as described by

<table>
<thead>
<tr>
<th>Subject</th>
<th>24 hr. milk output.</th>
<th>Plasma sugar.</th>
<th>Amino acid N.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cc.</td>
<td>mg. per 100 cc.</td>
<td>mg. per 100 cc.</td>
</tr>
<tr>
<td>K-k</td>
<td>560</td>
<td>86</td>
<td>5.14</td>
</tr>
<tr>
<td>O-l-v</td>
<td>480</td>
<td>88</td>
<td>5.09</td>
</tr>
<tr>
<td>Y-l</td>
<td>465</td>
<td>99</td>
<td>4.90</td>
</tr>
<tr>
<td>G-l-n</td>
<td>453</td>
<td>99</td>
<td>5.00</td>
</tr>
<tr>
<td>H-r-f</td>
<td>950</td>
<td>99</td>
<td>4.82</td>
</tr>
<tr>
<td>J-r-s</td>
<td>1200</td>
<td>102*</td>
<td></td>
</tr>
</tbody>
</table>

* Whole blood.

Shaffer and Hartmann. The method is standardized against solu-
tions of pure glucose. The new reagent will determine 10 mg. of
glucose per 100 cc. of original blood. It is thus well adapted to
the determination of fermentable and non-fermentable sugar in
blood. For the fermentation of glucose in the Folin-Wu filtrate
we used the method of Folin and Svedberg (29) or that of Somogyi
(30), without materially affecting the results.

The results are shown in Table II. The general average of
total sugar is 102 mg. compared with 95 mg. per 100 cc. of plasma.
The non-fermentable fraction varies from 15 to 30 mg., with an
average of 26 mg. per 100 cc. of blood, expressed as glucose. This
corresponds to the usual range and average, nor does there appear
any evidence of an increasing non-fermentable fraction with
increasing lactation. It may be concluded that in general, the blood sugar and amino acid N in women are unaffected by the degree of lactation.

Finally we record the milk output and the blood analyses of two women of exceptionally high lactating power. In order to emphasize the exceptional power of the subjects H-r-f and J-r-s we have included in Table III similar records of the four next high lactating women. The two exceptional subjects have more than twice the output of any of the other four. Compared with the ordinary lactating woman their milk output is nearly 4 times as great. The blood sugar of these two subjects and the amino acid N is normal. Moreover in subject J-r-s we had a further opportunity of study 6 weeks post partum. The amount of milk (as judged from the records of the premature baby nursery, and our own measurements) remained at the same average level of 1200 cc. a day. The blood sugar was 108 mg. per 100 cc. of whole blood, with a value for the non-fermentable fraction of 28 mg.

DISCUSSION.

While it is abundantly clear that the level of blood sugar and amino acid N in women remains at the normal non-lactating level and is not affected even by high milk production, before such results can have any bearing on the views of Widmark it must be shown that the milk output, or the lactose production, of the two classes can be comparable. The milk production of heavy milking cows may well be so great as to constitute a pathological phenomenon, even in those animals in which it is not so great as to give rise to the symptoms of milk fever.

First we have calculated the milk production of our two highest lactating subjects on the basis of a similar weight to the dairy cow, and compared the calculated output with the figures as given by Widmark and Carlens (1). Our subjects (H-r-f and J-r-s) weighed 48 and 52 kilos respectively and on the basis of the average weights of dairy cows, as shown in Table IV, their weights might vary from one-eighth to one-twelfth of the dairy animal, depending upon the breed with which the comparison is made. (Widmark and Carlens do not state the weights of their experimental animals.) On such a supposition our two subjects would produce an amount of milk varying from 8 to 15 kilos daily. Such a
Blood Sugar in Lactation

milk production according to Widmark and Carlens would produce a lowering of the blood sugar, from 85 mg. to 57 mg. Proportionately our two subjects should have shown a blood sugar value of around 67 mg. instead of the actual figures of 99 and 102 mg.

Secondly we have calculated the lactose production of our two subjects and compared it with that obtained from the data supplied to us by the Department of Agriculture of the Dominion of Canada. The data consist of the average milk production of four breeds of cow over a number of years obtained from animals qualifying for the Canadian Record of Performance at Ottawa. The calculations are shown in Table IV. On the common basis of 100 kilos of body weight subjects H-r-f and J-r-s are producing as much lactose as dairy animals of sufficient caliber to qualify in the Canadian Record of Performance.

Table IV.
Comparing Lactose Production of 2 High Lactating Women and Averages of High Lactating Cows.

<table>
<thead>
<tr>
<th>Cow</th>
<th>Average milk production of mature cows qualified in Record of Performance 1924-28.</th>
<th>Average milk production per day.</th>
<th>Average milk production per day.</th>
<th>Average milk production per 100 kilos body weight.</th>
<th>Lactose production per 100 kilos body weight.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>kg.</td>
<td>kg.</td>
<td>liters</td>
<td>liters</td>
<td>gm.</td>
</tr>
<tr>
<td>Jersey</td>
<td>400</td>
<td>4545</td>
<td>13</td>
<td>12.6</td>
<td>3.1</td>
</tr>
<tr>
<td>Guernsey</td>
<td>500</td>
<td>5000</td>
<td>14.3</td>
<td>13.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Ayrshire</td>
<td>500</td>
<td>5227</td>
<td>14.9</td>
<td>14.4</td>
<td>2.9</td>
</tr>
<tr>
<td>Holstein</td>
<td>636</td>
<td>7070</td>
<td>21.9</td>
<td>21.2</td>
<td>3.3</td>
</tr>
</tbody>
</table>

* The average milk production of mature cows qualifying in the Canadian Record of Performance is for one lactation period of 365 days. A few of the cows did not reach 365 days in one lactation period, though the milk production was sufficiently high to enable them to qualify. We have taken 350 days as the average lactation period.

† Average specific gravity of whole milk 1089.

‡ Average lactose content of cow's milk, 5.0 per cent. Average lactose content of woman's milk, 7.0 per cent.
From the above it is clear that woman can produce large amounts of milk and amounts of lactose equivalent to the production of heavy milking cows without affecting the level of the blood sugar or the amino acid N. The control of the amount of those substances circulating in the blood lies in internal secretion rather than in the output requirement.

**Note on Lipoid and Inorganic Phosphorus.**

In Table I are also included our average figures for lipoid and inorganic P. Both determinations were made on the plasma. Lipoid P was determined by extraction of the plasma according to the method of Bloor (31), removal of the mixture of alcohol and ether by evaporation, and then ashing the residue according to the method of Fiske and Subbarow (32) as outlined for total P of blood. The method gave figures slightly higher than that of Whitehorn (33). Inorganic P was determined by the method of Fiske and Subbarow. Meigs (19) cited the evidence which had led him and Blatherwick and Cary to believe that the milk fat was formed from lipid substances circulating in the plasma. Correlated with this was an increased inorganic P in the plasma returning from the mammary gland. Our figures show no connection between the lactation output and circulating lipoid P and inorganic P. Our average value (3.9 mg.) is slightly higher than those generally reported for inorganic P in lactation in women (34). 93 per cent of our figures lie in the range 3.3 to 4.5 mg. Fish (35) has recently found a lowered average inorganic P in serum of milking cows compared with the dry animal. Our figures support the opposite conclusion in women (36). The variation in lipoid P is more pronounced (8.0 to 14.8 mg.). The general average is 10.8 mg. with 62 per cent of our figures between 10 and 12 mg. Reference to serum Ca can be found in another paper (24).

**SUMMARY.**

Blood sugar and amino acid N are not affected by lactation in women.

The non-fermentable fraction of “blood sugar” remains within its ordinary range during lactation in women.

These statements are true, even in women of very high milk production.
Values are given for lipoid and inorganic P in plasma during lactation in women.

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