STUDIES ON THE CHEMICAL COMPOSITION OF BEEF
BLOOD.

III. THE BLOOD PICTURE OF CALVES ON A SOLE DIET OF MILK
OR OF MILK WITH THE ADDITION OF VARIOUS
SUPPLEMENTS.*

BY C. F. HUFFMAN AND C. S. ROBINSON.

WITH THE ASSISTANCE OF R. E. LARSON AND K. L. BURT.

(From the Chemical Laboratory and Department of Dairy Husbandry of the
Michigan Agricultural Experiment Station, East Lansing.)

(Received for publication, April 16, 1926.)

Although milk occupies a unique position as a food in that it
is a natural, complete ration for young animals, attempts to use
it as such for the raising of animals to maturity have failed in
practically all cases.

Davenport (1), Eckles (2), Fitch, Hughes, and Cave (3), and McCandlish
(4) found that calves developed normally on milk alone for a period of only
about 3 months after which they did not do well. McCandlish carried his
experiments through to a fatal termination. He describes the results as
follows:

"One very noticeable feature of the experiment was the occurrence of
fits. These fits were first apparent when the animal was between three and
four months of age and continued to occur at frequent but irregular inter-
vals up until about three weeks before the animals died. These fits were all
very similar and frequently started for no apparent reason and could al-
mast always be induced by leading the animals around for a few minutes.
The animal would fall down and bellow as if in pain; the jaws would stick
open and the legs become rigid; the muscles became tense and hard."

Two pigs which Herter (5) tried to raise on milk alone developed leg
weakness and were killed. On the other hand McCollum (6) succeeded in
raising a sow to sexual maturity with the production of a normal litter of
pigs. Moro (7), Bartenstein (8), and Meyer and Nassau (9) used guinea
pigs which succumbed in a much shorter time, in some cases in 3 to 4
days. Dogs appear to be unable to survive such treatment, Moro (7)

* Published with the permission of the Director of the Experiment Sta-
tion as Journal Article No. 35 from the Chemical Laboratory.

101
Fig. 2. Blood picture of Calf C36 on a diet of milk and supplements.
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C31</td>
<td>Milk alone.</td>
<td>162nd and 175th days.</td>
<td>See Fig. 1.</td>
<td>Died in convulsion.</td>
</tr>
<tr>
<td></td>
<td>C40</td>
<td>&quot; &quot;</td>
<td>461st day.</td>
<td>P 1.31 mm, CO₂ 23.4 mm, Ca 2.0 mm in terminal convulsion.</td>
<td>Died 48 hrs. after beginning of attack.</td>
</tr>
<tr>
<td>2</td>
<td>C13</td>
<td>Milk alone, 210 days. Wheat straw, CaCO₃, cod liver oil, and green grass added in succession.</td>
<td>200th day.</td>
<td>Ca 1.9 mm during convulsion.</td>
<td>Died 294th day, paralyzed for 8 days.</td>
</tr>
<tr>
<td></td>
<td>C15</td>
<td>Milk alone, 166 days. Cod liver oil and calcium phosphate added successively.</td>
<td>166th, 175th, 178th days.</td>
<td>Ca &lt; 2.0 mm during attacks.</td>
<td>Died 184th day.</td>
</tr>
<tr>
<td></td>
<td>C23</td>
<td>Whole milk, 96 days. Skim milk and CaCO₃, starch, acid phosphate.</td>
<td>83d, 92nd, 96th, 104th days.</td>
<td>Ca 2.0 mm during convulsion. Above this after 105th day.</td>
<td>&quot; &quot; 142nd &quot; &quot;</td>
</tr>
<tr>
<td>3</td>
<td>C14</td>
<td>Whole milk, 27 days. Same plus cod liver oil till death.</td>
<td>177th day.</td>
<td>Not secured.</td>
<td>Died in convulsion.</td>
</tr>
<tr>
<td></td>
<td>C27</td>
<td>Whole milk, 67 days. Same plus syrup of iron phosphate to end of experiment.</td>
<td>None.</td>
<td>Normal.</td>
<td>Removed from experiment 501st day.</td>
</tr>
<tr>
<td>C28</td>
<td>Whole milk, 27 days. Same plus sulfur to end of experiment.</td>
<td>222nd, 225th, 228th days.</td>
<td>Ca 1.83 mM 200th day. About 2 mM till death.</td>
<td>Died in convolution 228th day.</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>------------------------------------------------------------</td>
<td>----------------------------</td>
<td>---------------------------------</td>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td>C30</td>
<td>Whole milk, 48 days. Same plus raw linseed oil till death.</td>
<td>None.</td>
<td>Ca at a minimum (1.75 mM) on 300th day.</td>
<td>Stiffness coincided with low Ca.</td>
<td></td>
</tr>
<tr>
<td>C34</td>
<td>Whole milk plus paraffin oil.</td>
<td>108th day.</td>
<td>Ca, 1.05 mM 102nd day.</td>
<td>Died in convolution.</td>
<td></td>
</tr>
<tr>
<td>4 C16</td>
<td>Whole milk, 3 mos. At various times mineral mixture, cod liver oil, blood meal, and syrup of iron phosphate.</td>
<td>None.</td>
<td>Normal.</td>
<td>Taken from experiment 611th day.</td>
<td></td>
</tr>
<tr>
<td>C22</td>
<td>Whole milk 57 days. At various times cod liver oil, alfalfa tea, tankage, wood ashes, syrup of iron phosphate, wheat bran.</td>
<td>“</td>
<td>“</td>
<td>Taken from experiment 710th day.</td>
<td></td>
</tr>
<tr>
<td>C36</td>
<td>Whole milk 10 days. At various times corn and oats, skim milk, oat hulls, wheat bran, cod liver oil, bone meal.</td>
<td>141st, 146th days.</td>
<td>See Fig. 2.</td>
<td>Legs stiff, 135th day. Found dead 165th day.</td>
<td></td>
</tr>
<tr>
<td>C54</td>
<td>Herd ration, 50 days. Whole milk alone till death.</td>
<td>None.</td>
<td>Normal.</td>
<td>Died during an atypical attack on 174th day.</td>
<td></td>
</tr>
</tbody>
</table>
and Gibson and Conception (10) observing symptoms of leg weakness and posterior paralysis in puppies fed on milk alone. With rats the symptoms are somewhat different. Mattill and Conklin (11) found that, especially in females, the rate of growth was retarded and reproduction failed, but the disturbances described above were apparently not seen. Palmer and Kennedy (12) partly confirmed Mattill's results. With an "artificial milk" they succeeded in getting some of their rats to give birth to young but it may be a significant point to observe that after 15 to 21 days "the young began to exhibit weakness, with spasms, and were destroyed by their mothers."

The present report is based on data from fourteen calves which were fed rations of milk alone or milk supplemented with various materials as indicated. The changes in the inorganic phosphorus, chloride, calcium, and carbon dioxide in the blood have been followed in order to detect any variations from the normal. The methods of analysis used were the same ones described in a former article on the normal composition of beef blood (13).

On the basis of rations fed, the subjects arrange themselves into the following classes: (1) Those receiving milk alone. (2) Those receiving milk alone until after the onset of convulsion when some supplement was added. (3) Those receiving milk plus a single additional substance. (4) Those receiving milk and a grain or mineral mixture.

The general results are summarized in Table I and details of the blood pictures of two animals are shown in Figs. 1 and 2.

**DISCUSSION.**

Although the results reported are too few in number to permit the drawing of very positive conclusions, certain definite tendencies appear to be evident. It seems that calves subsisting on a diet of milk alone or milk supplemented only by certain supplements cannot usually be raised to maturity. Our experiences agree with those of other experimenters on calves and other animals, as outlined in the first part of this paper. Whatever may be the mechanism of this disturbance it is apparently operative on all sorts of animals irrespective of the character of their natural diets, since the same symptoms, at least, have been observed in calves, guinea pigs, pigs, and dogs. The symptoms observed by us are as follows:
The calves seem nervous and irritable; the coats become rough; the eyes fail to focus and assume a staring appearance. Some animals appear at times to become dizzy or confused, running backwards or forwards for short distances or turning in circles. Frequently, the balance is so disturbed that the calf falls to the ground, occasionally dropping forward with its head flexed between its front legs. No spasticity is apparent during these attacks, the muscles being completely relaxed. At other times, however, they stand, trembling for a few seconds, and fall on one side in violent convulsions. The legs are rigidly extended, the muscles becoming hard and tense; there is frothing at the mouth; respiration slows down with marked dyspnea. These attacks may last but a few minutes or, intermittently, for several hours. Calves under 6 months of age usually survive several such seizures but older calves succumb to the first attack. Occasionally, a stiffness of the muscles of the legs develops which may be of a permanent or only temporary nature.

On autopsy, the outstanding gross lesions in the majority of cases are multiple petechial and ecchymotic hemorrhages of the pericardium, heart, thymus, and other structures of the thoracic region in variable degrees. Degenerative changes in the liver and kidneys are observed in some of the cases with occasionally a gastroenteritis. The gross picture suggests some form of intoxication.¹

All of the five animals in Groups 1 and 2 when fed milk alone developed convulsions in from 83 to 200 days with the exception of C40 which showed no symptoms for 461 days. All died, three in spite of the addition of straw, cod liver oil, calcium carbonate or calcium phosphate to their ration. The one consistent and characteristic feature of the blood picture was a drop in the calcium to a value of 2 mM or below coincident with the attack. Evidently none of the supplements used exerted a curative effect when administered after the onset of the attack.

Of the five animals in Group 3 only one showed no marked symptoms. This animal received whole milk and syrup of iron phos-

¹ Postmortem examination has been made of all cases and a histological examination of the organs is in progress. This work is being done under the supervision of Dr. E. T. Hallman of the Department of Pathology, Michigan State College.
phate until it was removed from the experiment at the age of 501 days. No convulsions were observed and its blood picture was normal. On a ration of whole milk and cod liver oil, C14 died in a violent convulsion at the age of 177 days. As this was before the blood studies were undertaken data on the blood picture are not available. The results on C28 which received whole milk and sulfur are interesting in view of Marine's (14) belief that sulfur increased the susceptibility of dogs to parathyroidal tetany. Although no convulsions were observed in the case of C30, it developed a pronounced stiffness and coincident with it a hypocalcemia which disappeared simultaneously with the recovery of the animal. It was found dead on the 165th day.

Two of the four animals in Group 4 showed no typical symptoms and had normal blood pictures throughout the course of the experiment. It may be a significant fact that these animals, like C27, were on a ration which included syrup of iron phosphate. With reference to the sow which McCollum (6) succeeded in raising to maturity on milk alone, the statement was made that it had access to rusty iron pipes. On a ration of milk plus various concentrates, cod liver oil, and bone meal, C36 developed characteristic convulsions and a typical blood picture as shown in Fig. 2. Calf C54 was subjected to a treatment just the reverse of that given the animals in Group 2. It received a supplemented ration during the early part of the experiment and milk alone in the latter part. When attacked it did not show the typical convulsions associated with low blood calcium and there was no tetany. The animal backed around the yard, turning always to the left and frequently running backwards for some distance. It was taken into the barn where it died after falling and breaking its leg. A blood sample taken at the onset of the attack showed a blood calcium of 2.55 mm.

The fundamental cause of the symptoms noted is still problematical. Vitamins are apparently ruled out. Although skeletal abnormalities were occasionally found on autopsy the fact that cod liver oil failed, in every case, to prevent or mitigate the symptoms precludes the assignment of that particular substance, held to be essential in calcium retention, to the causal rôle. This contention is supported by metabolism results secured on C28 within 10 days of its death, which showed it to be in positive calcium and phosphorus balance.
The responsibility of vitamin B is rendered improbable. The milk used was from cows known to be on feed containing adequate quantities of this substance. The fact that C36 on a ration of yellow corn and oats, a ration high in vitamin B, developed the same symptoms substantiates this view. Both Eckles (2) and McCandlish (15) deny a vitamin causation. Loss in weight was not a symptom and it was frequently observed that the appearance of convulsions was preceded by an increased rate of growth.

The similarity of the symptoms of our animals and those of parathyroidectomized animals is striking. Parathyroid removal or impairment is accompanied by a depletion of the blood calcium. We have demonstrated a definite relationship between certain of the symptoms in our animals and this same condition. It appears that the threshold is slightly higher in calves than in dogs, tetany being observed in the latter usually when the blood calcium falls below 7.0 mg. per 100 cc. (1.75 mM) while in the former a condition of tetany, either latent or active, appeared to exist when the figures fell below 8.0 mg. per 100 cc. (2.0 mM). We have no record of true convulsions when the blood calcium exceeded this figure by more than experimental error. Active tetany did not always supervene when values lower than this existed but usually there were indications of its imminence.

There appears to be no relation between blood calcium and the symptoms other than tetany or muscular rigidity. We have frequently secured samples from animals either during or immediately after non-spastic attacks which gave normal values for calcium. This is true likewise in the case of C54 which was bled during the terminal attack when it was actively engaged in backward running and left turning.

Our attempts to mitigate the symptoms by feeding calcium salts were not so conclusive as might be desired because only the phosphate and carbonate were tried. The work of Berkeley and Beebe (16), Greenwald (17), Iljort (18), and Luckhardt and his coworkers (19, 20) indicates that these salts have a low value in the treatment of tetany.

At the onset of the attacks there was a rise in the inorganic phosphorus which was transient in character. There was, however, no constant nor quantitative relationship between the variations in this constituent and the blood calcium. Greenwald
(21) and Salvesen (22) have called attention to the tendency for the phosphate to rise, at least temporarily, in parathyroid tetany. Gross and Underhill (23) did not find high phosphorus values to be a constant feature in this condition. In our animals while increased phosphorus did not always accompany low calcium values an explanation may be afforded by the rapid readjustment of the phosphorus concentrations. Thus, in the case of C36 (Fig. 2) a sample taken 2 hours after the onset of the convulsion and all subsequent samples showed no increased inorganic phosphate. Whether or not an increased phosphorus is observed seems to depend upon when the sample is taken.

Binger (24), Salvesen, Hastings, and McIntosh (25), and Underhill, Gross, and Cohen (26) have all shown that the introduction of large amounts of phosphorus into animals may be accompanied by a depression of the blood calcium with the production of tetany.

The contention of Salvesen, Hastings, and McIntosh that high blood phosphate unassociated with low blood calcium is not accompanied by tetany is supported by our results. Preceding death, the inorganic phosphate in the blood of C36 reached the extremely high level of 6.61 mM, yet no signs of tetany appeared, the blood calcium being in the neighborhood of 3.0 mM. In Calf C31, on the other hand, tetany occurred with an inorganic phosphate content of 2.90 to 4.11 mM and a blood calcium of 2.0 to 1.75 mM.

There appeared to be a tendency for the chlorides to fall somewhat during a seizure but this change was not marked.

The explanation heretofore advanced for the results obtained from feeding milk alone to herbivores has been that, having been developed to take care of the bulky fodder of their natural ration, the gastrointestinal tract of such animals becomes atonic when roughage is denied them. This prevents the proper digestion of what food is ingested with the consequent formation of toxic products which, when absorbed, produce the results observed. Heretofore, no explanation of the mechanism of the action of such a toxin has been made. The production of parathyroid tetany has likewise been attributed to a toxemia of gastrointestinal origin.

At the present time the intimate relation between the parathyroids and the calcium-regulating agency of the body seems to have been conclusively demonstrated. Whether they act through the elaboration of a hormone which itself directly controls the calcium
solution and deposition or indirectly by exerting a detoxicating function for the protection of some other organ which regulates this process of mineral metabolism may perhaps be questioned. The result however appears to be the same; viz., the removal or injury of the parathyroid glands disturbs the calcium metabolism. If it may be reasoned conversely that a disturbance in the calcium metabolism indicates an impairment of the parathyroid function, it would follow that such a condition exists in our animals and we are thus afforded an explanation of the mechanism of the assumed toxemia.

The work of Dragstedt (27) in support of the theory of the detoxicating function of the parathyroids is especially interesting in connection with our experiments. By the use of a milk diet or a ration rich in lactose, which converts the intestinal flora from a putrefactive to a fermentative one, he has been able to control the tetany in parathyroidectomized dogs. We have been able to produce typical symptoms of parathyroid tetany in our calves raised on a diet of milk alone which should have prevented the establishment of a proteolytic flora at any time. The difference in our observations may perhaps be due to the greater length of the bovine intestine as compared with that of the dog. The lactose content of milk may be inadequate to maintain an aciduric condition throughout the longer gut. Some support for such an idea may be found in Inouye's (28) results which showed that the greater the casein content of the diet the greater the amount of lactose necessary to produce beneficial results. Work on this aspect of the problem is in progress and the results will be reported in a later paper.

SUMMARY.

A study has been made of the effects on calves of a ration of milk alone or of milk with the addition of various supplements.

The most striking result of such treatment is the development of convulsions resembling those due to the removal of the parathyroid glands.

The symptoms are accompanied by a lowering of the calcium content of the blood.

The inorganic phosphate, chlorides, and bicarbonate content of the blood show no characteristic changes.
There is no evidence from the results obtained that the condition is due to an acidosis.

BIBLIOGRAPHY.

STUDIES ON THE CHEMICAL COMPOSITION OF BEEF BLOOD: III. THE BLOOD PICTURE OF CALVES ON A SOLE DIET OF MILK OR OF MILK WITH THE ADDITION OF VARIOUS SUPPLEMENTS
C. F. Huffman, C. S. Robinson and With the assistance of R. E. Larson and K. L. Burt


Access the most updated version of this article at [http://www.jbc.org/content/69/1/101.citation](http://www.jbc.org/content/69/1/101.citation)

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 0 references, 0 of which can be accessed free at [http://www.jbc.org/content/69/1/101.citation.full.html#ref-list-1](http://www.jbc.org/content/69/1/101.citation.full.html#ref-list-1)