Lesions of the Nervous System in Vitamin Deficiency

I. Rats on a Diet Low in Vitamin A

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Plates 15 to 18

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Lesions of the peripheral nervous system have been recognized and described in animals fed diets deficient in the antineuritic vitamin B, but there has been relatively little written about nervous system lesions in association with diets deficient in vitamin A. Hart, Miller and McCollum (1) described histologic changes "not unlike those recorded for beri-beri" in the nervous system of swine fed certain wheat and grain mixtures, and they concluded that these changes were the result of toxic materials in the food rather than due to the absence of vitamin A. Steenbock, Nelson and Hart (2) described unsteadiness of gait in a dog fed a diet deficient in fat-soluble vitamin but made no mention of examination of the tissues of the nervous system. Mellanby (3–6) observed incoordination, spasticity and weakness in young puppies fed a diet of 10 per cent wheat germ which was at the same time deficient in fat-soluble vitamins. He described lesions consisting of scattered degeneration in the spinal cord and observed that the ascending fibers were particularly involved. He related these lesions to a positive harmful influence in the wheat germ in the absence of a defending chemical substance like vitamin A. More recently Suzman, Muller and Ungley (7) have described experiments in which adult dogs were fed a diet abundant in cereal and lacking in vitamin A conducted with the idea of attempting to produce lesions in the spinal cord, but they did not succeed in accomplishing this end.

In the Laboratory of the Department of Obstetrics in this institution, Dr. S. B. D. Aberle has been conducting experiments with rats on a diet deficient in vitamin A with no direct intention of observing nervous system lesions or manifestations. It was observed, however, in the course of the feeding that certain animals developed marked weakness and incoordination of the extremities. As a result of this observation we undertook a study of the tissues of the central and peripheral nervous systems of these animals. It is the purpose of the
present communication to present the results of the studies made on
the tissues of the central and peripheral nervous systems of many of
these rats.

Experimental Procedure

Diet Employed.—All the animals used in this study, with the exception of certain
controls, were placed on an artificial ration deficient in vitamin A when 21 to 24
days of age. The composition of the ration was:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Per cent</th>
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<tr>
<td>Casein</td>
<td>15–18*</td>
</tr>
<tr>
<td>Corn-starch</td>
<td>56–63*</td>
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<tr>
<td>Crisco</td>
<td>18–22*</td>
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<tr>
<td>Osborn-Mendel Salt Mixture IV</td>
<td>4</td>
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* It was found that the animals ate better when the proportion of the various
  constituents of the diet was changed weekly or biweekly. This was done within
  the limits indicated in the table.

The vitamin B complex was supplied in the form of yeast in quantity calcu-
lated and found by practice to be sufficient for the needs of this animal. Vitamin
D was supplied in the form of irradiated ergosterol or irradiated yeast. Vitamin
E was present in sufficient quantity in the crisco; vitamin C is apparently not needed
by the rat.

Material Studied and Technic Employed.—The nervous systems of a total of
twenty-three animals were examined. The animals were grouped into seven
classes in accordance with conditions of experiment to be specified for each group.

Blocks of the brains and spinal cords were fixed immediately upon removal from
the animals in 95 per cent alcohol, in a solution of formaldehyde, v.s.p. (1:10),
and in Müller's solution. The brachial plexuses, the sciatic and vagus nerves of
each animal were fixed in Müller's and in formaldehyde solution, as were the optic
nerves from five of the rats in Group A. The alcohol-fixed material was embedded
in celloidin and stained by the original Nissl method (toluidine blue). The for-
maldehyde-fixed material was stained for fat by the Scharlach R method and for
the demonstration of myelin sheaths by the Spielmeyer method. The material
fixed in Müller's solution was stained with osmic acid, embedded rapidly in cel-
loidin and sectioned at 30 microns. In many instances the spinal cords were
sectioned longitudinally as well as transversely, and an average of four blocks at
different levels were taken from each cord. About ten sections in serial were cut
from each block and mounted for histologic examination.

RESULTS

On gross examination no abnormalities were found in the brain, spinal cord or peripheral nerves of any of the animals.
In none of the animals except Rat 76 (Group A) were there any lesions in the brain demonstrable microscopically by any of the staining methods. In that animal the ventral pontile nuclei contained many vacuolated nerve cells in the Nissl preparations, but the Spielmeyer, Marchi and Scharlach R preparations were negative.

None of the optic nerves examined showed any pathologic change grossly or microscopically.

**Group A. Nine Rats on Diet Deficient in Vitamin A, from Mothers on Diet of 100 Per Cent Calf Meal during Pregnancy and Lactation.**

*Rat 65.*—This animal was on the special diet for a total of 54 days and had paralysis for a period of 20 days, at the end of which time it died. Its maximum weight was 81 gm., but at necropsy it weighed only 65 gm.

Nissl preparations of the spinal cord showed swelling and cytolysis of the anterior motor horn cells, but there was no increase in the glia. In the Marchi preparations there was much black pigment deposition at the points of entrance of the posterior nerves into the cord. Somewhat less pigment was scattered in the posterior columns and was also present in an irregular manner around the periphery of the cord. Much degeneration was present in the posterior nerve roots and to a somewhat less degree also in the anterior roots. Scharlach R and Spielmeyer preparations of the spinal cord showed no degeneration. The vagus and sciatic nerves and those of the brachial plexus showed degeneration of an equal degree by all the staining methods (Fig. 2).

*Rat 71.*—This animal was on the special diet for 44 days and was paralyzed for 9 days, when it was killed. It had lost 14 gm. of weight from a maximum of 81 gm.

The anterior motor horns contained swollen, chromatolytic nerve cells. There was no proliferation of glia. Marchi preparations showed numerous black granules on the periphery of the ventral side of the cord and only a few granules in the posterior columns. Granules were absent in the nerve roots. Scharlach R and Spielmeyer preparations of the cord showed no myelin degeneration. The peripheral nerves were the seats of extensive demyelination (Figs. 1 and 3).

*Rat 72.*—This rat was on the special diet for a period of 72 days and was paralyzed for 33 days, when it died. Its maximum weight was 102 gm. and at necropsy it weighed but 77 gm.

A few ganglion cells in the anterior motor horns of the spinal cord showed chromatolytic changes. Marchi preparations of the cord were not made. Spielmeyer stains revealed large clear vacuoles indicating degeneration on the margins of the cord. In one Scharlach R preparation there was found a collection of fat droplets in the white matter. Extensive demyelination was demonstrable in the brachial plexuses and sciatic nerves by both the Marchi and Scharlach R methods. The vagi showed no involvement.

*Rat 73.*—This rat was on the artificial diet for 53 days and was paralyzed for
14 days, when it was killed. It had maintained its weight fairly constantly at the maximum of 76 gm.

There were no changes in the spinal cord demonstrable by the Nissl technic, and Marchi preparations of the cord were not made. In the Spielmeyer stains there were present large clear vacuoles on the periphery; Scharlach R preparations failed to reveal fat. By the latter staining method, however, one of the dorsal nerve roots was shown to contain an abundance of brilliant red particles. All the peripheral nerves, including the vagi, were strongly positive for fat by both the Scharlach R and Marchi methods (Fig. 4).

Rat 74.—The total experimental period of this animal was 73 days, during the last 30 days of which it was paralyzed. This animal had lost but 7 gm. in weight from a maximum of 103 gm. It was killed.

The Nissl preparations of the spinal cord were negative. Marchi preparations of the cord were not made. By the Spielmeyer method there was once more observed a looseness of structure and vacuolization on the periphery. In this cord the vacuolization was also present symmetrically in the posterior columns. Scharlach R preparations were completely negative. Degeneration of marked degree was demonstrated by the Marchi method in the sciatic nerves and to a less degree in the nerves of the brachial plexus. The vagi showed no degeneration by this method. The distribution of the myelin degeneration could be confirmed in the Scharlach R preparations.

Rat 75.—This animal was on the special diet for 55 days and showed symptoms of paralysis for 6 days, at the end of which time it died. Its maximum weight was 120 gm. and at necropsy its weight was 108 gm.

Nissl preparations of the cord were negative; Marchi preparations were not made. By the Spielmeyer method there could be shown vacuoles on the periphery, but no fat could be demonstrated by the Scharlach R stain. Fatty degeneration of the myelin sheaths of the brachial plexuses and sciatic nerves were found in the Marchi and Scharlach R preparations.

Rat 76.—This rat was on the experimental diet for 71 days and was paralyzed for a period of 22 days, at the end of which it died. Its loss of weight amounted to 10 gm. from a maximum of 107 gm.

A few anterior motor horn cells in the spinal cord showed chromatolytic changes and one glia rosette was present in the crossed pyramidal tract. In the Spielmeyer preparations the myelin sheaths on the periphery of the cord appeared spongy and vacuolated, but Scharlach R preparations did not disclose the presence of fat. In both Marchi and Scharlach R preparations there was present some fatty change in the brachial plexuses and sciatic nerves. The vagi were not examined. The Spielmeyer preparations confirmed the presence of degeneration observed by the other methods.

Rat 78.—The total duration of the experiment was 53 days and the animal was paralyzed the last 20 days of its life. This animal was killed, having lost no weight.
There were no changes observed in the nerve cells of the spinal cord. There were demonstrated large vacuoles on the periphery of the cord by the Spielmeyer technic (Fig. 9), but Scharlach R preparations of the cord and the nerve roots were negative for fat. All the peripheral nerves, the vagi, brachial plexuses and sciatics, were found to contain moderate numbers of black granules in the Marchi stains.

Rat 79.—This rat was on the diet for 50 days and had paralysis for 18 days, at the end of which time it was killed. The animal gained weight steadily up to the time of its death, when it weighed 85 gm.

There were no changes in the spinal cord that could be demonstrated by the Nissl stains. In the Spielmeyer preparations of the cord there was seen marked degeneration of the posterior columns and to a less extent also on the periphery (Fig. 10). Scharlach R preparations failed to show fat; Marchi preparations were not made. Extensive degeneration of the medullary sheaths was present in the brachial plexuses and the sciatic nerves, but the vagi were completely normal.

Comment

In each of the nine rats lesions were found in the spinal cord consisting of degeneration of the medullary sheaths of the sensory tracts on the periphery. In four of the animals the posterior columns showed degeneration and in two, the entering posterior nerve roots. These changes were demonstrated by the Spielmeyer myelin sheath stain and by the Marchi method. In Rat 72, which was paralyzed for 33 days, fatty change was demonstrated in the white matter of the cord by the Scharlach R stain. In Rat 65 there was degeneration of the anterior nerve roots in addition to the posterior. It should be mentioned that the findings in the nerve roots were discovered quite by accident since no systematic attempt was made to include these in the blocks taken for sectioning. The lesions that were observed in them suggest the interesting possibility that the changes in the cord were secondary to and dependent on them.

Every one of the animals showed extensive degeneration of the medullary sheaths of the brachial plexuses and sciatic nerves; the vagi were degenerated in only four of the animals, and in another they were not examined. From the fact that the degeneration in the peripheral nerves could be demonstrated by the Scharlach R method in addition to the Marchi and Spielmeyer methods, the conclusion must be drawn that it was of longer duration in them than in the spinal cord. This

1 This process is often designated by the term polynyritis in the literature.
would support the view that the peripheral nerves were primarily involved, and that the demyelination continued to the spinal nerve roots from whence it spread to the spinal cord itself.

Four of the nine animals of this group showed changes in the ganglion cells of the spinal cord that were described as swelling, cytolysis or chromatolysis. It becomes at once apparent from a glance at the histories of these animals that the neuronal lesions were in no way dependent on the duration of paralysis or on the loss of weight. The fact was brought to light, however, that these changes occurred only in those animals which were necropsied after a lapse of several hours and not in those necropsied immediately after death. The same observation was made subsequently in some of the other animals of this study. In passing, it must be mentioned that similar changes in nerve cells are produced when toluidine blue (or even thionin and cresyl violet) is used to stain tissue fixed in a solution of formaldehyde instead of 95 per cent alcohol.

Group B. Two Rats on Diet Deficient in Vitamin A, from Mothers on Diet of Table Scrap during Pregnancy and Lactation.—

Rat 122.—This animal was on the special diet for a total of 98 days and showed paralysis only on its last day of life. Its maximum weight was 122 gm. and at necropsy it weighed 96 gm. It was killed.

Nissl preparations of the spinal cord were completely negative. Marchi preparations of longitudinal sections of the cord showed an exquisite picture of degeneration of the posterior columns, the motor tracts and the posterior nerve roots as they entered the cord (Fig. 6). The anterior roots were likewise involved, but to a much less degree. Scharlach R preparations of the spinal cord were entirely free of fat. Large vacuoles were present in the posterior columns and at the periphery of the cord in the Spielmeyer stain. A striking picture of degeneration of the myelin was seen in the peripheral nerves by the Marchi method. The Spielmeyer and Scharlach R preparations of these nerves, however, were negative.

Rat 125.—This animal was on the diet deficient in vitamin A for a period of 105 days. It displayed signs of paralysis for a period of 20 days, at the end of which time it was killed. Its maximum weight was 196 gm. and at necropsy it weighed 154 gm.

The brain and spinal cord of this animal were not studied. Severe degeneration of the medullary sheaths of the brachial plexuses and sciatic nerves was found in the Marchi stains, but the other staining methods yielded negative results.

Comment

It will be noticed that the two animals of this group, from mothers on a diet of table scrap which is adequate in vitamin A, developed signs
of paralysis at a much later time than the animals in Group A of this study. This merely confirmed the well known fact that animals are born with vitamin A stored in their tissues if their mothers receive an adequate supply of this vitamin during pregnancy.

The lesions in the peripheral nerves of these two animals were similar to those observed in the rats of Group A, but perhaps they were earlier lesions since they could be demonstrated in Marchi preparations only. It is of great interest to note that in the spinal cord of Rat 122 there was degeneration present in the motor as well as in the sensory tracts. It would seem that the lesions in the cord followed those in the peripheral nerves on the sensory side, and produced those in the peripheral nerves on the motor side.

**Controls**

*Group C. Two Rats on Diet Deficient in Vitamin A, from Mothers on Diet of Table Scrap during Pregnancy and Lactation. Animals Killed before Any Signs of Vitamin A Deficiency Appeared.*—

Rats 132 and 133.—Each animal was killed 35 days after being placed on the special regimen. The first animal gained 67 and the second gained 76 gm. during this period.

There were no changes of any kind in the spinal cords which could be demonstrated by any of the staining methods. Similarly, the brachial plexuses, and the vagus and sciatic nerves were negative for any lesions in their medullary sheaths.

**Comment**

In spite of prolonged subsistence on a diet deficient in vitamin A, the two animals of this group failed to show any changes in their nervous systems at necropsy. They were killed before showing any signs of the deficiency disease, which would indicate a close parallel between the clinical manifestations of nervous lesions and the anatomic changes responsible for them.

*Group D. Five Rats on Diet Deficient in Vitamin A. Animals Partially or Completely Cured of Symptoms of Paralysis.*—

Rat 68.—This animal developed signs of paralysis after 33 days on the special diet. These lasted for 34 days, to disappear with the repeated administration of cod liver oil. The animal was killed 3 days after the disappearance of the signs of paralysis.

Lesions were not found in the spinal cord by the Nissl technic. Tremendous vacuolization was present in the posterior columns and at the periphery of the cord in both Spielmeyer and Scharlach R preparations. Marchi stains were not
made of the cord. Definite but not very extensive degeneration of the myelin sheaths of the peripheral nerves could be demonstrated by the Marchi method. This finding, particularly in the sciatic nerves, was confirmed in the Spielmeyer and Scharlach R preparations.

*Rat 77.*—Signs of paralysis appeared after 43 days on the special diet, and persisted up to the time the animal was killed, which was 29 days later. However, there was progressive improvement in the signs with the repeated administration of cod liver oil.

Changes in the spinal cord could not be demonstrated by the Nissl method. Vacuolization of the posterior columns and periphery of the cord was pronounced in the Spielmeyer preparations. Although the vacuoles were demonstrable in the Scharlach R preparations, no fat was found. Marchi preparations of the cord were not made. A moderate amount of degeneration was found in the peripheral nerves by the Marchi method, but the other stains were negative.

*Rat 115.*—This animal failed to develop any signs of paralysis (its mother was on a table scrap diet) after being on the special diet for 58 days. It was given cod liver oil, nevertheless, for a period of 12 days, at the end of which it was killed.

The spinal cord was not examined. The peripheral nerves showed distinct but not very extensive myelin degeneration in the Marchi preparations and to a less extent also in the Scharlach R and Spielmeyer preparations.

*Rat 205.*—This animal developed paralytic signs after 48 days on the diet, and these signs lasted for 30 days, to disappear after the administration of cod liver oil over a period of 20 days. The rat was killed 4 days after the disappearance of the paralytic signs.

The spinal cord appeared to be normal in the Nissl stains. In the Marchi preparations there was evidence of degeneration in the crossed and uncrossed pyramidal tracts, and to a slight extent also in the posterior columns and at the periphery of the cord (Fig. 8). Degeneration of one of the posterior nerve roots could be traced into the cord. In the Spielmeyer stains there was found vacuolization in the zones corresponding to the black granules seen in the Marchi preparations. The Scharlach R preparations were entirely negative. Moderately extensive degeneration was found in all the peripheral nerves by the Marchi method.

*Rat 206.*—This rat developed paralytic signs after 52 days on the diet, and these disappeared at the end of 26 days following the administration of cod liver oil for a period of 22 days. The rat was killed 4 days after the disappearance of paralytic signs.

Nissl preparations of the spinal cord revealed an entirely normal picture. In the Marchi preparations of cross-sections of the spinal cord there was found extensive degeneration of the periphery and of one of the posterior columns (Fig. 7). At another level the crossed and uncrossed pyramidal tracts showed degeneration in addition to the sensory tracts. The degeneration could be confirmed in longitudinal sections of the cord. There was present some vacuolization in the Spielmeyer preparations in those regions in which myelin degeneration was demon-
strable by the Marchi method. Scharlach R stains, however, were entirely negative for fat. The peripheral nerves showed well marked degeneration in the Marchi preparations (Fig. 5).

Comment

Rats 68, 77, 205 and 206 showed signs of paralysis for periods varying from 26 to 34 days. Three of the rats recovered from the paralysis with the repeated administration of cod liver oil, and they were killed 3 or 4 days later in each instance. Rat 77, although showing definite improvement, failed to recover completely from the paralysis. In view of the improvement noted in the symptomatology it is surprising that at necropsy such extensive lesions were present in the spinal cords and peripheral nerves of these animals. Similar observations have been made in experiments on vitamin B deficiency where it was found that the administration of yeast concentrate to paralyzed animals produced an almost immediate recovery. Obviously the clinical improvement of these animals could not be caused by a sudden restitution of the injured nervous systems to normal. Indeed, on the basis of such observations some workers have concluded that the paralysis was not caused by the peripheral polynyeuritis. Such a view, however, seems to be unfounded.

The conclusion must be drawn from the present experience that it is possible to have little or no clinical evidence of nervous disease in the presence of even marked anatomic lesions in the nervous system during a certain period of recovery. What the anatomic picture in the nervous system would have been 14 or 30 days after recovery is obviously not answered by this "acute" experiment.

Again in Rat 205 there was evidence to suggest that some of the changes in the spinal cord were merely an extension of those in the nerve roots. In this animal and in Rat 206 the crossed and uncrossed pyramidal as well as the sensory tracts showed some degeneration.

The problem presented by Rat 115 is unique in this study. The animal had been on the diet deficient in vitamin A for 58 days without presenting clinical evidence of injury to the nervous system. It did, however, show evidence of dietary deficiency by the presence of cornified epithelium in the vaginal smears. At necropsy the peripheral nerves showed distinct but not extensive demyelination. It may
possibly be supposed that the animal would shortly have developed paralysis had it not been killed or given cod liver oil.

*Group E. Two Rats Fasted but Receiving Full Ration of Vitamins Including Cod Liver Oil.*

*Rat S74.*—This animal received but 1 gm. daily of the diet deficient in vitamin A in addition to the full ration of vitamins including cod liver oil. It died at the end of 17 days without developing signs of paralysis and after losing 33 gm. in weight.

There was a slight paleness at the periphery of the spinal cord but no vacuolization in the Spielmeyer preparations. The Scharlach R and Marchi preparations were entirely negative for myelin degeneration. The peripheral nerves presented an entirely normal picture by all the staining methods employed.

*Rat S76.*—This rat also received 1 gm. daily of the special diet in addition to the full ration of vitamins including cod liver oil. It died at the end of 16 days on this diet without showing signs of paralysis and after having lost 58 gm. in weight.

All the preparations of the spinal cord presented an entirely normal picture, the cord having been sectioned longitudinally and transversely. The peripheral nerves were free of degeneration except for one small zone in the Marchi preparations, where a few black granules were found.

*Comment*

The anatomic findings in these two animals showed fairly conclusively that inanition itself was not a factor in the production of lesions in the nervous system. Moreover, the two rats in this experiment lost much more weight than any of the rats in the other experiments. It was shown by Woollard (8) and by Zimmerman and Burack (9) that demyelination of the peripheral nerves was present in animals that were starved except for vitamin B, which was given in adequate amounts. It is noteworthy that these animals were at the same time deprived of vitamin A, which factor may have played an important rôle in the production of the lesions.

*Group F. One Rat on Diet Deficient in Vitamin A Supplemented with Cod Liver Oil. Mother on Diet of 100 Per Cent Calf Meal during Pregnancy and Lactation.*

*Rat 64.*—This animal was on the special regimen for 111 days, during which time it increased its weight from 41 to 162 gm. At no time did it show paralytic signs.

A complete investigation of the nervous system, central and peripheral, by the various histologic methods employed in this study revealed a normal picture throughout.
Comment

That the artificial diet employed in this study when supplemented with an adequate amount of vitamin A was capable of maintaining rats in a good state of nutrition and did not cause nervous lesions even when fed over a long period of time, was shown by this experiment.

**Group G. Two Rats on Diet of Table Scrap, from Mothers on Same Diet.**—Rats 164 and 165.—The first animal was killed when 89 and the second when 90 days old.

A complete investigation of the entire nervous system by all the histologic methods employed in this study revealed no pathologic changes.

**DISCUSSION**

The pathogenesis of lesions associated with vitamin deficiencies is not understood at the present time. According to some of the investigators mentioned previously, the lesions observed in animals fed diets rich in cereals and deficient in vitamin A are the result of injurious agents in the form of assumed “toxic substances” which act in the absence of a defending chemical substance like vitamin A. Since the diet employed in this investigation did not contain cereals, it is impossible to attribute the lesions to substances contained in these foods.

In this connection it is of interest to consider the experimental results of Burr and Burr (10, 11) who employed rats to observe the effect of feeding a diet poor in unsaturated fatty acids. Although they do not mention physiologic or anatomic evidence of lesions in the nervous system, they describe urinary symptoms and changes in the tail and skin which they regard as significant since the diseased conditions cleared up when unsaturated fatty acids were added to the diet. These investigators found that it was impossible to produce the changes when corn-starch was one of the components of the diet. Since the ration fed the rats employed in the investigation presented in this communication contained corn-starch and, moreover, since none of the rats developed symptoms like those described by Burr and Burr, it seems reasonable that one might eliminate the possibility of such a deficiency. Thus it seems that the diet employed in these experiments is adequate in all respects excepting its content of vitamin A. However, since we have no information which suggests a possible mechanism for the development of lesions in vitamin deficiencies, the question as to whether
their presence merely serves as a protective one cannot be answered at this time. Experiments are now in progress in this laboratory which we hope may yield results that will throw some light on this phase of the subject.

With regard to the lesions described, it seems desirable to emphasize the importance of several staining methods. In the experience of the present writer, lesions of a degenerative nature in the nervous systems of experimental animals have so frequently presented difficulties of interpretation that it seemed fully justifiable to attempt to confirm them by the various staining methods employed. This was calculated to give both a positive (in the Marchi and Scharlach R preparations) and a negative picture (in the Spielmeyer preparations) of any possible degeneration in the medullary sheaths. Lesions of this kind which have been described in this communication have thus been confirmed by at least two methods of staining.

**SUMMARY AND CONCLUSIONS**

Under the conditions of these experiments, which consisted essentially of maintaining rats on a ration adequate in all dietary essentials as far as is known except vitamin A, the following changes were produced in the nervous system.

1. Degeneration of the medullary sheaths of the brachial plexuses and sciatic nerves, and less often of the vagus nerves. Such lesions were not found in the optic nerves.

2. Degeneration of the medullary sheaths of the sensory tracts on the periphery of the spinal cord and in the posterior columns. Much less frequently similar lesions were found in both the crossed and uncrossed pyramidal tracts.

3. Changes of the same nature in the posterior nerve roots and less frequently in the anterior nerve roots of the spinal cord. Evidence was adduced to indicate that the changes in the sensory tracts of the spinal cord followed those in the posterior nerve roots.

With the onset of muscular weakness and incoordination in these animals anatomic changes like those just described were found at necropsy, but they were not present for any appreciable period preceding the onset of these clinical signs.

For a short but undetermined period following clinical signs of
recovery from the nervous disease, marked lesions were still present in the nervous system at necropsy.

These lesions in the nervous system were produced by a ration containing no cereals which might have contributed a "toxic" substance to account for the degeneration of the myelin sheaths. Neither does a deficiency in unsaturated fatty acids appear to have played a role in their development.

REFERENCES


EXPLANATION OF PLATES

PLATE 15

Fig. 1. Rat 71. Drawing of sciatic nerve. Scharlach R stain. × 450.
Fig. 2. Rat 65. Drawing of sciatic nerve. Much of the fat is phagocytosed. Scharlach R stain. × 450.

PLATE 16

Fig. 3. Rat 71. Photomicrograph of sciatic nerve. Spielmeyer stain. × 455.
Fig. 4. Rat 73. Photomicrograph of sciatic nerve. Marchi stain. × 120.
Fig. 5. Rat 206. Photomicrograph of sciatic nerve. Marchi stain. × 120.
Fig. 6. Rat 122. Photomicrograph of longitudinal section of spinal cord showing degenerated myelin sheaths in posterior nerve root and in posterior column. Marchi stain. × 120.

PLATE 17

Fig. 7. Rat 206. Photomicrograph of transverse section of spinal cord. Note the marked degeneration in the posterior columns on one side and on the periphery of the cord. Marchi stain. × 30.
Fig. 8. Rat 205. Photomicrograph of transverse section of spinal cord showing degeneration of myelin sheaths in the anterior and lateral columns and on the periphery. Marchi stain. × 35.
FIG. 9. Rat 78. Photomicrograph of transverse section of spinal cord. The vacuolated regions on the periphery corresponded to those containing black granules in the Marchi preparations. Spielmeyer stain. × 40.

FIG. 10. Rat 79. Photomicrograph of transverse section of spinal cord showing marked degeneration of the medullary sheaths in the posterior columns and on the periphery. Spielmeyer stain. × 35.
(Zimmerman: Nervous system in vitamin deficiency. I)
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