CAROTENE INTAKE, LEVEL OF BLOOD PLASMA CAROTENE,
AND THE DEVELOPMENT OF PAPILLARY EDEMA
AND NYCTALOPIA IN CALVES*

L. A. MOORE

In a previous publication Moore, Huffman, and Duncan (1) summarized the literature and reported observations on 24 cases of a type of blindness in the bovine due to a constriction of the optic nerve where it passes through the bony optic canal. The evidence indicated that the blindness was of a nutritional origin. Moore (2) has recently presented evidence to show that the blindness was due to a deficiency of vitamin A and was associated with the development of nyctalopia and papillary edema. Nyctalopia is a condition of night blindness in which the individual fails to see properly in dim light, but can see in bright light. Papillary edema is a swelling or an edema of the nerve head in the eye. In order to diagnose the latter condition it is necessary to examine the nerve head with an ophthalmoscope. For further details and a discussion of these conditions the previous paper may be consulted (2). Cunningham and Addington (3) have recently published results showing the type of blindness due to constriction of the optic nerve in calves whose dams received a ration of ground Hegari fodder and cottonseed meal. McNutt and Wall (4) have also reported the same type of blindness in feeder steers in Iowa. It is the purpose of this paper to show the relationship between carotene intake and the level of plasma carotene on the development of nyctalopia and papillary edema in calves when the carotene intake was under control.

EXPERIMENTAL

Plasma carotene determinations were made each week according to a recently published method (5). For the carotene determinations of the alfalfa meal the extractions were carried out by the method of Guilbert as modified by Peterson, et al. (6) and determined by the use of a photoelectric colorimeter.

Male calves of the Holstein and Ayrshire breeds were used. They received a low carotene ration after 40-90 days of age which consisted of skimmed milk and a concentrate mixture consisting of 240 pounds barley, 180 pounds rolled oats, 180 pounds wheat bran, 60 pounds linseed oil meal and 8 pounds salt. Previous to being placed on the ration the calves received whole milk and the low carotene concentrate ration. The concentrate ration contained 0.5 to 0.7 microgram of carotene per gram so that each calf received 2 to 3 micrograms of carotene per pound of body weight from this source. Wood shavings were used as bedding.

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After the calves were placed on the low carotene ration, ophthalmoscopic examinations were made weekly. The calves were tested for night blindness each week by attempting to run them into objects and observing their behavior in dim light, a method similar to that used by Guilbert and Hart (7). The calves were weighed every 10 days at which time adjustments were made in the amounts of carotene fed.
In order to compare the level of blood plasma carotene of a normally fed calf with the experimental animals, graph I shows the plasma carotene content of calf A25. This calf received whole milk to 80 days of age, a concentrate ration and alfalfa in liberal quantities after 30 days of age. It will be noted that a different scale for plasma carotene was used in this graph than in the graphs for the experimental animals.

Calf C407, an Ayrshire, was placed on the low carotene ration at 40 days of age and the principal results are shown in graph II. This calf was myopic by 2 to 3 diopters at the beginning of the experiment. At 81 days of age there was some suspicion of nyctalopia which was definite at 88 days. At 97 days of age there was some definite swelling of the nerve head and the orange yellow color of the tapetum lucidum was bleached. By this time the plasma carotene had dropped to 0.1 microgram per ml. At 105 days of age alfalfa was added to the ration which supplied 7 micrograms of carotene per pound of body weight or approximately one-half of the Guilbert and Hart (7) requirements. This was in addition to that received in the ration. The edema of the nerve head continued to increase so that the margins were completely blurred. The calf coughed considerably and scourred. The plasma carotene continued at an extremely low level. During part of this period the calf was only partially night blind. The left eye showed exophthalmus and the capillaries of the retina showed considerable distension. At 183 days of age the calf was in such poor condition that it was necessary to increase the carotene intake to 14 micrograms per pound. Nine days later the calf was no longer nyctalopic but showed exopthalmos in both eyes. The animal showed gradual improvement in condition and the plasma carotene gradually increased. The edema of the nerve heads decreased considerably. However, this animal never regained his full activity nor physical appearance, and always moved about rather slowly. He probably came very near to developing the permanent type of blindness due to constriction of the optic nerve so that the visual acuity was possibly decreased some by post papillitic atrophy.

Calf C398, an Ayrshire, was placed on the low carotene ration at 86 days of age as shown in graph III. This animal had a congenital posterior lenticous in both eyes making it difficult to examine the nerve head. At 206 days of age this animal showed nyctalopia and papillary edema. At 216 days when the swelling of the nerve heads had increased to 2 diopters, alfalfa was added to the ration supplying 14 micrograms of carotene per pound of body weight. Eighteen days later the calf was no longer night blind. The papillary edema receded very slowly and was still present after one year of supplemental feeding at the 14 microgram level. The plasma carotene increased gradually after the supplemental feeding.

Calf C404, also an Ayrshire, was placed on the low carotene ration at 78 days of age as shown in graph IV. At 129 days there was definite edema
of the nerve heads of both eyes, the right eye showed a choking of 1.5 D while the left eye showed a choking of one-half D. Partial night blindness was also observed and the tapetum lucidum of both eyes showed considerable bleaching. The plasma carotene had decreased to the 0.1 microgram level.

Alfalfa supplying 14 micrograms of carotene per pound of body weight was added at 131 days and after 8 days this calf was no longer night blind. The plasma carotene increased considerably and then decreased later for some unknown reason. At this time the nerve head of the right eye showed some increase in edema and at 242 days there were some indications of night blindness. At 435 days of age the condition of the eye ground showed little change from that noted at 218 days and although the tapetum lucidum took up some slight color it never assumed the orange yellow color which is normal for the structure. It will be noted that the plasma carotene remained quite low after the addition of the alfalfa and it was not until the latter stage of the experiment that the values rose above 0.2 microgram per ml.

Calf C402, a Holstein, was placed on the low carotene ration at 63 days of age, as illustrated in graph V, and showed evidence of papillary edema at 122 days of age at which time the plasma carotene had declined to a low level. Alfalfa supplying 14 micrograms per pound of body weight was added to the ration, and this allowance was increased later to 28 micrograms after which the plasma carotene increased from 0.04 to 0.5 microgram per ml. At 174 days the alfalfa was removed from the ration and the plasma carotene started to decline. At 213 days the calf died due to injuries not related to the experiment.

Calf C412, a Holstein, started to receive the low carotene ration at 90 days of age and at 161 days definite papillary edema developed as shown in graph VI. At 182 days definite nyctalopia was present. At 203 days the edema had increased considerably in the left eye so that there was a choking of 2 D. Many of the capillaries and small vessels at the edge of the nerve head also showed considerable fusiform dilation at this time. At 225 days the pupil of the left eye did not react to light stimulation and showed mydriasis. By means of covering each eye separately it was found that in daylight the calf was completely blind in the left eye but could still see well out of the right eye. However, in the dark the animal showed complete night blindness. Both eyes showed some exophthalmus. It will be noted that the plasma carotene had remained at an extremely low level during this period. At 228 days carotene was added to the ration in the form of alfalfa hay in an attempt to preserve the sight of the right eye. The attempt was successful for at the age of 480 days the calf could still see. The addition of the alfalfa promoted an immediate rise in the plasma carotene.

Calf C403, a Holstein, was placed on the low carotene ration at 52 days of age and night blindness developed at 125 days of age as shown by graph VII. Papillary edema was not present. At 127 days alfalfa supplying
carotene at the rate of 28 micrograms was added. Five days later the night blindness had disappeared and the carotene content of the blood plasma increased from 0.03 to 0.34 microgram per ml. by 169 days at which time the alfalfa was discontinued. "Caritol" supplying 28 micrograms of carotene per pound was added at 179 days. However, the plasma carotene appeared to decrease further so that at 205 days the alfalfa was substituted after which there was a steady increase in the level of plasma carotene.

Calf C400, an Ayrshire, as shown in graph VIII, was placed on the low carotene ration at 82 days of age and at 142 days the right eye showed a choking of 1 D and considerable edema was present on the dorsal edge of the nerve head. The left eye showed no choking but the nerve head was somewhat hazy. By this time the plasma carotene level had dropped to .04 microgram per ml. At 148 days there was considerable hemorrhage on the retina of the left eye along the vertical vessel. The hemorrhage was 2 cm. in length and 1 cm. in width as seen through the ophthalmoscope. There was also some involvement of the anterior chamber. At this time there was
no indication of night blindness. At 150 days alfalfa was added to supply 56 micrograms of carotene per pound of body weight. At 162 days both eyes showed a choking of 2 D and the nerve margins were entirely blurred. The hemorrhage in the left eye was present until 185 days although it gradually decreased in size during this period. At 193 days the feeding of alfalfa was discontinued whereupon the plasma carotene began to decrease. At 227 days it had dropped to 0.1 microgram per ml. and the calf showed nyctalopia. At 236 days carotene feeding was resumed at the previous rate and 8 days later evidence of night blindness had disappeared. The plasma carotene showed a gradual rise and attained values up to 0.6 microgram per ml. The edema of the nerve heads seemed to persist and the area previously covered by hemorrhage gradually assumed a greenish blue color. At 350 days the edema of the left eye had receded considerably and about two-thirds of the margins of the nerve head were discernible. The fibers of the nerve head could again be seen. At 415 days the edema in both eyes had largely disappeared and both eyes appeared to be quite normal except for the discolored area in the left eye due to previous hemorrhage.

Calf C399, a Holstein, was placed on the low carotene ration at 86 days of age as shown in graph IX and at 150 days showed evidence of papillary edema with a choking of 2 D in the left eye but was not night blind. At this time alfalfa was added supplying 14 micrograms of carotene per pound. At 159 days the calf showed evidence of nyctalopia and had a convulsion in the pen at the time of testing for night blindness. Because of the animal's apparent poor condition the allowance was further increased to 28 micrograms. At 164 days the right eye showed a choking of 1.5 D and the left eye 3 D. The development of a posterior polar cataract was observed in the right eye. At 166 days the alfalfa intake was increased so as to supply 56 micrograms of carotene per pound. The alfalfa was discontinued at 208 days and at 226 days nyctalopia was observed again. The plasma carotene had dropped to 0.2 microgram per ml. "Caritol" was added at 230 days and the calf was no longer night blind 6 days later. The "Caritol" was supposed to supply 56 micrograms of carotene per pound of body weight. The level of plasma carotene increased for a while and then decreased. The "Caritol" mixture apparently underwent auto-oxidation after a preliminary induction period so that no comparison could be made as to the effectiveness of this source of carotene.

The calf was in rather poor condition at 419 days, had a few convulsions and showed incoordination. The plasma carotene had decreased to the 0.05 microgram level, and at 425 days alfalfa supplying 10 micrograms of carotene per pound of body weight was added. During this period, observations on night blindness were not made because of the further development of the cataract in the right eye which would complicate the observations. At 458 days the calf went entirely blind so that the 10 microgram level did not
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prevent the further development of this condition. It will be noted that the plasma carotene level remained at about 0.2 microgram per ml. At this level of carotene intake the incoordination disappeared but the calf never seemed to pick up in physical appearance to any extent.

DISCUSSION

From the results obtained from this group of Holstein and Ayrshire calves it was found that when the level of plasma carotene fell to approximately 0.13 microgram per ml. or below, nyctalopia and papillary edema were likely to develop in a short while. Furthermore, if continued, the permanent type of blindness might also develop as in the case of calves C412 and C399. C412 remained at an extremely low level for over 3 months before the blindness developed. There are of course individual variations.

When the calves were placed on the low carotene ration at 40 to 90 days of age, nyctalopia developed in from 48 to 73 days while one animal, C398, went for 120 days which seemed to be the exception. The calves received whole milk as the only source of vitamin A up to the time they were placed on the low carotene ration. Papillary edema developed at about the same time although there were some variations. These variations are due to the fact that the two conditions are the result of two different processes as explained in a previous paper. It seems probable that with the method used only the later stages of night blindness were detected.

The nyctalopia could be cured in from 5 to 18 days by the addition of carotene to the ration.

From the results obtained from Calf C407, the addition of 7 micrograms of carotene per pound of body weight to the basal ration, which would make the total intake about 9 micrograms per pound, was not sufficient to raise the level of plasma carotene above 0.2 microgram per ml. This level did not prevent nyctalopia or further development of papillary edema. Furthermore, the calf showed evidence of bronchitis, diarrhea and general unthriftiness during this period all of which are evidence of insufficient vitamin A intake. When the carotene intake from alfalfa was increased to 14 micrograms the nyctalopia and bronchitis disappeared and the general appearance of the animal improved.

Calf C399 which received 10 micrograms of carotene per pound of body weight after 425 days of age, plus that in the basal ration making the total intake about 12 to 13 micrograms, maintained plasma carotene at about the 0.2 microgram level. This would indicate that the calf was receiving about the minimum maintenance level. This intake would be just slightly below the minimum requirements set up by Guilbert and Hart (7).

From the results obtained from calves C407, C398, and C404 where the carotene intake was adjusted at 14 micrograms per pound of body weight plus that contained in the basal ration which would make the total intake
about 16 micrograms per pound, the level of plasma carotene increased very gradually but never attained very high values. This gradual increase would indicate that some slight storage of vitamin A was taking place at this level. It will be noted that there are individual variations in this respect, C404 remaining below 0.2 microgram per ml. for a considerable period. It was felt throughout the experiment that this calf was always on the verge of vitamin A deficiency.

It will be noted further that at this level of intake while nyctalopia was prevented, the papillary edema in calf C404 showed some increase, C398 was static for a considerable period and C407 showed some decrease. Apparently nyctalopia may be prevented and the outward appearance may be normal at this level of intake but it may not be sufficient to keep the cerebrospinal pressure down to normal levels as indicated by the papillary changes. Data on this particular relationship will be reported at a later date.

In calves C412 and C403 which received 28 micrograms of carotene per pound of body weight the level of plasma carotene rose to as high as 0.7 microgram per ml. of plasma showing considerable contrast to the 14 microgram levels. At this level of intake the calves appeared very thrifty and active. The level of plasma carotene of C400 which received 56 micrograms of carotene per pound of body weight was not any higher than for calves C412 and C403 which received only 28 micrograms and probably indicates individual variation.

By comparing the level of plasma carotene of Calf A25 which received alfalfa hay in liberal quantities with the plasma carotene level of the calves used in this experiment it will be seen that there is considerable difference. In this experiment the plasma carotene values were usually below 0.8 microgram per ml. while Calf A25 attained values up to 3.0 micrograms per ml. during the same period of growth. Mature Holstein cows on pasture may attain carotene values up to 15.0 micrograms per ml. of plasma (8). It would seem therefore that in the bovine the level of blood plasma carotene is subject to wide variations.

The presence of carotene in blood plasma after the removal of the greater part of it from the ration is difficult to explain since the liver is supposed to convert it into vitamin A. It would be reasonable to suppose that shortly after its removal the carotene in the blood plasma would decrease rapidly and be absent in a few days. However this does not appear to be true. In calves C402, C403, and C400 there was a gradual decrease in the level of plasma carotene after the removal of the alfalfa from the ration and not a sudden drop. Unpublished data from mature cows show that when they are removed from a normal ration to a low carotene ration the decrease in blood carotene is gradual. Semb, Baumann and Steenbock (9) suggest that the blood stream can function as a significant storage reserve for carotene.

The results of this investigation show that the carotene requirements
reported by Guilbert and Hart (7) for cattle are approximately correct when the criteria of the development of nyctalopia is employed.

It should be kept in mind that the results obtained on the level of plasma carotene were with Holstein and Ayshire calves. Different values on the same level of carotene intake might be expected with the Jersey or Guernsey breed.

**SUMMARY AND CONCLUSIONS**

1. Calves placed on low carotene rations at 40 to 90 days of age developed nyctalopia in from 48 to 73 days.
2. Papillary edema developed at approximately the same time although there were some variations.
3. An intake of about 9 micrograms of carotene per pound of body weight was not sufficient to prevent nyctalopia or an increase in papillary edema.
4. An intake of about 16 micrograms per pound of body weight was sufficient to maintain the plasma carotene at 0.2 microgram per ml. and above in Holstein and Ayrshire calves.
5. An intake of 16 micrograms per pound of body weight was sufficient to prevent nyctalopia and maintain fair general health.
6. When the plasma carotene values fell below about 0.13 microgram per ml. nyctalopia and papillary edema followed. This value is for Holstein and Ayrshire calves.
7. The carotene requirements of Guilbert and Hart (7) for the bovine are approximately correct where nyctalopia is used as a criterion.

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**REFERENCES**

