

IS THE NEURITIS-PREVENTING VITAMINE CONCERNED IN CARBOHYDRATE METABOLISM?

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VEDDER and CLARK (1912), reporting observations on polyneuritis gallinarum based on experiments lasting for several years during which time over 200 fowls were used, make the following statement with regard to the relation between the amount of polished rice eaten and the time of development of neuritis.

It has been generally observed that the great majority of fowls fed on polished rice usually lose their appetites after about a week on this diet, and thereafter eat only small amounts of rice. There are always a few fowls however which eat greedily up to the very last, and will eat far greater amounts than the usual ration allowed. Several deductions have been drawn from this fact with regard to the development of neuritis. Some observers have thought that those fowls that have eaten well throughout the experiment have been protected from the development of the disease by this increased consumption of rice, and therefore have been inclined to regard polyneuritis as the result of simple inanition. On the other hand, other observers have thought that those fowls that ate the most rice developed the disease soonest, and have regarded this as an argument in favour of the theory that polyneuritis gallinarum is caused by some toxin contained in the polished rice. We have observed fowls that always ate well, and yet developed neuritis sooner than usual, and we have observed fowls that ate large quantities of rice throughout the experiment, but whose depletion period was longer than normal. Again some of the fowls that have eaten poorly have developed neuritis promptly, while others have not developed the disease at all. Therefore it is believed that the amount of rice eaten has little to do with the development of the disease, which depends rather on the idiosyncrasy of the fowl with regard to the amount of neuritis-preventing substance required.

Later, Braddon and Cooper (1914) and Funk (1914) published experiments which they thought demonstrated that when fowls or pigeons were fed on polished rice or starch, with or without a fixed amount of anti-neuritic vitamine, the greater the proportion of carbohydrate in the food, the quicker was the onset of polyneuritis. From this evidence these investigators concluded that the vitamine played an active part in the metabolism of carbohydrates.

Here is a direct contradiction as to the experimental facts, for the statement of Vedder and Clark cannot be reconciled with the statements and experiments of Braddon and Cooper and of Funk. The subject has been deemed worthy of further investigation for it is a matter of considerable scientific and practical importance. It is obviously important for the physiologist to determine the exact rôle of the vitamins in metabolism. The sanitarian must also have exact information as to the amount of vitamin required in order that he may prescribe a diet that will always prevent beriberi. The writer has suggested in various publications that the antineuritic vitamin acts as a building stone which is essential for the metabolism of certain tissues of the body and more particularly of the nervous system. If this view is correct, it follows that each individual requires a definite amount of vitamin irrespective of the amount of carbohydrate eaten. The amount required varies somewhat for individuals depending upon personal idiosyncrasy, the amount of labour performed and other circumstances, but this variation is relatively slight. That is in practical terms, if a certain definite amount of beans or rice polish supplying the vitamin be consumed, and this amount be sufficient to supply the demand for vitamin, beriberi will never develop no matter how large the amount of rice or other carbohydrate consumed in the ration.

On the other hand if the view advocated by Braddon and Cooper and by Funk is correct, it follows that the more carbohydrate is eaten, the more vitamin must be supplied; thus if four ounces of beans are prescribed as a preventive, this might be sufficient to prevent beriberi while one pound of polished rice is eaten daily, but if two pounds of rice were eaten daily with the same quantity of beans, the individual would be in danger of developing beriberi.

I have endeavoured to perform some experiments that would throw more light on this matter, and explain the apparent conflict in the experimental facts.

Experiment 1. This experiment was performed in collaboration with Mr Rommel, Chief of the division of Animal Husbandry of the U.S. Department of Agriculture. The experiment was outlined under the direction of Mr Rommel and myself, but the observations were made and recorded by unprejudiced workers who did not know what the experiment was intended to prove. On January 18, 1916, six young cockerels were placed in individual coops and fed on an exclusive diet of polished rice. The birds were allowed to eat all they desired, but the amount supplied each day was weighed into special feed boxes so constructed

that no rice could be lost, and the amount remaining uneaten was weighed at the end of each day, so that the actual amount consumed by each bird was recorded every day. The fowls were weighed at the beginning and at the end of the experiment, and the time at which symptoms of paralysis appeared were carefully noted. On February 22, 1916, the experiment was repeated using five cocks. The results of this experiment are shown in Table I, in which all the birds used are arranged in order

TABLE I.

Fowl no.	Original weight	Total amount of rice eaten before development of neuritis	Percent. of total rice eaten before development of neuritis compared to original body weight	Average daily amount of rice eaten	Percent. of body weight eaten daily	No. of days after experiment began when neuritis developed	Weight lost	Remarks
1	3600	2647	73.5	132.3	3.67	20	96	Moderate paralysis
2	1824	1095	60.0	64.4	3.53	17	312	Marked paralysis
3	3216	2271	70.6	98.7	3.06	23	192	Symptoms so slight that they could only be detected on careful examination
4	3744	2535	67.7	105.6	2.82	24	95	Symptoms slight
5	2640	1665	63.0	69.3	2.62	24	297	Paralysis pronounced. Died of polyneuritis three days later
6	3104	1355	43.6	67.7	2.18	20	965	Paralysis marked but not complete. Bird could move when stirred
7	3456	1611	46.6	70.0	2.02	23	750	Symptoms trifling. Could stand and walk but with evidence of paralysis
8	2832	1113	39.3	53.0	1.87	21	961	Symptoms only slight paralysis of legs
9	3840	1275	33.2	70.8	1.84	18	960	Rapid and complete paralysis
10	3744	1171	31.2	53.2	1.42	22	744	Symptoms of neuritis mild
11	2304	690	29.9	32.8	1.42	21	480	Moderate paralysis

depending upon the percentage of rice eaten as compared with their original body weight. From this table it is possible to see at a glance the lack of relation between the amount of rice eaten and the time of development of neuritis. All figures for the weights of the fowls and amounts of rice eaten are expressed in grams.

This experiment indicates that when fowls are fed on polished rice *ad libitum*, the rapidity of onset of polyneuritis bears no relation to the amount of rice eaten. Certainly it is evident that neuritis does not develop more quickly in those birds that eat the largest amounts of rice. This bears out my previous observations, which were also made on birds allowed to eat as much rice as they desired.

Funk and Braddon and Cooper on the other hand fed their birds by hand. Thus Funk (1914) performed the following experiment. Doves

were fed by hand on polished rice in various quantities. One group received one half a gram daily, another group 5 grams daily and still other groups 10 and 20 grams daily. Funk stated that the doves receiving one half a gram of rice died of simple starvation without a trace of polyneuritis, while the result of the experiment on the remainder of the doves was as follows:

	5 grams	10 grams	20 grams
Appearance of polyneuritis	39 days	36 days	22 days
Death	42 ,,	38 ,,	22 ,,

I repeated this experiment but used fowls because they are easier to feed by hand.

Experiment 2. Twelve fowls of the same breed and approximately the same size and age were divided into three groups. An endeavour was made to feed the first group 100 grams of rice daily, the second group 50 grams of rice daily, and the third group 25 grams of rice daily. Polished rice was used and the birds were hand fed. However it was very soon found that it was impracticable to feed the fowls in Group 1 as much as 100 grams of rice daily. After a few days of such feeding they were unable to digest this amount of rice with sufficient rapidity, and the rice accumulated in their crops. If feeding was then continued, after a few days more their crops became so distended with rice that the introduction of more rice became impossible without killing the bird by the pressure developed by the swelling rice. As soon as it was found that the proposed amounts of rice could not be fed without mechanically killing the birds, the amount actually administered was weighed, and the actual amounts of rice so fed are indicated in Table II in comparison with the amounts originally proposed.

TABLE II.

No. of fowl	Original weight	Proposed feeding		Amount actually fed				Result of experiment
		Daily amount (grams)	Percent. of body weight to be fed daily	Total amount polished rice fed prior to death	Percent. of body weight fed before death	Average daily amount of rice fed (grams)	Percent. body weight fed daily	
1	942	100	10.61	1200	127.3	85.7	9.09	Died 14 days after exp. started
2	1290	100	7.75	1250	96.9	73.5	5.69	„ 17 „ „
3	1292	100	7.75	1325	102.5	69.7	5.39	„ 19 „ „
4	1595	100	6.26	1400	87.7	73.6	4.60	„ 19 „ „
5	1100	50	4.5	850	77.2	44.7	4.06	„ 19 „ „
6	1075	50	4.6	900	83.7	45.0	4.01	„ 20 „ „
7	1315	50	3.8	1150	87.2	50.0	3.80	„ 23 „ „
8	1505	50	3.3	800	53.1	42.1	2.79	„ 19 „ „
9	1132	25	2.2	600	53.7	25.0	2.20	Polyneuritis after 24 days
10	1249	25	2.0	425	34.2	21.2	1.69	„ „ 20 „
11	1244	25	2.0	—	—	—	—	No polyneuritis after 32 days when the experiment was discontinued
12	1292	25	1.9	—	—	—	—	

The results of this experiment agree with those obtained by Funk and by Braddon and Cooper in so far as they refer to the death of the birds. That is, the birds receiving the largest amounts of rice died first. But it was very evident that they did not die of polyneuritis. After about two weeks, the birds receiving the larger amounts of rice lay prostrated in the cages, too weak to stand up, but they did not show any symptoms of paralysis of the legs or retraction of the neck. Their crops were enormously distended. I am satisfied that the first four birds of the series died from the results of over-feeding, and that had the full 100 grams been fed daily, their death would have been brought about even more swiftly. It seems probable that Funk's results are to be explained in the same way. Funk recognized the fact that his doves fed on one-half a gram of rice daily died of starvation rather than of polyneuritis. It is quite as possible to kill an animal by overfeeding as by underfeeding.

The experiments of Braddon and Cooper are open to the same criticism; in some of them the birds were fed as much as one-fifth or 20 per cent. of their body weight daily, while it appears that fowls will not eat more than 4 per cent. of their body weight voluntarily, and that they are killed (without polyneuritis) by forced feeding of polished rice in amounts ranging from 6 to 9 per cent. of their body weight. It should be stated that the nerves of my fowls were examined and a certain degree of degeneration was found by the Marchi method. However in no case was this comparable to the extent of degeneration found in the nerves of fowls which have succumbed to polyneuritis, and it must be remembered that Vedder and Clark showed that degeneration began in the nerves of fowls after only seven days feeding on polished rice. Degeneration begins before the symptoms of polyneuritis appear, and continues after the bird is cured, so that the finding of moderate degrees of degeneration is no proof that the bird died of polyneuritis, and cannot be used to controvert the opinion that the cause of death in these experiments was overfeeding and not polyneuritis.

In order to confirm this conclusion, I repeated the experiment using unpolished rice. Twelve fowls were divided into three groups. The first group was fed 150 grams of unpolished rice daily, the second 75 grams, and the third group 50 grams. Table III shows the amounts fed in proportion to the body weight, and the results of the experiment.

TABLE III.

No. of fowl	Original weight	Daily amount of unpolished rice fed	Percent of body weight fed daily	Results
1	1580	150	9.49	Residue accumulated in crop after 19 days feeding. Alive at end of 30 days when experiment was discontinued. Would probably have died had feeding been continued
2	1630	150	9.20	do. do. do.
3	1710	150	8.77	Residue accumulated in crop after 11 days feeding. Died after 23 days feeding, with crop greatly distended
4	1810	150	8.28	Residue accumulated in crop after 11 days feeding. Died after 24 days feeding, with crop greatly distended
5	1550	75	4.83	Remained well for 30 days when feeding was discontinued
6	1580	75	4.74	do. do. do.
7	1610	75	4.65	do. do. do.
8	1740	75	4.31	Residue accumulated in crop after 15 days feeding. Died after 29 days feeding, crop greatly distended
9	1220	50	4.09	Remained well for 30 days when feeding was discontinued
10	1530	50	3.26	do. do. do.
11	1560	50	3.20	do. do. do.
12	1690	50	2.95	do. do. do.

Since birds fed on unpolished rice never develop polyneuritis, the death of these birds when fed from 4 to 9 per cent. of their body weight of unpolished rice, indicates that these birds were killed by overfeeding. The results obtained are somewhat irregular and it may be seen that the birds receiving the largest amounts did not in all cases show distress first. This is probably to be explained on the basis of individual idiosyncrasy. It is well known that weight for weight some individuals eat more than others. It is probable also that the results would have been more consistent had the experiment been continued a little longer. However the experiment was so revolting that it was only continued until sufficient information was obtained to prove definitely that birds can be killed by overfeeding on a diet that cannot produce polyneuritis.

Experiment 3. If polyneuritis develops in birds fed on food containing no carbohydrate, such as sterilized meat or sterilized egg, this would appear to show that the antineuritic vitamine is essential to the body in some way other than as a factor in carbohydrate metabolism. Accordingly meat and eggs were sterilized in the autoclave at 120° C. for half-an-hour, since many experiments have indicated that the antineuritic vitamine is destroyed in most foods at this temperature. Four fowls were fed on a daily ration of 50 grams of sterilized egg, half white and half yolk, and another group of fowls was fed on a daily ration of 50 grams of sterilized meat. The results of this experiment are indicated in Table IV.

TABLE IV.

Fowl	Food	Developed neuritis	Remarks
1	egg		Died in 16 days with inflammation of crop
2	"	56 days	Completely paralyzed in 58 days, and died in 63 days
3	"	63 "	" " " 69 " " 71 "
4	"	64 "	Completely paralyzed in 70 days. Treated with autolyzed yeast extract and recovered
1	meat	70 "	Completely paralyzed in 72 days, and died in 75 days
2	"	73 "	" " " 79 " " 83 "
3	"	95 "	" " " 101 " " 102 "
4	"	101 "	" " " 112 " " 114 "

From this it will be seen that fowls fed on sterilized egg or sterilized meat develop polyneuritis with great regularity, but only after a considerably longer depletion period than is observed in fowls fed exclusively on polished rice. This may be because the vitamine is not entirely destroyed in these foods by the sterilization, or because nutrition may be maintained better on these foods even in the absence of vitamine, than is the case when rice alone is fed. The nerves of all these fowls were examined by the Marchi method and showed the typical degeneration that accompanies polyneuritis gallinarum. Since there was no carbohydrate whatever in the diet of these fowls, we must conclude that the antineuritic vitamine is essential to the body in some other manner than as a factor in carbohydrate metabolism.

Experiment 4. If the antineuritic vitamine is concerned in carbohydrate metabolism, it might be expected that fowls fed on a considerable amount of polished rice in addition to sterilized meat or egg, would develop polyneuritis faster than birds fed on sterilized meat or egg alone. Accordingly four fowls were fed on a ration of 25 grams of polished rice and 25 grams of sterilized egg. Four other fowls were fed on a ration of 25 grams of sterilized meat and 25 grams of polished rice daily. The rice used was the same as that used in Experiment 2 in which the fowls fed on 25 grams developed neuritis. The meat and egg were the same as that fed in Experiment 3, for Experiments 3 and 4 were performed at the same time, and the meat and egg were sterilized daily for both experiments so that there could be no possible difference between the meat and egg used in the two experiments. As a matter of convenience the birds were placed for the day in small individual coops containing a receptacle in which the weighed food was placed. The birds were then allowed to eat at pleasure, but at the end of the day any food remaining was fed by hand. During the first few weeks of the experiment the fowls ate well, and little remained to be fed by hand; but about the third week they lost appetite

and thereafter had to be fed largely by hand. From time to time individual fowls would appear to recover their appetites and for a few days would eat nearly all of their ration voluntarily. One bird never stopped eating and was practically never fed by hand. The results of this experiment are indicated in Table V.

TABLE V.

Fowl	Food	Neuritis	Remarks
1	egg and rice	none	Died in 40 days from forced feeding. No signs of neuritis
2	" "	"	Remained well for 111 days
3	" "	"	" " "
4	" "	"	" " "
1	meat and rice	41 days	None of the fowls in this group died. They developed complete paralysis of the legs, so that they were unable to stand, but some of them (1 and 3) made partial recoveries while still eating the same diet. No. 4 remained well 111 days, when the experiment was discontinued
2	" "	85 "	
3	" "	91 "	
4	" "	none	

As none of the birds in the group fed on egg and rice developed neuritis, it was necessary to show that it was not impossible for these particular birds to succumb to this disease. They were therefore placed on an exclusive diet of polished rice, and No. 2 developed neuritis 8 days later and died of the disease in 15 days, No. 3 developed neuritis in 19 days and No. 4 developed neuritis in 14 days.

In a similar way the fowls in the group fed on meat and rice were also placed on an exclusive diet of polished rice at the end of 111 days when the experiment was concluded. No. 1 died of neuritis in 8 days, No. 2 in 17 days, No. 3 in 15 days and No. 4 in 20 days.

This experiment indicates decidedly that when fowls are fed on sterilized meat or sterilized egg plus an equal quantity of rice, they do not develop neuritis any faster than when fed on sterilized meat or sterilized egg alone. On the contrary the reverse was the case. The fowls fed on egg and rice did not develop neuritis at all while the experiment lasted; and the fowls fed on sterilized meat and rice not only did not develop the disease faster on the average than the fowls fed on sterilized meat alone, but on the contrary appeared to show some tendency to spontaneous recovery on this diet, and all of the birds in Experiment 4 ended the experiment in better condition than the birds in Experiment 3. We cannot conclude therefore that the addition of rice to an already deficient diet hastened the onset of the disease, as we would expect, were Funk correct in his view that the vitamine is essential in carbohydrate metabolism. On the contrary, the addition of rice, probably by affording a more balanced ration, actually deferred the onset of polyneuritis.

CONCLUSIONS.

1. Fowls fed on polished rice and allowed to eat *ad libitum*, consumed from 30 to 70 per cent. of their body weight, and from 1.4 to 3.6 per cent. of their body weight daily before the development of polyneuritis.

2. Under these conditions, the rapidity with which polyneuritis develops bears no relation to the amount of rice eaten, but depends upon the idiosyncrasy of the fowl to this deficiency.

3. Experiments performed to determine the relation of the antineuritic vitamine to carbohydrate metabolism by hand feeding birds with varying amounts of carbohydrate foods are fallacious if the amounts fed are too excessive or too minute. The birds receiving too much die from overfeeding and the birds receiving too little die of starvation.

4. Fowls fed on sterilized meat or sterilized egg will develop polyneuritis.

5. When fowls are fed on equal parts of sterilized meat and rice or sterilized egg and rice, they develop neuritis more slowly than when fed on sterilized egg or sterilized meat alone.

6. These experiments all indicate that the antineuritic vitamine is not concerned in carbohydrate metabolism.

DISCUSSION.

In prescribing a diet to prevent beriberi, it is believed that it is sufficient to ensure the consumption of such a quantity of antineuritic foodstuffs (beans, rice polishings, barley, etc.) as experience has indicated will prevent the disease, without any reference to variations in the amount of carbohydrate consumed.

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