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NERVES IN THE ABSENCE OF
EMBRYONIC NERVE FIBERS,
FOLLOWING EXPERIMENTAL
NONTRAUMATIC DEGENERATION: A
DISERTATION, PP. 61-107**

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A DISSERTATION
SUBMITTED TO THE FACULTY
OF THE OGDEN GRADUATE SCHOOL OF SCIENCE
IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
DEPARTMENT OF ANATOMY

BY
ELBERT HOWARD CLARK

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ELBERT CLARK

From The Anatomical Laboratory, University of the Philippines

THIRTY-TWO FIGURES

INTRODUCTION

The present study is based upon experiments in which degeneration and regeneration of medullated nerve fibers were brought about under new experimental conditions. The results obtained relate, for the most part, to phases of the subject upon which the evidence has heretofore been incomplete. In this investigation, an experimental obstacle which has been responsible for the strikingly contrary observations between the supporters of auto-regeneration on the one hand and the advocates of an out-growth of the axis cylinder on the other, has been entirely avoided. I refer to an ingrowth of foreign nerve fibers through the scar tissue into a regenerating medullated nerve. This obstacle was avoided by inducing degeneration in the peripheral medullated nerves of the domestic fowl by a prolonged exclusive feeding of polished rice, and subsequent regeneration by a return to an adequate nutritive diet.

In 1897 Eijkman first described 'polyneuritis' in fowls which had been kept for three or four weeks on an exclusive diet of polished rice. This has since been confirmed by numerous other investigators and Frazer and Stanton ('11) have noted and illustrated 'Wallerian degeneration' in the nervus ischiadicus of the domestic fowl which developed paralysis on a polished rice¹ diet.

¹ White rice, polished rice or decorticated rice is the clear white table rice of commerce. It is rice, which, after having the husk taken off, is further sub-

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July 18, 1914

In another place² I have described more in detail the changes occurring in the nervous system of such fowls. Here it was also pointed out, in agreement with Frazer and Stanton and others, that "The neuritis produced in fowls by a prolonged diet of polished rice is, so far as the best evidence indicates, a neuritis due to a deficiency of some food constituent or constituents necessary for the maintenance of the metabolic and functional activity of the nervous system."³

In the paralysis of fowls brought about by an exclusive diet of polished rice the medullated fibers of the sciatic undergo a rapid degeneration. This degeneration, however, is much slower than that produced as a result of transection of the nerve. Moreover, for the rice-fed fowls, the following conditions obtain: In

jected to a process of 'milling' or polishing. "In this process the fruit wall or pericarp, the layers subjacent to it (the subpericarpal layers) as well as the embryo are removed," Frazer and Stanton ('11). These authors give the following as the average composition of polished and unpolished rice:

	PROTEIN	FAT	CARBO- HYDRATE	ASH	MOISTURE
	per cent	per cent	per cent	per cent	per cent
Polished rice.....	7.7	0.25	77.23	0.25	14.3
Unpolished rice.....	9.0	1.65	75.52	1.08	12.75

Unpolished rice or red rice is rice which has not been subjected to the polishing process, and which as a consequence still has the pericarp, subpericarpal layers and the embryo. Fowls fed exclusively upon unpolished rice for long periods never develop neuritis as when fed exclusively upon polished rice. Further, neuritis in fowls as the result of an exclusive rice diet can most frequently be cured by placing the fowl on an exclusive diet of unpolished or red rice. There are several qualities of white rice, which, aside from the quality of the grain, are denoted by the amount of polishing to which the rice has been subjected. As might be expected the most highly polished grade is the most effective in producing paralysis in the fowl.

² Edward B. Vedder and Elbert Clark. A study of polyneuritis gallinarum. Philippine Journal of Science, vol. 7, no. 5, Sec. B, p. 423.

³ Richard P. Strong and B. C. Crowell have produced experimentally in man a similar neuritis by the prolonged feeding of a diet of which polished rice formed by far the main constituent. In one case which resulted fatally, the peripheral nerves showed marked degeneration (The etiology of beri-beri. Phil. Jour. Science, B, vol. 7, p. 271). John M. Little has also described beri-beri in man resulting from an almost exclusive diet of white bread (Beri-beri caused by fine white flour. Jour. Amer. Med. Assoc., vol. 58, p. 2029).

degeneration the fibers are intact and all traumatic and inflammatory effect produced by cutting the tissues and the nerve or of tying the latter are obviated; the process of degeneration can be stopped at almost any stage or greatly prolonged, and several stages of degeneration are to be observed in different fibers of the same nerve. In regeneration, the possibility of an ingrowth of fibers from other nerves into the regenerating nerve under observation is obviated and recovery of the animal can be accomplished after any stage of degeneration of the peripheral nerves. And lastly, the slowness of the cycle of degeneration and recovery, makes it possible to draw a sharper distinction between the process of degeneration and regeneration in medullated nerve fibers. At the present time these experimental conditions are especially desirable.

PARALYSIS IN FOWLS RESULTING FROM AN EXCLUSIVE DIET OF POLISHED RICE

A typical case of a fowl which has become unable to walk after a diet of polished rice is found in that of No. 54 whose history is as follows: No. 54, brown hen, fed polished rice since February 7, 1912; 25 days later, on March 3, the first definite signs of unsteadiness in the legs were noted. March 4, the bird was found balanced on its 'haunches,' was scarcely able to rise and could not take more than two or three haphazard steps without tumbling over in a heap. The diet was changed to a 'regenerative' diet consisting of whole grain, meat scraps, bread, grass, etc. March 14, could stand up very unsteadily for a few seconds but was scarcely able to take a step. March 20, same—never stood up nor attempted to walk unless forced and assisted in this. April 3, good general appearance but was scarcely able to walk. April 10, improved, but walked with much difficulty. May 3, apparently entirely recovered within the last few days.

It should be noted that many fowls on the polished rice diet lose complete control of the lower part of the legs. Others show wing drop, droopiness of the head and inability to swallow.

Still others show complete collapse.⁴ The greatest variety of symptoms are manifested by various birds, but loss of control of the legs is the most frequent. Fowls showing the latter symptom, with otherwise fair to good general condition, were the ones selected for this study; nerves of these show a more pronounced degeneration, and recovery in this class of fowls is more easily accomplished. Twenty to thirty days on the white rice diet is the usual length of time before symptoms of neuritis are manifested. Some birds resist for 35 or 40 days, and two fowls⁵ that were receiving a small quantity of calcium lactate with the rice did not 'come down' till the fifty-first and sixtieth day respectively. Nitrogenous and fatty foodstuffs in very small amounts added to the rice also greatly defer the development of the neuritis. For more complete data on this interesting affection and for feeding experiments, reference should be made to the recent article by Vedder and Clark ('12).

DEGENERATION

A few remarks should be made at this point concerning the nature and extent of the degeneration in the medullated fibers of the sciatic nerve in fowls of the class under consideration. In the nerves of 60 chickens, which had been fed 20 days or more on an exclusive diet of polished rice, degeneration in the fibers of the sciatic nerve was observed by the aid of the Marchi method in every case regardless of what symptoms were manifested by the fowl before death. Many of these were confirmed by the Weigert method for staining the myelin sheath. Several fowls fed as long as 35 to 40 days showed no signs of weakness in the legs but well marked nerve degeneration. The nerves from each of twelve fowls fed from 7 to 22 days consecutively

⁴ Several workers have observed that fowls occasionally do not lose weight on the polished rice diet. Frazer and Stanton ('11) who have kept very complete records report several fowls which kept their weight up for as long as 35 days. Other fowls even showed a gain in weight.

⁵ Courtesy of Dr. R. B. Gibson of the Department of Physiology; from experiments being conducted by him to study the influence of an addition of various salt mixtures to the white rice on the production of this affection, to be reported shortly.

with no leg weakness showed, by the same methods, myelin degeneration in their fibers. It was a constant observation that different fibers of a given nerve present the greatest variation in the degree of their degeneration. In two fowls killed after feeding 7 days on white rice, small areas of blackening after treatment by the Marchi method were observed in approximately one-third of the fibers of the sciatic. These areas very seldom involved the entire diameter of the individual fiber at any one point and the great majority ranged from 1 to 8 microns in diameter (fig. 32).

In the sciatic nerve of those fowls fed for a longer time and which developed a typical paralysis in the legs, every fiber showed larger areas of blackening. Advanced degeneration was found in from 10 per cent to 20 per cent of the fibers. The change shown by these latter fibers presents an identical picture of degeneration with that in medullated fibers of a mammalian nerve 10 to 14 days after section, but for the nuclei of the neurilemma sheath. The nuclei of the neurilemma sheath have undergone little or no multiplication. This will be again referred to and more fully discussed in the consideration of the "embryonic nerve fiber." By both the Marchi method and the Weigert method for the medullary sheath, the change of the medullary sheath substance into fatty globules and droplets appears complete in some fibers. As I have pointed out in a previous paper ('12),

Fibers showing advanced degeneration are marked by accumulation of degenerated myelin in large globules and droplets, a swelling and bulging of the nerve sheath at these points and a disintegration of the axis cylinder. The largest globules usually appear vesicular and in their center, segments or fragments of the axis cylinder are frequently to be seen. In these larger, and in some of the smaller globules also, the stainable material is found at the periphery and appears laminated. This laminated appearance is very characteristic in Weigert preparations and is the rule in the larger globules. Usually 3 distinct layers are clearly visible, of which the outer is the thickest. Other incomplete layers and fragments are seen centrally.

But for an increase in the number of nuclei of the neurilemma sheath, this description applies with equal exactness to fibers of similar preparations of the peripheral segment of the sciatic nerve of a fowl 7 days after section. Figures 2, 3, 4 and 5