RELATION OF DIET OF SWINE TO DEVELOPMENT OF LOCOMOTOR INCOORDINATION RESULTING FROM NERVE DEGENERATION [1]

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INTRODUCTION

A troublesome locomotor disorder among pigs, manifested by incoordination in the use of the legs, abnormal posture, and lameness, which has been of common occurrence in the Bureau's herd at the United States Department of Agriculture, Beltsville Research Center, Beltsville, Md., was described in an earlier paper (*1*).[2] The observations there reported suggested both diet and breeding as possible causative factors, particularly among pigs confined in small pens and fed in record-of-performance tests. The role of breeding was suggested by the high incidence of lameness among inbred litters, and some significance was placed on the abnormally low free-choice intake of calcium- and phosphorus-rich components of the diet.

Although a lack of either vitamin A or vitamin D is recognized as causing characteristic types of lameness and paralysis, the disorder apparently persisted under a regimen considered adequate in these vitamins for growing and fattening pigs. It appeared that if the disease were of dietary origin, the cause was possibly an obscure derangement of calcium and phosphorus metabolism or suboptimum levels of an unknown vitamin or vitaminlike factor in the stock diet. An infection of swine erysipelas in the herd was also considered as a possible complicating factor since a small proportion of the growing pigs had swollen joints and other symptoms of this disease, which also occasionally resulted in lameness. However, no consistent gross lesions of the bones or joints, other than some possibly due to injury, were detected in the animals suffering from the type of incoordination under investigation.

Further study of the problem was accordingly undertaken along the following lines: Determination of the effects of mineral elements in the diet; search for easily available feeds for use as supplements or replacements in the stock diet which would completely prevent or cure the disease; and, in order to facilitate the identification of the deficiency factor, the formulation of an experimental diet or diets capable of producing the symptoms. Control of the lines of breeding of the animals used in experimental lots and of the incidence of erysipelas was coordinated with the dietary treatments. The results obtained are reported in this paper.

REVIEW OF LITERATURE

A disease characterized by posterior paralysis and incoordination of movement was described by Wehrbein (*7*) of the Iowa State College

[1] Received for publication July 11, 1940.
[2] Italic numbers in parenthesis refer to Literature Cited, p. 316.

of Agriculture in 1916. Degeneration of the myelin sheath and of the brachial and sciatic nerves was observed. Efforts to demonstrate pathogenic organisms failed. In more recent years, Eveleth and Biester (*2*), also of the Iowa State College, have continued the work and have reviewed the reports of other investigators from the standpoint of the possible involvement of vitamin A and of the vitamin B complex in the nerve degeneration in various species. The complexity of the problem is evidenced by the conclusions of the Iowa investigators, which indicate that the incoordination and myelin degeneration in the nervous systems of swine are not necessarily associated in all cases and that neither vitamin A nor the vitamin B complex is responsible for the myelin degeneration.

In work on young pigs fed artificial diets, Wintrobe, Mitchell, and Kolb (*7*) observed poor growth, marked ataxia, and severe nerve and spinal-cord degeneration when the content of yeast was gradually reduced and thiamin and riboflavin substituted in the ration. In work at the Beltsville Research Center (*6*) on the vitamin B_1 requirement of young swine, nerve and spinal-cord degeneration have also been encountered in animals fed autoclaved diets with and without the addition of thiamin.

The observations of Hogan and coworkers (*3*) are also of interest because of their relation to sows and suckling pigs and because the development of the abnormal gait seemed to depend on sudden changes in the nutritive value of one or more constituents of the diet. These investigators reported serious losses during certain years in the pig crop, whereas in others the disease was mild in form or absent.

Hughes (*4*) has worked with purified diets in which the components of the vitamin B complex were varied. He observed marked lameness in pigs fed a diet low in riboflavin, although other groups on riboflavin-rich diets that were in turn low in thiamin, nicotinic acid, or other fractions of the B complex were not free of lame pigs.

Besides these reports, information in the possession of the Bureau, including communications from a number of workers at various State experiment stations, indicates that the disorder is of serious economic importance and is more prevalent in some years than in others.

EXPERIMENTAL PROCEDURE

Beginning with the spring farrow of 1937 and continuing through the spring farrow of 1939, groups of pigs were fed in concrete-floored pens under essentially the same conditions as those prevailing in record-of-performance tests except for dietary differences. Two experiments, one with spring and the other with fall pigs, were conducted each year. In the earlier experiments, the number of lots was restricted to six, and litters containing at least six pigs were utilized in order to provide litter mates in each lot. These litters were selected so far as possible from inbred stock which had shown a predisposition toward lameness, in an attempt to accentuate the effects of the various diets either in completely protecting against or in intensifying the symptoms. After 1937, this inbred stock became so depleted in the herd that it was not possible to continue this procedure. In the more recent experiments, it has been necessary also to depart somewhat from the use of complete litter-mate groups and

to select closely related pigs of similar age, sex, and weight. The pigs were generally placed on experiment at 10 to 12 weeks of age.

The diets were prepared from the general supply of feeds purchased for use in swine feeding at Beltsville. The stock diet consisted of No. 2 yellow corn, digester tankage of 60 percent protein content, linseed meal, alfalfa-leaf meal made from sun-cured hay, and a mineral mixture. This mineral mixture consisted of ground limestone, 50 percent; steamed bonemeal, 27.97 percent; common salt, 20 percent; iron oxide, 2 percent; potassium iodide, 0.02 percent; and copper sulfate, 0.01 percent. This mixture constituted 0.8 to 1.0 percent of the stock diet. The supplemental or replacement feeds were varied, being chosen because of known or supposed mineral, vitamin, or protein value and as contrasting feeds for replacement of the corn, tankage, linseed meal, or alfalfa-leaf meal.

The diets were adjusted, through changes in quantities of corn or other cereal and tankage, or its substitute, to furnish approximately 18 percent of protein to pigs between the weights of 40 and 100 pounds, 15 percent to those between the weights of 100 and 160 pounds, and 12 percent to those with weights of more than 160 pounds. Whenever linseed and alfalfa-leaf meals were used, they generally constituted 5 percent of the diet of the pigs in the lowest weight group, 4 percent of that of the middle group, and 3 percent of that of the highest weight group.

The diets fed were grouped in five series and are shown in table 1. In series A, particular attention was given to the effect of minerals on the production of lameness. As shown in the table, group 2 received a low mineral diet, and group 8 received a supplement of manganese chloride. Oats were used in group 6 in part because of their relatively high manganese content. Group 5 was given access to a small unpaved area of natural clay soil free of vegetation to determine whether the lacking element or elements in the diet could be obtained from the soil. Skim milk, green forage, and liver were fed in part for their mineral content but more in a search for a natural feed that would be consistently protective against the disease. The green forage consisted of both freshly cut green soybeans and alfalfa. It was estimated that the quantity fed corresponded to approximately 5 percent of the dry forage in the diet.

In series B, the use of corn-gluten meal in place of tankage and alfalfa-leaf and linseed meals was prompted by the deficiency of the first-named feed in riboflavin, as indicated by early assays for vitamin G, and the desire to determine the possible role of riboflavin in the prevention of the disease. Oats were used in group 2 because of the favorable results obtained in series A. Liver was used in the next group for its high riboflavin content and also for its richness in other members of the vitamin B complex. In one group molasses was also used for its richness in certain factors, including vitamin B_6. Casein, washed with acidulated water and extracted with alcohol, was added in one group to improve the quality of protein mixture and as a control on the other diets to which natural feeds were added. Fortified cod-liver oil was added to the diets of series B, as well as to those of series C and D, in order to provide an adequate supply of vitamins A and D in all rations regardless of composition and treatment.

TABLE 1.—*Experimental set-up for the five series of tests*

Pig group No.	Trials	Pigs used in test	Proportion of basal mixture used	Diet supplement or treatment
	Number		*Percent*	
SERIES A—BASAL MIXTURE OF CORN, TANKAGE, ALFALFA-LEAF MEAL, AND LINSEED MEAL				
1	2	Spring and fall	99.2	Mineral mixture, 0.8 percent (stock control diet).
2	2	do	100	None.
3	2	do	100	5 pounds of skim milk per day.
4	3	Spring	100	1 pound of green forage per day.[1]
5	1	do	99.2	Same as group 1; pigs on earth runway.
6	2	Spring and fall	70	Oats, 30 percent.
7	1	Fall	97	Dried pork liver, 3 percent.
8	1	do	100	Manganese chloride, 72 p. p. m.
SERIES B—BASAL MIXTURE OF CORN, CORN-GLUTEN MEAL, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL				
1	1	Spring	100	None.
2	1	do	70	Oats, 30 percent.
3	1	do	98	Dried pork liver, 2 percent.
4	1	do	95.5	Casein, 4.5 percent.
5	1	do	85	Molasses, 15 percent.
SERIES C—BASAL MIXTURE OF TANKAGE, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL				
1	2	Spring and fall	13.1	Corn, 86.9 percent.
2	2	do	13.1	Barley, 86.9 percent.
3	2	do	13.1	Wheat, 86.9 percent.
SERIES D—SIMPLE BASAL DIET OF CORN, TANKAGE, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL OR STOCK CONTROL DIET OF ALFALFA-LEAF MEAL AND LINSEED MEAL ADDED TO SIMPLE BASAL DIET				
1	3	2 spring and 1 fall	100	Simple, unheated (control).
2	3	do	100	Stock, unheated (control).
3	2	Spring and fall	100	Simple, heated.
4	1	Spring	100	Stock, heated.
				Simple, heated, supplemented by—
5	1	Fall	90	Corn-gluten meal, 10 percent.
6	1	do	97	Dry liver, 3 percent.
7	1	do	90	Rice bran, 10 percent.
8	1	do	92.3	Dried whey, 7.7 percent.
				Stock, heated, supplemented by—
9	1	Spring	85.3	Dried whey, 14.7 percent.
10	1	do	85.3	Whey concentrate, 14.7 percent.
11	1	do	99	Wheat-germ oil, 1 percent.
SERIES E—CURATIVE TRIALS ON VARIOUS DIETS				
1	1	Fall	100	Stock control, same as series D, No. 2.
2	1	do	100	Dried skim milk in place of tankage in series D, No. 2.
3	1	do	100	Animals fed with groups 1, 2, 6, 7, and 8 in series A.

[1] Alfalfa-leaf meal omitted from basal mixture.

In series C, comparison was made of corn, barley, and wheat, when constituting a high percentage of the diet, for the prevention of lameness.

In series D, the basal diet and a simplification of it, in which the linseed and alfalfa-leaf meals were omitted, were subjected to dry

heat at 115°–120° C. for 40 hours in the case of the former diet and 30 hours in the latter. Poultry-nutrition studies have shown that a factor or factors essential for the nutrition of the chick are destroyed by the heat treatment. The dermatitis produced by the feeding of a heated diet has been cured or prevented by the feeding of the vitamin B complex fraction designated as the filtrate fraction, and recent work has been reported (*5*) on the protective properties of pantothenic acid. Apparently, thiamin, riboflavin, vitamin B_6, and possibly nicotinic acid are not inactivated or destroyed by the heat treatment. At the time that the first trials on the feeding of heated diets were planned (1938), it seemed evident that the factors just named were also not involved in the lameness derangement in pigs. In series D, as indicated in table 1, various supplements were used with the heated diets. The whey concentrate used in group 10 was prepared in the laboratories of the Bureau of Dairy Industry. In obtaining this product, whey from rennet-coagulated curd was evaporated and approximately two-thirds of the lactose allowed to crystallize out. Cod-liver oil was added to all diets at the time that new supplies of feed were placed in the self-feeders.

In series E, three groups of pigs are included that were segregated from the herd or from record-of-performance lots after definite signs of lameness had developed and were fed in an endeavor to determine whether cures or alleviation of symptoms could be obtained. One group received the stock diet, another a modified stock diet in which dried skim milk replaced the tankage, and the third consisted of a litter of five pigs that had been distributed among 5 lots in series A.

The pigs were kept on the test diets for periods of 12 to 24 weeks. As the experiments progressed, it was found that symptoms of lameness and incoordination were generally easily detected within a 12-week feeding period; consequently, the test period was shortened in later experiments. The mixed diets were self-fed and the consumption of each lot recorded. The pigs were weighed and examined weekly. A scoring system was set up by which to record the relative severity of the disease. Entire absence of symptoms was scored as 0; initial signs of lameness, as 1; more advanced lameness with tendency to weakness in pasterns and peculiar motion of rear legs, as 2 (fig. 1, *A*); definite incoordination shown by weaving motion and the throwing forward of the rear legs, also difficulty in rising and tendency to sit on the haunches, as 3; marked symptoms of those enumerated as 3, in which the animal had great difficulty in walking and frequently collapsed, as 4; and extreme paralysis, in which the animal was barely able to rise or to move about with the forelegs, as 5 (fig. 1, *B*).

At the conclusion of the feeding period, the animals from most of the groups were slaughtered for laboratory studies. Samples taken included blood for erysipelas tests, (made by the Pathological Division of the Bureau); also nerve and spinal cord tissue and the femur bones.

A histological study of the sciatic nerve and spinal cord of approximately 95 animals was made. Several peripheral nerves of the first few animals studied were sectioned for examination, but in the later work only the sciatic nerve and the spinal cord were taken for routine study since these tissues show the degeneration consistently when the other nerves are involved. The samples of nerve tissue were removed from the warm carcasses immediately after slaughter, and sections were

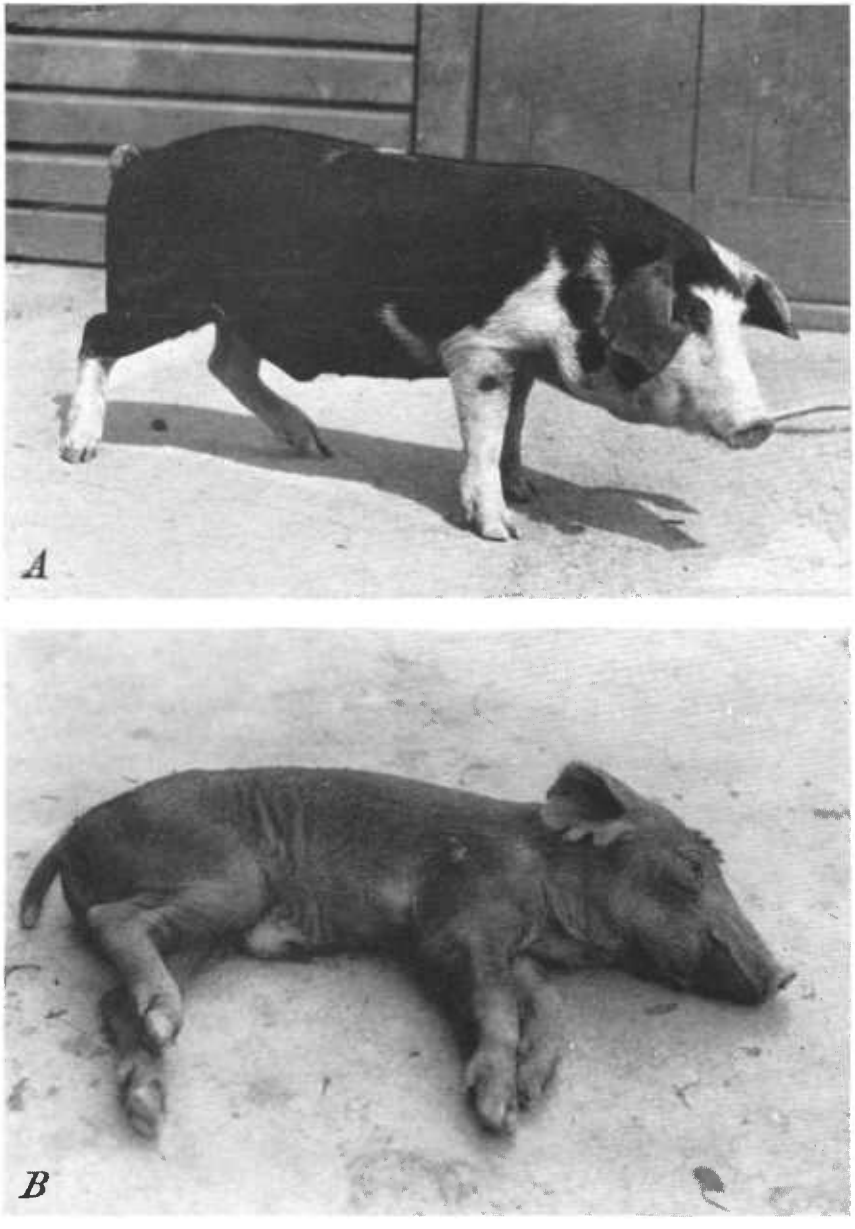
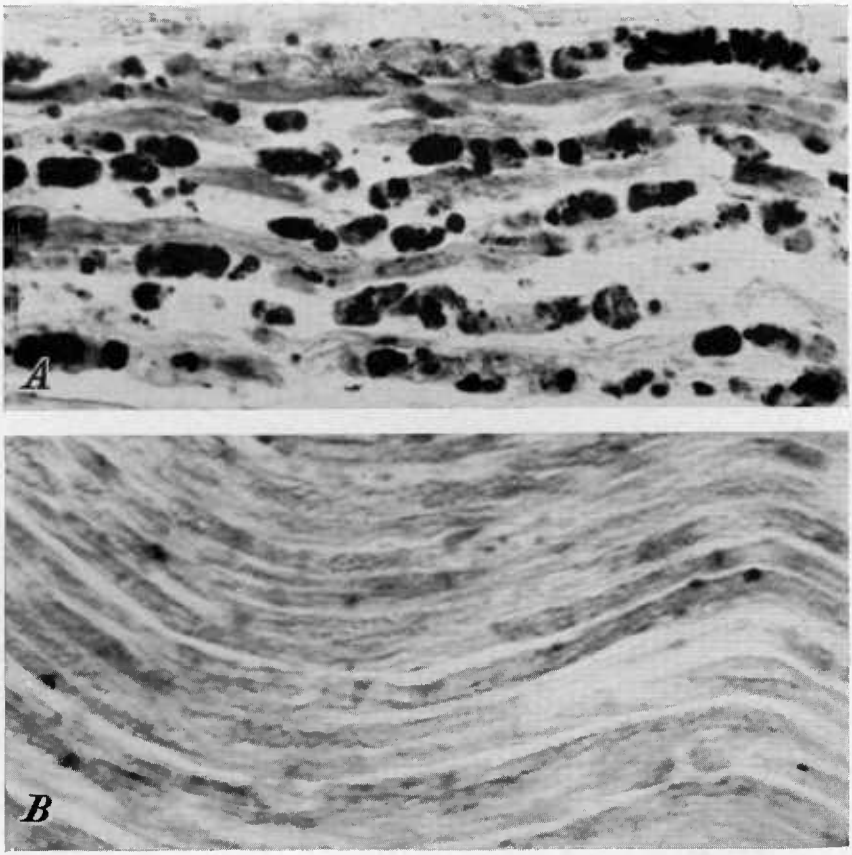
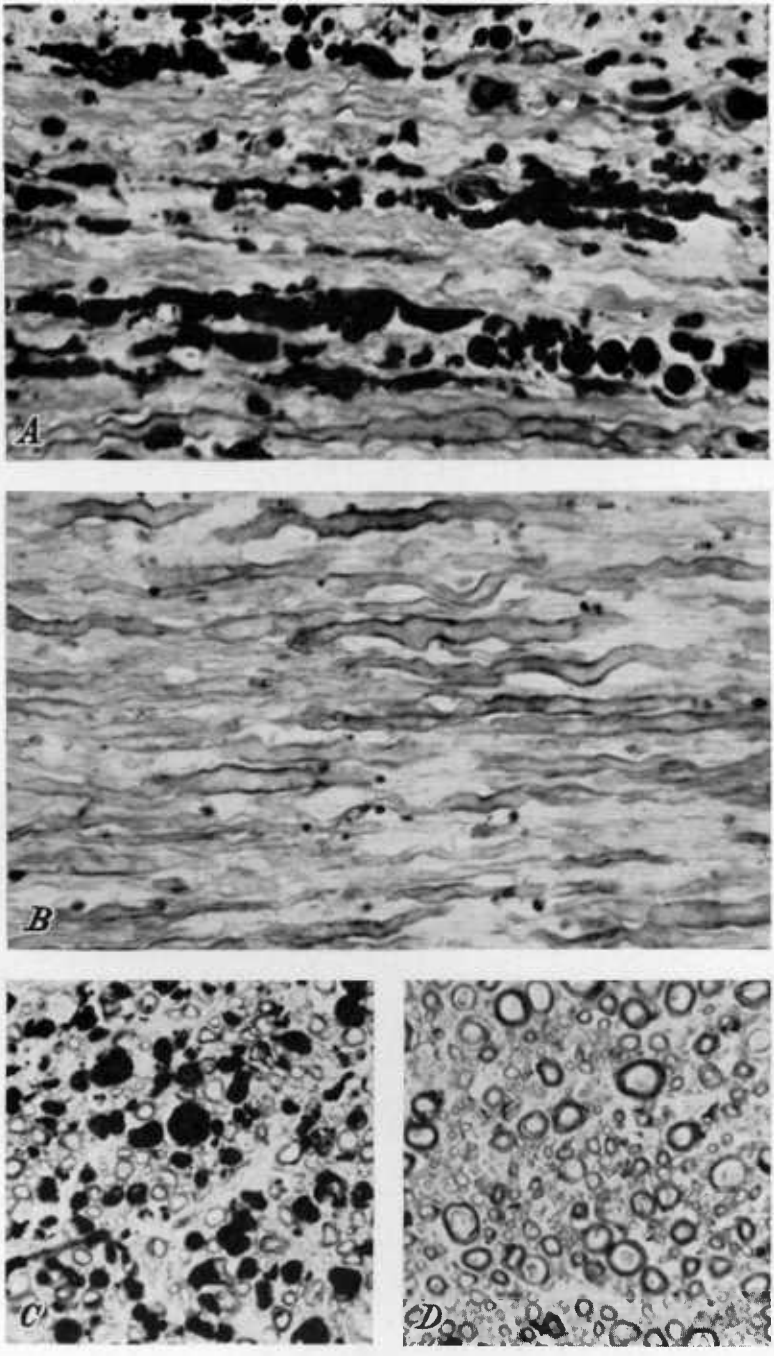


FIGURE 1.—*A*, Pig showing incoordination in the use of the hind legs. *B*, Pig with extreme paralysis, which developed while the animal was fed the heated diet No. 3 in series D.

prepared for study by the Marchi method. This procedure consists in placing the fresh tissues in a solution of potassium dichromate until the normal myelin is largely oxidized and then transferring to a water solution of osmium tetroxide and potassium dichromate to oxidize



A, Longitudinal section of the sciatic nerve from a typical animal with advanced locomotor incoordination showing massive demyelination of nerve fibers (black globular areas); *B*, longitudinal section of the sciatic nerve from a normal animal showing intact myelinated fibers.



A, Longitudinal section of a dorsal column of spinal cord from a partially paralyzed pig showing degeneration of myelinated tracts; *B*, longitudinal section of a dorsal column of the spinal cord from a normal animal showing normal medulated fibers; *C*, cross section of *A*; *D*, cross section of *B*.

further the degenerated myelin and ordinary adipose tissue. Oxidation of the products of the degenerated myelin sheaths results in a deposition in these areas of a lower oxide from reduced osmium tetroxide, which is black in color. The tissues were embedded in celloidin or paraffin, then cut and mounted in the usual way. The slides were either counterstained or examined directly for myelin degeneration, as shown by the globular black areas in plates 1 and 2. The absence, presence, and severity of myelin degeneration were scored on a numerical basis paralleling the method of scoring the live animals for lameness.

Supplementary to the hog-feeding experiments, a number of rat-feeding comparisons were made to determine the possible dietary deficiencies of the heated diets from the standpoint of rate of growth and feed utilization.

EXPERIMENTAL RESULTS

GROWTH OF PIGS AND INCIDENCE OF LAMENESS

Table 2 shows the results obtained with the pigs on the various series of diets. In series A, the animals in all eight groups grew at normal rates and remained on the diets until most of them weighed more than 200 pounds. As shown in the table, every group contained at least 1 affected animal. Of a total of 77 animals, 27 showed signs of lameness and incoordination. To a large extent, the cases were of a mild form. Perhaps the most striking result was the high incidence among the pigs fed green forage. The animals of this group (No. 4), like those of group 2, did not receive a mineral mixture, and the affected animals in these two groups showed a greater degree of lameness than those in any of the other groups.

Oats and dried liver were reasonably effective supplements. The former was fed as 30 percent of the diet, which is considered near the maximum for the most efficient utilization.

Most of the animals used in series A consisted of litters from the spring and fall farrows of 1937, many of which were selected from the inbred stock suspected as being predisposed toward the development of lameness. The data indicate that little was gained from the use of such stock to accentuate the effects of ordinary diets on the incidence and severity of incoordination. This finding has been confirmed by subsequent results with pigs representing a large number of lines of breeding and showing a varying incidence of incoordination from season to season.

In series B, the results obtained show rather definitely that the use of corn-gluten meal did not render the diets less effective in preventing lameness and incoordination. No affected pigs were found in either the control group or the group receiving oats, and only one mild case was recorded in each of the remaining groups. Growth on the control diet was poor. Although the rates of gain were highest with the feeding of liver and of casein, growth was still subnormal. Oats increased gains somewhat and molasses only slightly.

In series C, the three groups, regardless of the supplement fed, had similar rates of gain and final weights. The lowest incidence, as well as degree, of lameness was observed in the group receiving the barley supplement.

TABLE 2.—*Growth and incidence of lameness of groups of pigs on the five series of diets*

SERIES A.—BASAL MIXTURE OF CORN, TANKAGE, ALFALFA-LEAF MEAL, AND LINSEED MEAL

Pig group No.	Pigs	Diet supplement or treatment	Average weight		Average daily gain	Feed per 100 pounds of gain	Lame animals	Average score for lameness
			Initial	Final				
	Number		*Pounds*	*Pounds*	*Pounds*	*Pounds*	*Number*	
1	11	Mineral mixture; control diet	43.6	204.6	1.50	370.9	3	0.67
2	11	None	48.6	214.1	1.72	356.4	5	.82
3	10	Skim milk	43.5	206.6	1.72	344.3	3	.50
4	18	Green forage	56.8	198.8	1.46	425.8	11	.98
5	5	Same as group 1; pigs on earth runway	39.4	229.8	1.72	357.0	1	.10
6	10	Oats	46.8	219.7	1.68	381.7	1	.10
7	6	Liver	54.7	213.9	1.63	384.8	1	.10
8	6	Manganese	54.7	218.7	1.82	348.3	2	.25

SERIES B.—BASAL MIXTURE OF CORN, CORN-GLUTEN MEAL, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL

1	5	None	55.8	132.4	0.50	543.4	0	0.0
2	5	Oats	55.6	138.6	.75	467.3	0	.0
3	5	Liver	57.0	269.2	1.11	376.3	1	.2
4	5	Casein	61.3	171.1	.93	438.1	1	.17
5	5	Molasses	56.8	152.8	.58	569.2	1	.20

SERIES C.—BASAL MIXTURE OF TANKAGE, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL

1	12	Corn	67.8	208.8	1.52	369.8	8	0.86
2	13	Barley	81.4	208.2	1.63	388.5	1	.04
3	13	Wheat	81.3	208.2	1.59	370.8	7	.42

SERIES D.—SIMPLE BASAL DIET OF CORN, TANKAGE, MINERAL MIXTURE, AND FORTIFIED COD-LIVER OIL OR STOCK CONTROL DIET OF ALFALFA-LEAF MEAL AND LINSEED MEAL ADDED TO SIMPLE BASAL DIET

1	17	Simple, unheated (control)	63.8	211.8	1.54	363.7	11	0.90
2	17	Stock, unheated (control)	62.8	230.3	1.78	359.6	6	.41
3	12	Simple, heated	53.6	115.6	.52	451.7	12	2.59
4	6	Stock, heated	65.8	66.2	0	[1]	6	2.25
		Simple, heated, supplemented by—						
5	6	Corn-gluten meal, 10 percent	57.7	107.7	.48	402.7	3	1.00
6	6	Dry liver, 3 percent	56.8	207.1	1.52	336.1	2	.75
7	6	Rice bran, 10 percent	58.5	151.7	.93	397.5	2	.58
8	6	Dried whey, 7.7 percent	60.0	202.0	1.41	353.2	2	.67
		Stock, heated, supplemented by—						
9	6	Dried whey, 14.7 percent	77.0	182.5	1.21	408.4	1	.33
10	6	Whey concentrate, 14.7 percent	74.7	162.7	.99	488.8	3	.67
11	6	Wheat-germ oil, 1 percent	70.7	98.5	.31	810.2	6	1.75

SERIES E.—CURATIVE TRIALS ON VARIOUS DIETS

Pig group No.	Pigs	Diet	Average weight		Average daily gain	Feed per 100 pounds gain	Lameness scores	
			Initial	Final			Beginning	End
	Number		*Pounds*	*Pounds*	*Pounds*	*Pounds*		
1	5	Same as series D, No. 2	83.8	146.0	0.87	-------	2.6	2.5
2	5	Dried skim milk in place of tankage in series D, No. 2	109.2	204.2	1.64	383.6	2.2	3.3
3	5	Animals fed with groups 1, 2, 6, 7, 8 in series A	70.8	215.0	1.85	380.2	2.0	1.3

[1] Daily consumption per pig approximately 1.95 pounds.

In series D, groups 1 and 2, the controls fed the unheated diets, grew normally but showed a seemingly high incidence of lameness, particularly group 1. The feeding of the unsupplemented heat-treated diets resulted in lameness and incoordination in varying stages in all 18 animals fed. Growth was also retarded in all pigs and in fact stopped in group 4. This group was on test for an average of 78 days. One animal died and others appeared near death as the experiment closed.

The supplements used stimulated growth in varying degrees. Dried pork liver, fed at a level of 3 percent, was very effective, and the commercial dried whey product, fed with the simple diet at a level of 7.7 percent, produced nearly as good growth. The whey concentrate, which was fed at a level approximating 210 cc. of fresh whey to 85 gm. of heated diet, was insufficient to prevent lameness completely although none of the three affected animals showed advanced incoordination. Of the five supplements used, wheat-germ oil was entirely ineffective in prevention of lameness, whereas the corn-gluten meal, liver, rice bran, and whey products were all moderately effective at the levels fed. The striking results obtained with the heated diet in the production of lameness, together with the protection afforded by these supplements when added to the heated diet, leave little doubt of the nutritional origin of the disease.

CURATIVE TESTS

In series E, the diets fed to the three groups of affected animals that had been segregated from their litter or lot mates failed to cure the lameness and incoordination. The results are shown in table 2. Although there was a minor improvement in the average scores of groups 1 and 3, the average of all three groups shows no improvement. The 5 pigs in group 2, which received dried skim milk, showed a decided increase in the severity of the disease. The failure of the curative tests may be due to the limited degree to which regeneration of nerve tissue can take place in the animal body.

RAT-FEEDING EXPERIMENTS

The rat-feeding experiments, the results of which are given in table 3, showed that the growth of rats was retarded by the heat treatment of the diets almost as much as it was in the pigs. The simple unheated diet, as used in pig series D, group 1, produced significantly poorer growth than the stock diet. In turn, the animals on the heated simple diet were retarded in growth and required more feed per unit of gain than those on the unheated diet.

The lack of a marked response from the addition of 5 percent of casein, extracted with water and dilute alcohol, indicates that quality of protein was not the limiting factor. Alfalfa-leaf meal fed at a 5-percent level, wheat germ at 10 percent, and rice bran at 5 percent appeared to be more effective supplements than the casein. When the daily allowance of rice bran was 1 gm. per day, or approximately 8 percent of the total food intake, the growth rate was nearly as great as when the unheated diet was fed, and was greater than for the wheat-germ supplement, of which the daily intake also averaged 1 gm., although constituting 10 percent of the diet. In the feeding of fractions of the rice bran, it was found that the filtrate fraction remaining

after the thiamin, riboflavin, and vitamin B_6 had presumably been removed by adsorption treatments was the most effective preparation of the series. Neither thiamin nor riboflavin preparations were of material benefit, thus supporting the findings with the rice-bran absorbate preparation that neither of these vitamins was a limiting factor in growth.

TABLE 3.—*Results of rat-feeding experiments on the heated pig diets of series D with various supplements*

Rat group No.	Rats used in experiments	Diet fed	Average gain in 12 weeks	Feed per gram of gain
	Number		*Grams*	*Grams*
1	8	Simple, unheated (control)	144.9	7.15
2	8	Stock, unheated (control)	185.1	6.55
3	14	Simple, heated	68.7	9.92
		Simple, heated, supplemented by —		
4	6	Casein, 5 percent	86.3	7.58
5	6	Alfalfa-leaf meal, 5 percent	100.2	7.37
6	6	Linseed meal, 5 percent	89.7	8.29
7	6	Wheat germ, 10 percent	96.2	8.49
8	4	Rice bran, 5 percent	98.0	7.96
9	4	Rice bran, 8 percent	138.3	7.22
10	4	Rice bran, absorbate	96.0	8.03
11	4	Rice bran, eluate	86.5	9.92
12	4	Rice bran, filtrate	135.5	7.75
13	6	Liver extract	164.7	6.33
14	6	Whey concentrate	145.8	6.45
15	6	Thiamin, 30 micrograms per week	80.3	8.71
16	6	Riboflavin, 105 micrograms per week	76.0	9.19

Liver, and to a less extent the whey concentrate, as prepared in the Bureau of Dairy Industry, were effective in promoting better growth than the unheated diet. The results as a whole appear to support the data presented by various workers that a factor of factors found in the so-called filtrate fraction obtained in the separation of the vitamin B complex are destroyed by prolonged dry-heat treatment.

HISTOLOGICAL STUDIES OF TISSUES OF PIGS

Histological examinations of tissues of pigs showed that a degeneration of the myelin sheaths in certain peripheral nerves and the spinal cord was probably a primary factor in the development of the locomotor symptoms evidenced in lameness and incoordination. As the work progressed, the similarity of the lesions to those reported by the Iowa investigators (*2*) and to those of Wintrobe and coworkers (*8*) became evident.

The nature of the degenerative changes in the myelin sheath of nerve fibers of the sciatic nerve and the spinal cord, as shown by the Marchi procedure, is illustrated in plates 1 and 2. Varying degrees of degeneration were found, sometimes involving only an occasional nerve fiber or tract and sometimes widespread areas.

The degenerative changes in the spinal cord were confined principally to the dorsal columns and dorsal nerve roots, although some demyelination was found in the ventral columns also. The dorsal columns of the cord are made up principally of ascending branches from the dorsal root fibers, and they convey posture, locomotor, and other sensations. An interruption of conduction in these tracts will lead to incoordination and finally a complete inability to walk, depending on the extent and location of the degeneration.

Table 4 presents a summary of the results of the histological examinations expressed numerically and of the outward symptoms of locomotor involvement as shown by the lameness score. The average scores for the outward symptoms are in general agreement with those for the nerve examinations. In most instances, the number of animals involved are not greatly different for the two scoring indices. Besides the animals included as having definite lesions, a number of others not included in the table had slight changes, from the normal structure, in the sciatic nerve and spinal cord, a condition which may or may not indicate early lesions. Even the unheated stock diet protected less than two-thirds of the animals. The finding of abnormalities in the pigs receiving green forage is confirmed by the histological studies on 10 animals. The data on this group indicate a condition intermediate between those on the unheated simple diet and those on the stock diet. The heated diet resulted in the greatest amount of spinal-cord degeneration, just as it did in general incoordination. The addition of dried whey in group 8 of series D prevented the extreme degeneration noted in group 3 of that series, and the higher level of whey used in group 9 was even more effective. Although the whey concentrate furnished considerable protection, it did not appear to be equal to the dried whey on an estimated liquid-whey basis. The addition of wheat-germ oil to the heated stock diet was of little if any avail in the prevention of lameness or of nerve degeneration. Rat tests showed the wheat-germ oil to be reasonably potent as a source of vitamin E, and it seems unlikely that the substances which confer vitamin E activity are involved in the nerve degeneration in question.

TABLE 4.—*Results of histological examinations on nerve tissues compared with data on incoordination*

Series	Group No.	Diet treatment or supplement	Pigs used	Incoordination data		Histological data on—			
						Sciatic nerve		Spinal cord	
				Pigs affected	Average score	Pigs with definite lesions	Average score	Pigs with definite lesions	Average score
			Number	*Number*		*Number*		*Number*	
A	4	Green forage	10	6	0.85	7	1.00	7	1.20
B	1	Control, corn-gluten meal	1	0	.00	1	.50	1	.50
B	2	Oat supplement	1	0	.00	0	.00	0	.00
B	3	Dried pork-liver supplement	1	0	.00	0	.00	0	.00
B	5	Molasses supplement	2	1	.50	1	.25	1	.25
C	2	Barley	6	1	.08	0	------	0	------
C	3	Wheat	6	4	.50	3	.50	4	.67
D	1	Simple, unheated	15	12	1.00	11	1.43	14	1.47
D	2	Stock, unheated	16	6	.44	7	.41	7	.56
D	3	Simple, heated	12	12	2.59	12	3.17	12	3.42
D	4	Stock, heated	[1] 4	4	2.63	4	3.00	4	3.50
D	8	Simple, heated, supplemented with dried whey	6	2	.58	3	1.83	4	1.00
		Stock, heated, supplemented with—							
D	9	Dried whey	6	1	.33	2	.33	2	.50
D	10	Whey concentrate	6	2	.50	3	1.00	4	1.17
D	11	Wheat-germ oil	[1] 4	4	1.13	3	1.75	4	2.00

[1] Two additional animals died near the close of the experiment in advanced stages of paralysis, and no histological studies were made.

A comparison of the results for groups 2 and 3 of series C, which received barley and wheat respectively, with those for group 1 of series D, which received corn as the principal ingredient of the diet, showed that wheat proved little different from corn but that barley conferred a high degree of protection. Among the pigs examined, those fed barley and those fed corn-gluten meal were the only ones that showed no definite cases of nerve degeneration. A limited number of rats from the experiments already described were examined for myelin degeneration. Animals fed the heated diet with the cod-liver oil fed in separate dishes showed degeneration, and at least one of six animals showed evidences of incoordination.

DISCUSSION

From the results thus far obtained, it seems reasonably certain that the locomotor symptoms and evidences of nerve and spinal-cord degeneration that have been found are similar to those reported by other investigators. However, Eveleth and Biester (*2*) concluded that the incoordination and myelin degeneration were caused by different etiological agents since severe incoordination was not always associated with advanced myelin degeneration. In some of their experiments, the feeding of diets deficient in vitamin A resulted in development of incoordination but only mild nerve degeneration.

Wintrobe and associates (*8*) describe demyelination in the peripheral nerves, the posterior root ganglia, and the posterior (or dorsal) columns of the spinal cord. Animals showing the degeneration had manifested "a peculiar slapping gait" and "were particularly awkward in turning." In the advanced stages, the animals became less active and sat with the hind legs sprawled in unnatural positions. The animals received an artificial diet from an early age, and the evidence pointed to a dietary deficiency of one or more components of the vitamin B complex other than thiamin or riboflavin.

In the present experiments, it was possible to control the production of the disease, within limitations, by the use of natural feedstuffs and thereby clarify some of the questions raised by the other investigators. Unlike the findings of the Iowa group (*2*), the results of the present work show a rather close association of incoordination with myelin degeneration. It seems apparent that the locomotor symptoms developed following the degeneration of fibers in the nervous system.

Thus far, repair of the degenerated fibers accompanied by disappearance of the symptoms of incoordination has not been observed. However, this result does not seem to be unusual, since a highly potent protective diet was not tested on the affected animals and regeneration of nerve tissue in the animal body is limited.

The finding that diets of the type commonly used in hog feeding, when subjected to heat treatment, will produce the disease has made it possible to study the problem in greater detail and with more certainty than formerly. There seems to be little doubt that the symptoms in live animals and myelin degeneration found histologically are similar in animals on heated diets and animals frequently affected on so-called normal diets. Heating of the diets undoubtedly destroyed or inactivated a nutritive factor or factors that are in some way related directly or indirectly to the nutrition of nerve fibers. Failure of animals to grow normally on the heated diets suggests that

more than one nutritive factor may be destroyed by heating. Observations on the growth of lame animals fed on unheated diets, including the stock or record-of-performance diet, as compared with normal animals under the same conditions, indicate that lame animals are frequently but not necessarily slower in rate of growth. Accordingly it is possible that the myelin-degeneration-preventive material is different from the growth factor destroyed by heating.

The results obtained on the heated diets have strengthened the opinion already expressed that breeding as a factor in predisposing the animals toward development of lameness is of much less concern than was at one time suspected. The absence of any serious cases of lameness in a number of litters from stock that had shown a high incidence in earlier work has contributed to this opinion.

Interference with normal bone development as a factor in the development of lameness has been eliminated by some work on the ash content of the femur bones.[3] However, the data on percentage of ash in the fat and moisture-free bone showed no relation to lameness or to diet. Another phase of the studies, namely, incidence of swine erysipelas, has been given some attention. Results of serological tests on blood serums, carried out in the laboratories of the Pathological Division of the Bureau, showed frequent positive cases of erysipelas, but there was no association of this disease with incoordination. However, lameness resulting from diseased joints due to erysipelas infections may be confused with the initial signs of incoordination due to dietary deficiency.

The identity of the lameness- and nerve-degeneration-preventive factor is still obscure. Evidently it is not present in large quantities in the usual swine feeds. Results suggest that barley and oats may be more effective preventives than corn and wheat. Liver, skim milk, whey, rice bran, and corn-gluten meal are among the feeds tested that possessed considerable value yet at the levels fed were not effective in all animals.

SUMMARY

The experimental work herein reported was carried on at the United States Department of Agriculture, Beltsville Research Center, Beltsville, Md., from the spring farrow of 1937 through the spring farrow of 1939. The pigs were generally placed on experiment at 10 to 12 weeks of age and were kept on test for 12 to 24 weeks. The disease, which frequently occurs among pigs confined in small pens with concrete floors, is characterized by incoordination in the use of the legs, abnormal posture, and lameness.

The diets used were prepared from the general supply of feeds purchased for use in swine feeding at Beltsville. The stock diet consisted of No. 2 yellow corn, digester tankage of 60-percent protein content, linseed meal, alfalfa-leaf meal made from sun-cured hay, and a mineral mixture. Various supplements or replacement feeds were used, being chosen because of known or supposed mineral, vitamin, or protein value or as contrasting feeds for those replaced in the stock diet.

Myelin degeneration of the nerves and spinal cord was demonstrated in the affected animals. The extent of degeneration was in general parallel with the severity of incoordination.

[3] Unpublished data.

When the normal diets were heated at 115°–120° C. for 30 to 40 hours, incoordination and myelin degeneration were generally produced in all animals. Heating greatly increased the incidence and severity of the disease. The incidence of the disease was high on stock diets commonly used for growing and fattening hogs.

Supplemental or replacement feeds incorporated into the basic diets, including the heated diets, gave favorable results in some cases although complete protection was infrequent. Of the various feed materials investigated, liver, concentrated milk products, barley, and oats afforded the greatest protection.

Animals that did not receive a mineral supplement in the diet tended to show a greater degree of lameness than those receiving such a supplement.

The results indicate a deficiency disease of nutritional origin. The dietary factor appears to be present in variable or insufficient quantities in many of the feeds commonly used in hog feeding and is destroyed or inactivated by dry-heat treatment.

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