THE RELATION BETWEEN THE INGESTION OF COLOSTROM OR BLOOD SERUM AND THE APPEARANCE OF GLOBULIN AND ALBUMIN IN THE BLOOD AND URINE OF THE NEW-BORN CALF.

By PAUL E. HOWE, Ph.D.

(From the Department of Animal Pathology of The Rockefeller Institute for Medical Research, Princeton, N. J.)

(Received for publication, September 26, 1923.)

In connection with a problem relating to the ingestion of colostrum and the appearance of protein in the urine of calves, analyses have been made of the proteins in the blood of the calves studied and also a differential analysis of the proteins of the urines in at least one urine in each case. A preceding paper contains the observations made with regard to the details of feeding, the time of appearance and disappearance of the protein in the urine, and discussions of the cases (1).

Presentation of Data.—The blood serum was analyzed according to procedures which have been described (2). The urines were analyzed according to similar procedures. The accuracy of the method in the case of urine was tested by adding blood serum to the urine and analyzing the mixture; with the samples of urine used the distribution of the proteins agreed with the analysis of the blood alone. When small amounts of protein were present the urines were fractioned by adding the proper amount of solid sodium sulfate. It is possible that in such cases, when the concentration of urea was high, the procedure was only approximate. On the other hand, when the protein content was high enough so that but 0.5 cc. of urine to 15 cc. of salt solution could be used, the interference of other urine constituents was negligible.

Calves Fed Colostrum.—The blood and urine of sixteen cases were studied in which calves ingested colostrum by nursing the dam or from a bottle. In each case the appearance of the globulin fractions in the blood (3) and of the various protein fractions in the urine was demonstrated. Data from representative cases are included
GLOBULIN AND ALBUMIN IN BLOOD AND URINE

in the accompanying tables. Analyses of the colostrum fed are also included. The data in Tables I to IV show that the quantity of blood globulin remains at a relatively high level after protein has disappeared from the urine. The gradual disappearance of absorbed

**TABLE I.**

*Calf 708. Fed Colostrum Soon after Birth.*

Calf born Feb. 8, 10.30 a.m. It was fed colostrum as follows: Feb. 8, 11.35 a.m., 1,135 cc., 5.15 p.m., 1,000 cc.; Feb. 9, 8.10 a.m., 1,000 cc., 12.30 p.m., 700 cc.

**Urine.**—A positive test for protein was obtained up to 11 a.m., on Feb. 10; the next sample, 6.10 a.m., Feb. 11, was negative.

<table>
<thead>
<tr>
<th>Sample collected.</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Egg-globulin N.</th>
<th>Pseudo-globulin N.</th>
<th>Total globulin N.</th>
<th>Albumin N.</th>
<th>Non-protein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 8, 11.20 a.m.</td>
<td>0.699</td>
<td>0.009</td>
<td>0.057</td>
<td>0.113</td>
<td>0.179</td>
<td>0.488</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Fed colostrum at 11.35 a.m., Feb. 8.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 9, 7.50 a.m.</td>
<td>0.855</td>
<td>0.137</td>
<td>0.179</td>
<td>0.136</td>
<td>0.452</td>
<td>0.391</td>
<td>0.012</td>
</tr>
<tr>
<td>&quot; 12, 2.30 p.m.</td>
<td>0.770</td>
<td>0.125</td>
<td>0.108</td>
<td>0.101</td>
<td>0.334</td>
<td>0.412</td>
<td>0.024</td>
</tr>
<tr>
<td>&quot; 28</td>
<td>0.894</td>
<td>0.839</td>
<td>0.085</td>
<td>0.129</td>
<td>0.093</td>
<td>0.307</td>
<td>0.508</td>
</tr>
<tr>
<td><strong>Urine.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb. 8, 4.00 p.m.</td>
<td>0.294</td>
<td>0.012</td>
<td>0.009</td>
<td>0.004</td>
<td>0.013</td>
<td>0.006</td>
<td>0.263</td>
</tr>
<tr>
<td>&quot; 9, 8.20 a.m.</td>
<td>0.895</td>
<td>0.053</td>
<td>0.040</td>
<td>0.034</td>
<td>0.117</td>
<td>0.157</td>
<td>0.610</td>
</tr>
<tr>
<td>&quot; 10, 6.15 &quot;</td>
<td>0.764</td>
<td>0.046</td>
<td></td>
<td></td>
<td>0.064</td>
<td>0.076</td>
<td>0.624</td>
</tr>
<tr>
<td><strong>Colostrum.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.304</td>
<td>1.024</td>
<td>0.388</td>
<td>0.364</td>
<td>0.189</td>
<td>0.283</td>
<td>0.048</td>
<td></td>
</tr>
</tbody>
</table>

*In this and the following tables the results are expressed as grams of nitrogen per 100 cc.

protein from the blood has been previously demonstrated (4). The data in Table III are presented to show that the permeability of the kidney as well as of the alimentary tract persists for some time. In this case the feeding of colostrum was delayed for 22 hours after birth during which time milk was fed. Following the ingestion of colostrum there was an accumulation of protein in the blood and the various protein fractions appeared in the urine.
Two facts are brought out in Table IV: (a) After a calf has received colostrum and protein has appeared in the blood and in the urine and has disappeared from the urine, a second ingestion of colostrum will be followed by an increase in protein in the blood and the reappearance of protein in the urine. (b) The time during which absorption from the intestinal tract can take place may be as long as 69 hours.

### TABLE II.

**Calf 1026. Fed Colostrum Soon after Birth.**

Calf born Mar. 8, 7.30 a.m. Fed colostrum as follows: Mar. 8, 9.10 a.m., 1,225 cc., 3.20 p.m., 1,000 cc., 9.30 p.m., 1,000 cc.; Mar. 9, 5 a.m., 1,000 cc., 11.30 a.m., 1,000 cc.

**Urine.**—Protein positive in the urine at 12 noon, Mar. 10, and the next sample at 5.40 a.m., Mar. 11, negative (trace).

<table>
<thead>
<tr>
<th>Sample collected</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Pseudo-globulin N.</th>
<th>Total globulin N.</th>
<th>Albumin N.</th>
<th>Non-protein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mar. 8, 9.00 a.m.</td>
<td>0.684</td>
<td>0.000</td>
<td>0.047</td>
<td>0.141</td>
<td>0.188</td>
<td>0.468</td>
</tr>
<tr>
<td>Fed colostrum immediately after bleeding.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar. 8, 3.20 p.m.</td>
<td>0.833</td>
<td>0.115</td>
<td>0.173</td>
<td>0.105</td>
<td>0.393</td>
<td>0.316</td>
</tr>
<tr>
<td>10, 10.00 a.m.</td>
<td>1.005</td>
<td>0.160</td>
<td>0.232</td>
<td>0.145</td>
<td>0.537</td>
<td>0.396</td>
</tr>
<tr>
<td>Mar. 9, 2.30 p.m.</td>
<td>1.535</td>
<td>0.101</td>
<td>0.059</td>
<td>0.086</td>
<td>0.256</td>
<td>1.147</td>
</tr>
<tr>
<td>10, 8.00 a.m.</td>
<td>0.486</td>
<td>0.012</td>
<td>0.012</td>
<td>0.274</td>
<td>0.298</td>
<td>0.030</td>
</tr>
<tr>
<td>Colostrum.</td>
<td>2.455</td>
<td>0.783</td>
<td>0.786</td>
<td>0.094</td>
<td>0.009</td>
<td>0.889</td>
</tr>
</tbody>
</table>

**Calves Fed Cow Serum.**—In two cases blood serum of the cow was fed to calves instead of colostrum. In the first case 500 cc. of blood serum was fed to a calf 21 hours after birth. There was no appreciable rise in the proteins of the blood nor did protein appear in the urine in more than traces. There may have been greater difficulty in absorbing protein at 21 hours than at birth, but the results
obtained agree with unpublished data in which the ingestion of 500 cc. of blood serum soon after birth was not sufficient to cause a measurable increase in the blood proteins of calves. The second case in which blood serum was fed was successful in indicating the

**Table III.**

*Calf 930. First Fed Colostrum 22 Hours after Birth.*

Calf was born Apr. 13, at 1.50 p.m. It was fed milk until 12 noon, Apr. 14, when it was given 1,500 cc. of colostrum. Colostrum (1,000 cc.) was again fed at 8 p.m., and on Apr. 15 at 5 a.m. and at 11.25 a.m.

**Urine.—** Protein in the urine was negative until 8.20 p.m. on Apr. 14, when the tests became positive and remained so until 5.35 a.m. on Apr. 17, at which time there was a slight trace of protein.

<table>
<thead>
<tr>
<th>Sample collected</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Pseudo-</th>
<th>Albuni-</th>
<th>Non-pro-</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>globulin N.</td>
<td>globulin N.</td>
<td>protein N.</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>Blood.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 13, 3.30 p.m.</td>
<td>0.723</td>
<td>0.000</td>
<td>0.057</td>
<td>0.166</td>
<td>0.213</td>
</tr>
<tr>
<td>&quot; 14, 11.45 a.m.</td>
<td>0.728</td>
<td>0.031</td>
<td>0.030</td>
<td>0.161</td>
<td>0.222</td>
</tr>
<tr>
<td>Fed colostrum 22 hrs. after birth.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 14, 8.00 p.m.</td>
<td>0.884</td>
<td>0.080</td>
<td>0.161</td>
<td>0.140</td>
<td>0.331</td>
</tr>
<tr>
<td>&quot; 15, 11.25 a.m.</td>
<td>0.981</td>
<td>0.225</td>
<td>0.097</td>
<td>0.149</td>
<td>0.471</td>
</tr>
<tr>
<td>&quot; 16, 9.10 &quot;</td>
<td>0.902</td>
<td>0.069</td>
<td>0.208</td>
<td>0.124</td>
<td>0.401</td>
</tr>
<tr>
<td>May 23.</td>
<td>0.917</td>
<td>0.044</td>
<td>0.125</td>
<td>0.092</td>
<td>0.261</td>
</tr>
<tr>
<td>Urine.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 15, 11.35 a.m.</td>
<td>2.085</td>
<td>0.000</td>
<td>0.098</td>
<td>0.212</td>
<td>0.300</td>
</tr>
<tr>
<td>Colostrum.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 14.</td>
<td>3.238</td>
<td>1.309</td>
<td>1.007</td>
<td>0.327</td>
<td>0.217</td>
</tr>
</tbody>
</table>

The appearance of protein in the blood and the excretion of protein in the urine. In this case larger amounts of blood were fed, 1,000 cc. and later 300 cc. The data are contained in Table V.

**DISCUSSION.**

The data presented support the inference that the protein present in the urine of new-born calves which have received colostrum is
derived from the colostrum as follows: (a) In every uncomplicated case in which protein has appeared in the urine of new-born calves following the ingestion of colostrum, euglobulin and pseudoglobulin I have appeared in the blood (4). (b) When colostrum has been with-

TABLE IV.
Calf 27. The Effect of a Second Ingestion of Colostrum after Protein Had Dis-appeared from the Urine, as the Result of a First Ingestion.

Calf was born May 1, at 12.30 p.m., and allowed to suckle the dam. Subsequently it was fed milk until protein disappeared from the urine, when it was again fed colostrum (69 hours old) as follows: May 4, 9.10 a.m., 1,000 cc., 2 p.m., 1,000 cc., 8. p.m., 1,000 cc.; May 5, 5 a.m., 1,000 cc.

Urine.—Protein was present in the urine from 2 p.m. on May 1, to 5 p.m. on May 2, when it was negative (trace). Following the second feeding of colostrum the urine became positive, May 5, 4.30 a.m., and was again negative (trace) on May 9.

<table>
<thead>
<tr>
<th>Sample collected</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Euglo-</th>
<th>Pseudo-</th>
<th>Total</th>
<th>Albumin N.</th>
<th>Non- protein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 1, 4.55 p.m.</td>
<td></td>
<td>0.743</td>
<td>0.025</td>
<td>0.030</td>
<td>0.140</td>
<td>0.199</td>
<td>0.489     0.055</td>
</tr>
<tr>
<td>&quot; 4, 8.45 a.m.</td>
<td></td>
<td>0.765</td>
<td>0.030</td>
<td>0.013</td>
<td>0.199</td>
<td>0.242</td>
<td>0.485     0.038</td>
</tr>
<tr>
<td>Fed colostrum at 9.10 a.m., 2 p.m., and 8 p.m. on May 4, and at 5 a.m. on May 5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>May 5, 9.30 a.m.</td>
<td></td>
<td>0.789</td>
<td>0.118</td>
<td>0.083</td>
<td>0.157</td>
<td>0.258</td>
<td>0.463     0.068</td>
</tr>
<tr>
<td>&quot; 22</td>
<td></td>
<td>0.803</td>
<td>0.115</td>
<td>0.051</td>
<td>0.111</td>
<td>0.317</td>
<td>0.544     0.042</td>
</tr>
</tbody>
</table>

Urine.

<table>
<thead>
<tr>
<th>Sample collected</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Euglobulin N.</th>
<th>Pseudoglobulin N.</th>
<th>Total Globulin N.</th>
<th>Albumin N.</th>
<th>Non-protein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2, 5.35 a.m.</td>
<td>1.011</td>
<td></td>
<td>0.148</td>
<td>0.434</td>
<td>0.091</td>
<td>0.772</td>
<td></td>
</tr>
<tr>
<td>&quot; 5, 5.30 &quot;</td>
<td>0.961</td>
<td></td>
<td>0.148</td>
<td>0.434</td>
<td>0.091</td>
<td>0.772</td>
<td></td>
</tr>
</tbody>
</table>

Colostrum (second feeding).

<table>
<thead>
<tr>
<th>Casein</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Euglobulin N.</th>
<th>Pseudoglobulin N.</th>
<th>Total Globulin N.</th>
<th>Albumin N.</th>
<th>Non-protein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.783</td>
<td>0.948</td>
<td>0.715</td>
<td>0.756</td>
<td>0.055</td>
<td>0.285</td>
<td>0.034</td>
<td></td>
</tr>
</tbody>
</table>

held from a calf for some hours after birth the globulin fractions have not appeared in the blood in appreciable amounts and no protein has appeared in the urine, but upon the subsequent ingestion of co- lostrum these proteins have appeared in the blood and urine. (c)
The proteins in the urine consist of the euglobulin, pseudoglobulin I and II, and albumin fractions.

There is but one point which needs particular discussion and that is with regard to the albumin which appears in the urine with the globulin fractions and in many cases in relatively large amounts.

The direct absorption of *albumins* by the new-born calf is not so

**TABLE V.**
*Calf 1034. Fed Blood Serum.*

Calf was born Apr. 9, at 1.30 p.m. At 4.35 p.m., it was fed 1,000 cc. of blood serum of a cow and at 10.30 p.m., 300 cc. of blood serum.

*Urine.*—Protein was present in the urine collected at 5.20 a.m. on Apr. 10, and again at 4.45 p.m. The urine collected at 5.30 a.m. on Apr. 11, showed only a faint cloudiness, negative.

<table>
<thead>
<tr>
<th>Sample collected</th>
<th>Total N.</th>
<th>Serum N.</th>
<th>Euglobulin N.</th>
<th>Pseudoglobulin N.</th>
<th>Total globulin N.</th>
<th>Albinin N.</th>
<th>Nonprotein N.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 9, 4.25 p.m.</td>
<td>0.676</td>
<td>0.000</td>
<td>0.000</td>
<td>0.149</td>
<td>0.149</td>
<td>0.468</td>
<td>0.059</td>
</tr>
<tr>
<td>Fed blood serum at 4.35 p.m.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 9, 10.30 p.m.</td>
<td>0.969</td>
<td>0.191</td>
<td>0.090</td>
<td>0.165</td>
<td>0.446</td>
<td>0.477</td>
<td>0.046</td>
</tr>
<tr>
<td>&quot; 10, 9.35 a.m.</td>
<td>0.761</td>
<td>0.026</td>
<td>0.106</td>
<td>0.140</td>
<td>0.272</td>
<td>0.430</td>
<td>0.059</td>
</tr>
<tr>
<td>&quot; 24.</td>
<td>0.833</td>
<td>0.030</td>
<td>0.051</td>
<td>0.144</td>
<td>0.226</td>
<td>0.553</td>
<td>0.055</td>
</tr>
<tr>
<td>Urine.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr. 10, 5.20 a.m.</td>
<td>1.131</td>
<td>0.037</td>
<td>0.066</td>
<td>0.011</td>
<td>0.114</td>
<td>0.036</td>
<td>0.913</td>
</tr>
<tr>
<td>Blood serum (cow).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.398</td>
<td>0.151</td>
<td>0.216</td>
<td>0.150</td>
<td>0.697</td>
<td>0.504</td>
<td>0.056</td>
</tr>
</tbody>
</table>

strikingly demonstrable as the absorption of the globulin fractions because albumins are already present in the blood of a calf. An examination of all of our data relating to the absorption of protein by new-born calves does not disclose a definite increase in albumin coincident with the accumulation of globulins in the blood. There are cases in which the data might be interpreted as indicating a slight increase in albumin but there are other cases in which such a change is not evident.
A satisfactory explanation of the presence of the albumin fraction in urine is not at hand. In the formulation of any theory it is necessary to remember that the quantity of albumin in colostrum is roughly only about twice that found in milk. When milk is fed an appreciable amount of albumin does not appear in the urine. In one experiment in which the ratio of albumin to globulin in the ingested colostrum was 1:5, the ratio in the urine was 1:1. In this case the possible interference of urea was essentially eliminated. This fact is difficult to reconcile with the simple assumption, which appears to be evident in the case of the globulins, that there is a permeability of the kidney as well as the gastrointestinal tract for a short time after birth and that the globulin excreted in the urine arises unchanged from the globulin of the colostrum. A possible explanation might be that the albumin is derived, in part at least, from the absorbed globulin. Such an explanation involves theories with regard to the relation between the various protein fractions for which there is comparatively little satisfactory evidence. Evidence which we have presented for the calf (4) and other unpublished data indicate that variations in albumin in the blood are relatively independent of the variations in the globulin fractions.

It is apparent that the absorption of unchanged protein and the excretion of protein in the urine appear to be intimately related. On the other hand, at the time the absorption and excretion of protein has ceased relatively large amounts of the euglobulin and pseudoglobulin I fractions are still present in the blood. These fractions continue to decrease over a period of 4 to 6 weeks until the concentration of the blood of the post-colostrum phase of the calf is reached (4). This final decrease is independent of the excretion of protein in the urine of the new-born which lasts only a few days.

The cause of the albuminuria in the young has not, so far as we can find, been ascribed hitherto to the direct absorption and excretion of the proteins of colostrum. The bearing of this view on the interpretation of the literature has been briefly touched upon in a preceding paper of Smith and Little (1).

In a previous study of the fat content of the feces of young calves (5) we showed that the feces of the young calf which were passed a few days after birth contained considerable amounts of protein and
that the proteins, euglobulin, pseudoglobulin, and albumin, were present. A survey of the total nitrogen determinations of feces presented at that time on calves which had not received colostrum and on those which had received colostrum shows that the total fecal nitrogen of the former set of calves was lower than for the latter set. At about the same time we separated, by salting out with ammonium sulfate, from the urine of a calf 1 day old, euglobulin, pseudoglobulin, and albumin. The evidence presented in the preceding papers and in this paper indicates that the protein of the feces soon after birth probably has its origin in the high protein-containing colostrum ingested at birth.

SUMMARY.

The coincidence of the appearance of euglobulin and pseudoglobulin I in the blood and urine of the new-born calf following the ingestion of colostrum and the absence of these proteins when milk is fed support the inference that the proteinuria of the new-born calf is due to the ingestion of colostrum. In this passage the proteins are in part unaltered.

The absorption and excretion of the proteins of blood serum have been observed.

The high protein content of the feces of young calves—during the first few days—is to be ascribed, in part at least, to ingested colostrum.

BIBLIOGRAPHY.