

MAGNESIUM STUDIES IN CALVES

I. TETANY PRODUCED BY A RATION OF MILK OR MILK WITH VARIOUS SUPPLEMENTS*

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Attempts to raise calves to maturity on a ration of whole milk alone have consistently failed (1-4). McCandlish (5), however, succeeded in raising some calves to maturity when the whole milk ration was supplemented with alfalfa hay. The result of a continued whole milk ration, which has been described in detail elsewhere, is a train of symptoms resembling those following extirpation of or injury to the parathyroid glands, and the frequent occurrence of a hypocalcemia led to the proposal of this as an explanation of the neuromuscular disturbances observed in these cases. Although hypocalcemia was the outstanding abnormality seen in the cases studied up to the time of that report (3) attention was also called to the fact that sometimes it was absent. As experiments multiplied, it became apparent that from so many cases with normal blood calcium the disturbances could not be the result of transient low values and so missed in the blood sampling, but that the symptoms were consistently produced when the blood calcium was normal.

A few determinations of blood magnesium had been made and, although they were known to be low, the significance of hypomagnesemia was not appreciated until the work of Kruse, Orent, and McCollum (6) demonstrated its importance. The similarity of the symptoms of magnesium deficiency and those seen in our animals together with the low magnesium values in our records pointed to this as the possible explanation of the failure of milk

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alone as a food and prompted a reinvestigation of the subject from this angle.

Methods

The blood was withdrawn from the jugular vein into a centrifuge tube containing a small amount of lithium citrate and centrifuged for 30 to 35 minutes. 10 cc. of the clear plasma were pipetted into 40 cc. of 5 per cent trichloroacetic acid, thoroughly mixed, centrifuged for 10 minutes, and filtered. Aliquots of this filtrate were used for determining calcium, phosphorus, and magnesium. Plasma calcium and inorganic phosphorus were determined by methods previously described (7). Plasma magnesium was determined colorimetrically by a modification of the Briggs technique (8). 15 cc. of the calcium oxalate filtrate, 1 cc. of 2 per cent KH_2PO_4 , and 1 cc. of concentrated ammonia were placed in a centrifuge tube and rubbed down with a rubber policeman in order to have the magnesium ammonium phosphate in a finely divided state. The tubes were placed in the refrigerator for 12 to 15 hours to allow complete precipitation. The tubes were then centrifuged for 15 minutes, the supernatant liquid removed, and the precipitate carefully washed twice with an ammoniacal 20 per cent alcohol solution. The precipitate was dissolved and the phosphorus was determined by the Briggs technique (8).

Symptoms of Magnesium Deficiency in Calves

Among the early symptoms of a magnesium disturbance in calves are irritability, nervousness, and anorexia. The animal, apparently temporarily blinded, will run into obstacles, or becoming confused will turn in circles until its balance is completely destroyed. As the convulsions become more violent, the calf may fall on its side with the legs alternately rigidly extended and contracted; there is frothing at the mouth and profuse salivation. These attacks may last continuously for several minutes or, intermittently, for a longer time. Young calves seem to be able to withstand several such convulsions but older calves usually succumb to the first attack.

It is practically impossible to distinguish between the form of tetany in calves which is associated with hypocalcemia and the tetany which is associated with hypomagnesemia unless blood studies are made. Vasodilatation has not been observed.

Results

As previously stated, many calves manifested tetany with normal blood calcium and inorganic phosphorus when fed the rations indicated in Table I. The rations were always milk alone

TABLE I

Calves on Whole Milk Ration Which Died in Tetany with Normal Plasma Calcium and Inorganic Phosphorus

Calf No.	Age at death	Weight	Mg intake per day	Mg intake per kilo body weight	Blood		Supplement
					Ca	P	
	<i>days</i>	<i>kg.</i>	<i>gm.</i>	<i>mg.</i>	<i>mg. per 100 cc.</i>	<i>mg. per 100 cc.</i>	
C-14	174	75.9	1.04	13.70	13.3	3.95	Cod liver oil
C-25	491	205.9	1.61	7.82	9.8	8.04	None
C-40	465	211.4	1.55	7.33	11.2	5.77	"
C-42	348	182.7	1.63	8.92	10.5	6.89	"
C-52	276	140.5	1.12	7.97	9.6	7.20	Mineral*
C-53	272	192.3	1.63	8.48	10.6	5.48	None
C-54	173	134.6	1.11	8.25	10.9	8.30	"
C-58	413	291.4	1.57	5.39	11.6	6.06	†
C-61	325	158.6	1.25	7.88	10.8	6.66	†
C-62	606	146.8	1.49	10.15	9.4	5.90	†
C-65	210	126.4	0.96	7.59	10.3	5.19	None
C-68	260	115.9	1.16	10.01	11.0	4.81	†
C-69	329	188.6	1.21	6.41	10.8	7.17	Linseed oil
C-95†	41	51.4	0.65	12.66	12.2	8.93	None
C-96†	60	61.4	0.76	12.38	10.3	5.39	"
C-120	300	210.5	1.63	7.74	10.4	6.41	Parathormone
C-121	149	129.5	1.09	8.42	12.7	6.91	"
C-123	446	331.4	1.91	5.76	14.3	5.30	Cod liver oil
C-124	246	199.5	1.52	7.62	12.3	7.21	" " "
C-126	481	378.2	2.18	5.76	11.1	6.51	Mineral

* This mineral mixture contained Mn, F, Si, Al, and Fe. The other mineral mixture contained only Fe, Cu, and Mn.

† Syrup of iron phosphate.

‡ These calves manifested tetany which was not fatal.

or milk with such supplements as cod liver oil, syrup of iron phosphate, parathormone, or a mineral mixture containing iron, copper, and manganese. As shown in Table I the magnesium intake varied from 0.65 to 2.18 gm. per day, whereas the intake per kilo of body weight varied from 5.39 mg. to 13.70 mg.

Calf C-14 died in tetany with a blood calcium of 13.3 mg., inorganic phosphorus 3.95 mg., and magnesium 0.88 mg. per 100 cc.

TABLE II

Age, Weight, Magnesium Intake, and Blood Calcium, Phosphorus, and Magnesium of Calves Which Manifested Tetany When Fed a Ration of Milk with Various Supplements

Calf No.	Age	Weight	Mg intake	Mg intake per kilo body weight	Blood		
					Ca	P	Mg
	<i>days</i>	<i>kg.</i>	<i>gm.</i>	<i>mg.</i>	<i>mg. per 100 cc. plasma</i>	<i>mg. per 100 cc. plasma</i>	<i>mg. per 100 cc. plasma</i>
C-178	10	48.2	0.41	8.51			
	20	49.1	0.62	12.63	13.3	7.19	
	30*	54.1	0.69	12.75	12.7	8.39	
	40	58.7	0.77	13.12	11.1	7.23	1.53
	50	64.6	0.86	13.31	12.0	7.53	1.66
	60	70.5	0.91	12.91	12.4	8.02	2.29
	70	76.9	1.00	13.00	12.7	7.49	1.53
	80	85.5	1.08	12.63	12.4	8.40	1.75
	90	93.7	1.08	11.53	13.1	7.96	1.83
	100	93.7	1.08	11.53	12.0	7.53	
	110*	93.7	1.58	16.86	11.6	5.48	1.61
C-179	119	93.7	3.60	38.42	12.2	7.44	1.93
	10	41.4	0.40	9.66			
	20	44.5	0.60	13.48			
	30	50.9	0.65	12.77	13.1	7.82	
	40	59.1	0.73	12.35	11.7	7.91	
	50	62.3	0.83	13.32	12.4	8.31	1.78
	60	68.7	0.91	13.25	12.9	8.81	2.16
C-181	64*	77.3	0.93	12.03	12.5	7.23	1.53
	180†	157.3	1.31	8.33	12.8	9.26	1.87
	190	165.5	1.31	7.92	13.3	8.50	1.83
	200	172.7	1.33	7.70	12.2	8.72	1.71
	210	177.7	1.42	7.99	12.1	8.28	1.69
	220	191.7	1.42	7.40	11.4	8.01	1.38
	230	200.5	1.42	7.08	11.7	8.03	1.38
	240	206.4	1.42	6.88	11.8	8.33	1.65
	250	216.4	1.42	6.56	11.6	7.78	1.39
	260	221.4	1.42	6.41	11.1	6.01	1.58
	270	220.0	1.42	6.45	12.8	6.93	1.58
	280	225.0	1.54	6.84	10.9	7.19	1.29
	290	226.4	1.50	6.62	10.7	8.12	1.23
	300*	228.2	1.43	6.26	9.8	6.83	1.22

TABLE II—*Concluded*

Calf No.	Age	Weight	Mg intake	Mg intake per kilo body weight	Blood		
					Ca	P	Mg
	<i>days</i>	<i>kg.</i>	<i>gm.</i>	<i>mg.</i>	<i>mg. per 100 cc. plasma</i>	<i>mg. per 100 cc. plasma</i>	<i>mg. per 100 cc. plasma</i>
C-186	180†	109.1	1.76	16.13	10.8	9.06	1.50
	190	112.7	1.76	15.62	10.4	10.17	1.60
	200	115.9	1.76	15.19	10.3	7.44	1.54
	210	130.5	1.76	14.60	10.5	8.45	1.91
	220	121.4	1.76	14.50	10.8	8.87	1.38
	230	119.5	1.76	14.72	9.8	9.06	1.41
	240	118.2	1.71	14.47	9.5	7.35	1.29
	250	122.7	1.48	12.07	10.0	8.50	1.44
	260	125.0	1.48	11.83	10.6	8.06	1.32
	270	130.5	1.48	11.34	9.5	7.88	1.50
	280	137.6	1.76	12.78	10.8	6.30	1.35
	284*	128.6	1.76	13.67	12.3	8.06	1.77
C-187	180†	121.9	1.76	14.44	9.8	7.40	1.26
	190	124.2	1.76	14.17	9.4	7.02	1.44
	200	127.4	1.76	13.81	10.2	6.75	1.36
	210	129.7	1.76	13.57	10.5	7.23	1.73
	220	131.0	1.76	13.44	10.0	7.48	2.05
	230	131.0	1.76	13.44	9.5	7.62	1.35
	240	130.6	1.71	13.09	7.0	7.58	2.69
	244*	130.1	1.45	11.15	9.7	5.41	1.12

Calf C-178 was fed whole milk to 31 days of age, when the ration was supplemented with cod liver oil. At 108 days of age the mineral mixture, containing Fe, Cu, and Mn was added. Calf C-179 was fed whole milk and cod liver oil. Calf C-181 was fed whole milk plus cod liver oil and the mineral mixture.

Calves C-186 and C-187 were fed skim milk, cod liver oil, yeast, and the mineral mixture.

* Tetany.

† Started on experiment at birth; data for first 170 days are omitted.

of plasma. Much lower phosphorus values have been frequently observed with normal or slightly higher than normal calcium values without the least evidence of irritability or tetany. The terminal phosphorus values of Calves C-53, C-65, C-68, C-96, and C-123 are slightly subnormal but not sufficiently low to bring about low phosphorus-high calcium tetany. Calves C-25, C-52, and C-62 also died in tetanic convulsions with calcium values of

9.8, 9.6, and 9.4 mg. respectively, which are certainly not sufficiently low to produce low calcium tetany.

The normal range of calcium and inorganic phosphorus for calves of the ages included in this discussion varies from 10 to 13 mg. and 6 to 8 mg. per 100 cc. of plasma respectively.

Table II summarizes the magnesium intake per day by 10 day periods and the corresponding plasma values for calcium, inorganic phosphorus, and magnesium of five typical additional animals. Calves C-178, C-179, and C-181 were fed whole milk with various supplements, while Calves C-186 and C-187 were fed a low fat ration consisting of skim milk with various supplements. Calves C-181, C-186, and C-187 were placed on experiment at birth, but the blood data for the first 170 days are omitted to save space.

Calf C-178 was fed whole milk until 31 days of age, when tetany was first observed. The blood calcium was 12.7 mg. and inorganic phosphorus 8.39 mg. per 100 cc. of plasma. Blood magnesium was not determined at this time. The ration was supplemented with cod liver oil. This animal again came down with tetany at 108 days of age. The blood calcium, inorganic phosphorus, and magnesium values at this time were 11.6, 5.48, and 1.61 mg. respectively. A mineral mixture supplying iron, copper, and manganese was added at this time. 11 days later the calf was found dead. The blood magnesium value just prior to death was 1.93 mg. This value was subnormal for a calf of this age, although the magnesium intake appeared to be adequate.

Calf C-179 had a convulsion at 64 days of age on a ration of whole milk and cod liver oil. At the time of the convulsion, the blood calcium, inorganic phosphorus, and magnesium values were 12.5, 7.23, and 1.53 mg. per 100 cc. of plasma respectively.

Calf C-181 was fed whole milk from birth together with enough cod liver oil to meet the vitamin D requirement. A mineral mixture (Fe, Cu, Mn) was also fed to supply the recognized mineral deficiencies of a milk ration. The blood magnesium values were all below 2 mg. per 100 cc. of plasma after 100 days of age. In order to increase the energy content of the ration, 2 pounds of 20 per cent cream were fed per day starting at 286 days of age. The blood magnesium values show a progressive decrease until the onset of the fatal convulsion. All of the blood calcium and phosphorus values were well within the normal range.

Calf C-186 was fed a ration consisting of skim milk, cod liver oil, yeast (25 gm. per day), and the mineral mixture. Starch was added to the ration at 234 days of age for energy. This calf had magnesium values which averaged above 2 mg. per 100 cc. of plasma during the first 90 days. After this age the blood magnesium showed a tendency to diminish. The terminal blood values for this calf were secured from a blood sample taken during the final convulsive state, so that increased values may be due to the convulsion itself.

Calf C-187 was fed the same ration as Calf C-186. The magnesium values averaged above 2 mg. per 100 cc. of plasma during the first 60 days but after that time there was a tendency for the magnesium to decrease. After 210 days of age the magnesium values began to show large fluctuations with one low calcium value. Although the animal was very irritable during this time, tetany was not observed. The final magnesium value was 1.12 mg., which is extremely low for a calf. This animal died during the night and the condition of the pen indicated that considerable struggling had occurred before death.

All the animals mentioned in Table II were observed in tetanic convulsions once or twice during the course of the experiment. This does not preclude, however, the possibility of additional convulsions at times when the calves were not under observation. It is very probable that additional convulsions did occur in some of the calves because of their extreme irritability. At times it was possible to precipitate a convulsion during bleeding or when leading a calf from one stall to another.

DISCUSSION

The results of this investigation help to explain the many failures of whole milk as a sole ration for calves. Low magnesium tetany does not occur on the average calf's ration because these animals are able to utilize magnesium more efficiently when they have access to roughage. Cow's milk contains approximately 0.01 per cent magnesium, indicating that young calves have a small but definite requirement for this element. It seems altogether possible that the magnesium requirement should increase with normal growth, the same as the requirements increase for calcium and phosphorus. The calcium and phosphorus requirements are

maintained by increasing the milk intake but the same is not true for magnesium. Apparently there is a failure in the magnesium metabolism which prevents the animal from utilizing the available magnesium.

Our earlier work indicated that the tetany of calves on a whole milk ration must have been due to low blood calcium (3), although these statements occurred on p. 109: "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." Since our earlier report many more calves have died in tetany on a ration of whole milk or milk and various supplements with normal blood calcium and phosphorus. A few low blood magnesium values were recorded when this investigation was first begun, but no attention was given to them at that time because the importance of magnesium in nutrition was not appreciated.

Hemoglobin, blood sugar, and plasma carbon dioxide and chloride determinations were made from time to time but the results were all normal or only slightly subnormal. There were no cases of severe anemia. In later experiments sufficient vitamin D was furnished by cod liver oil, viosterol, sunshine, or by heavy feeding of whole milk to protect the animals from rickets.

It is of importance to note that the plasma calcium and inorganic phosphorus values are well within the normal range but that low plasma magnesium values are a constant finding. The magnesium values also suggest the possibility of individual variations and that periods of low plasma magnesium may precede or accompany the tetanic convulsions. The calcium values may drop to below 10 mg. per 100 cc. of plasma in a few periods but the general tendency is above 10 mg. Calves which develop true blood calcium tetany invariably have values below 7.5 mg. The magnesium deficiency in calves is apparently not associated to any extent with alterations in the levels of plasma calcium and phosphorus.

Normal blood magnesium values range from 2.25 to 2.75 mg. per 100 cc. of plasma, although larger temporary fluctuations may occur without any apparent cause. The Ca:Mg ratio in calf blood is normally 4:1 to 5:1, whereas a sustained whole milk ration

increases this ratio to 8:1 to 10:1, owing solely to a decrease in the blood magnesium. The blood magnesium values are of chief interest in that they show a progressive decline with the severity of the irritability, excitability, and neuromuscular activity. The magnesium intake was usually less than 2 gm. per day regardless of the size of the calf. The magnesium intake per kilo of body weight at the time of tetany ranged from 6.3 mg. per kilo in the case of Calf C-181 to 16.9 mg. per kilo in the case of Calf C-178. Low blood magnesium in these cases was probably not associated with the high fat content of the ration since Calves C-186 and C-187 were fed skim milk, starch, and not more than 20 cc. of cod liver oil per day.

The normal blood calcium-low magnesium tetany observed in calves resembles the tetany occurring in rats and dogs fed a low magnesium diet. However, the intake of magnesium per kilo of body weight was much greater in our calves than in the case of rats and dogs as reported by Kruse and coworkers (6). Sjollem and Seekles (9) and Sjollem (10) reported that the serum calcium and magnesium values were low in cattle suffering from grass tetany. The symptoms of grass tetany are similar to the symptoms observed in our calves. In grass tetany the blood calcium values averaged about 6.5 mg. and the magnesium values less than 1.0 mg. per 100 cc. of serum with a Ca:Mg ratio of 14:1. Our calves manifested tetany with a normal blood calcium and a low blood magnesium with a Ca:Mg ratio of 8:1 to 10:1. It is significant, however, that there is the same downward trend in the magnesium values. The average normal serum magnesium value given by Sjollem and Seekles (9, 10) for cows is 1.66 mg. and 0.46 mg. for cows with grass tetany, which is in contrast with our normal plasma magnesium range for calves of 2.25 to 2.75 mg. and 1.2 to 1.6 mg. for calves suffering from low magnesium tetany.

SUMMARY

1. Tetany occurred in twenty calves fed whole milk or milk with several different supplements, which had normal blood calcium and inorganic phosphorus. Systematic blood magnesium determinations were not made on these animals.
2. Data are also included on five more typical calves which died

in tetany, with normal blood calcium, inorganic phosphorus, but low blood magnesium.

3. Tetany in calves associated with low blood magnesium was indistinguishable from low blood calcium tetany unless blood calcium and magnesium studies were made.

4. Magnesium tetany occurred on a ration high in fat as well as on a ration low in fat.

5. Calves which manifested tetany with normal blood calcium and low magnesium had a blood calcium to magnesium ratio of 8:1 to 10:1.

6. These results partially explain why several investigators have been unable to raise calves to maturity on whole milk rations.

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