BOTULISM

A REPORT OF FOOD-POISONING APPARENTLY DUE TO EATING OF CANNED STRING BEANS, WITH PATHOLOGICAL REPORT OF A FATAL CASE *

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CLINICAL REPORT, BY DR. WILBUR

A meal of roast beef, string bean salad with mayonnaise dressing, gelatin pudding, coffee and whipped cream was partaken of by a group of young people at a sorority supper held at Stanford University on Nov. 25, 1913; twenty-four ate of the bean salad and of these twelve were taken ill within the succeeding few days with symptoms of botulism. The string beans were from two separate lots, one dark green in color, purchased at a grocery store and packed by a canning association; the others, light green in color, were put up the summer before at the home of one of the girls attending the dinner. These latter beans were apparently prepared by the process of sterilization recommended by the U. S. Department of Agriculture Bulletin, that is, boiling in the final container for one hour on three successive days. There was no food or meal taken in common by all of those poisoned except the one in question. Among those made ill was one of the waiters, who had likewise partaken of the beans. The fact that two or three of the first patients had also eaten mushrooms confused the diagnosis slightly at first. Of the twelve taken ill one died about two weeks after the meal. All of the rest had bulbar disturbances of varying degree but all made a satisfactory recovery.

The early symptoms came for the most part at the end of thirty-six to forty-eight hours and because of the eye manifestations several first consulted an eye specialist, Dr. Howard Black of Palo Alto, and he together with Dr. Thomas M. Williams were in attendance on the patients whom I had the opportunity of studying. While there was marked variability in the course and seriousness of the disease picture all were enough alike so that the description of one patient will illustrate the phenomena observed.

Girl, aged 23, Tuesday evening, Nov. 23, 1913, ate the dinner including the canned string beans of the light green color together with a little rare roast beef. The following day she felt perfectly normal except that at 10:00 in the evening the eyes felt strained after some sewing. Thursday morning,

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thirty-six hours after the meal, when the patient awoke, the eyes were out of focus, appetite was not good and she felt very tired. At night she had still no appetite, was nauseated and vomited the noon meal apparently undigested. Friday morning, two and one-half days after the meal, the eyes were worse, objects being seen double on quick movement, and it was noticed that they had a tendency to be crossed. A peculiar mistiness of vision was also complained of. She was in bed until late in the afternoon, when she visited Dr. Black. She had had some disturbance in swallowing previous to this time and stated that it felt as if "something came up from below" that interfered with deglutition. The fourth day she remained in bed, was much constipated, and noticed a marked decrease in the amount of urine voided. There was at no time pain except for occasional mild abdominal cramps, no headache, subnormal temperature, and a normal pulse. The fourth and fifth days the breathing became difficult at times and swallowing was almost impossible. The patient complained of a dry throat with annoying thirst. The sixth day there were periods of a sense of suffocation with a vague feeling of unrest and as if there might be difficulty in getting the next breath. The upper lids had begun to droop. The voice was nasal. When the attempt was made to swallow liquids they passed back through the nose. The patient felt markedly weak.

Physical examination at this time showed ptosis of both upper eyelids, dilatation of the right pupil, sluggish reaction to light of both pupils, apparent paralysis of the internal rectus of the left eye, normal retina, inability to raise the head, control apparently having been lost of the muscles of the neck, inability to swallow, absence of taste. The tongue was heavily coated and the throat was covered with a viscid whitish mucus clinging to the mucous membrane. The soft palate could be raised but was sluggish, particularly on the right side. The exudate on the right tonsil was so marked that it resembled somewhat a diphtheritic membrane. The seventh day there was some change in the condition; occasional periods occurred when swallowing was more effective, and there was less tendency to strangle. On the eleventh day there was some improvement of the eyes, still strangling on swallowing, sensation of taste was keener, and the general condition improved. The twelfth day the patient was able to move her head, but was unable to lift it except when she took hold of the braids of her hair and pulled the head forward. The eyes could be opened slightly, speech was less nasal and more distinct, and improvement in swallowing was marked. At the end of two weeks the patient was able to take soft diet freely, and at four weeks she was up in a chair for a couple of hours complaining only of general weakness and inability to use her eyes. At the end of five weeks she was able to leave the hospital and return to her home and later to resume her regular work.

The foregoing description is typical of the cases seen and corresponds to the picture of botulism, which was first clearly differentiated as a clinical entity by Van Ermengen, who, following his study of the epidemic of Ellezelles, demonstrated that the symptoms were due to a toxin formed by an anaerobic organism, the *Bacillus botulinus*. In the patients seen by me there was a wide variation in the severity of the disease, some having only transient disturbance of vision or of swallowing, others such complaints as "jaws seemed very tired," "apparent inability to chew food," "tongue seemed hard to move," "sleepy all the time," "could not walk fast," "throat filled up with mucus all the time," "tried to attend classes, legs and arms were almost powerless," "hard work climbing stairs," and "throat

felt as if there was shelf in it beyond which food could not pass but it did not hurt." The complaint of seeing double and of the mist passing over the eyes was comparatively common. The gradual onset of the symptoms and their marked variability were the most striking features. At one time a patient would show marked inability to swallow, while a little later a soft meal would be taken without difficulty. There was very little difference for some time in the severity of the clinical picture between the fatal case and some of the others. The details of these cases were reported by Dr. Thomas M. Williams at the meeting of the California State Medical Society in April, 1914.

FATAL CASE

Young healthy woman, aged 23, on the second morning following the ingestion of the meal at which time the beans were taken, complained that objects were often seen double. There was no headache or vomiting; urination apparently as usual. A laxative had been taken because of constipation and the bowels had acted. On the fourth morning the patient was unable to eat because of the inability to swallow. There was no pain. Later on in the day she swallowed with difficulty. On the sixth morning her mouth was dry, there was considerable thirst, no abdominal colic, no appetite, marked asthenia, with the muscular power in the left arm less than normal. Voice was slightly nasal with inability to articulate distinctly. Temperature was 97.8 to 99 F., pulse 104. There was ptosis of both upper lids; both pupils were dilated but reacted to light, with normal fundi. The breath was foul, tongue coated and it and the pharynx covered with sticky, whitish, viscid mucus. There was considerable edema of the uvula.

The condition did not change very much in the next few days except that the patient felt very weak, was unable to raise the head without help, at times would swallow well, at other times was unable to take the simplest food, and the pulse became more rapid and dicrotic. Blood-pressure was normal. At one time she became quite talkative and complained that her jaws did not open naturally and she could not see well but for the most part she was quiet and slightly depressed.

On the tenth day she brought up with very much difficulty some mucus which had been interfering greatly with her throat and had a period in the afternoon when she was unable to swallow, had difficulty in breathing and cold extremities. Later on she was able to take an egg-nog, but complained of a spontaneous choking sensation. In the night to the distress from these attacks was added an inability to breathe through the nose.

On the twelfth day involuntary movements of the bowels occurred. Some relief from the choking, breathless sensation was gained by swabbing the throat. The patient vomited some dark green fluid after a large, soft involuntary stool and began to feel very warm and excited, axillary temperature going up to 100.4. After a period of chills, great restlessness, choking sensation, increasing temperature and higher pulse rate together with the signs of hypostatic pneumonia, the patient had a collapse from which she recovered on the administration by Dr. Williams of an intravenous transfusion of normal salt solution. She vomited later a considerable amount of blood and although her breathing became more superficial, her weakness more evident, the sensorium remained perfectly intact.

On the thirteenth day she died following a respiratory disturbance apparently due to sudden paralysis of the diaphragm, since the heart continued to beat for some time. Various form of stimulant and other treatment were administered without avail. The necropsy, performed by Dr. William Ophüls,

was practically negative except for areas of collapse and bronchopneumonia in the posterior parts of the lungs, and certain lesions of the central nervous system, which will be described later.

SYMPTOMS AND SIGNS

When one sees a series of cases presenting such striking features as those enumerated in the two described the difficulty of making a diagnosis of botulism is not great, but it is easy to see how a sporadic case could be readily overlooked or confused with various other conditions, such as luetic bulbar paralysis, anterior poliomyelitis, etc. The symptoms noted by the various writers who have described epidemics of this type are all of the same general character.

DIGESTIVE AND SECRETORY SYSTEMS

Contrary to the usual idea of food-poisoning, there is apt to be freedom from pain except perhaps for some colic, occasional vomiting, and only at times diarrhea, in patients who have been poisoned with botulismus toxin. Obstinate constipation is the rule, the intestinal tract being paralyzed by the ingested poison. Bürger¹ reports the washing out from the stomach of food particles eaten five days previously, on the evening of the day when the infected ham was taken for breakfast. Slow absorption from this alimentary tract paralysis probably explains in part the gradual onset of the symptoms and also the finding by Kob of toxin in the blood of a child eight days after the ingestion of the infected food. Very little peristalsis was to be heard over patients seen by me except after the use of brisk cathartics and enemas. The late involuntary stools and the other gastro-intestinal features in some cases may be due to a central effect on the vagus. The first stool passed by a patient was described by Van Ermengen² as dark and full of mucus. Anorexia is common, and the foul breath, coated tongue, viscid, sticky, whitish mucous secretion with the generally dry mouth is accompanied apparently by a paralysis of the secretory activity of many glands (parotid enlarged at times) extending in some patients even to the lacrimal glands, so that Schumacher³ reports the inability of a woman to shed tears when told of her husband's death. At times tears are secreted freely, and, as in one of our patients, the eyes appear watery and injected.

NERVOUS SYSTEM

The most striking effect on the nervous system is the difficulty in vision with the normal background, dilated pupils, ptosis, and

1. Bürger: Ueber zwei Gruppen von Botulismus mit zwölf Erkrankung- und fünf Todesfällen, *Med. Klin.*, 1913, ix, 1846.

2. Van Ermengen: *Ztschr. f. Hyg. u. Infektionskrankh.*, 1897, xxvi, 1.

3. Schumacher: *München. med. Wchnschr.*, 1913, lx, 124.

paralysis of the various eye muscles with double vision and the disturbance in deglutition. Dizziness, sleeplessness, marked muscular weakness with no disturbance of the sensorium, no headache and no anesthesia or paresthesia are characteristic. At times various paralyses of the different skeletal muscles particularly about the neck are seen. Practically all the cranial nerves except the first and second have shown involvement in described cases; that is, ptosis, mydriasis, disturbances of accommodation (third and fourth cranial nerves), inability to cry (lacrimal nerve of the fifth cranial), dryness in the mouth (seventh and ninth cranial), disturbance of deglutition partially due to lessened secretion and partially due to nervous disturbances leading to difficulty in chewing and the muscular side of swallowing (ninth, tenth and eleventh cranial nerves), mask-like expression (seventh cranial), at times difficulty in hearing (eighth cranial), variation in speech to aphonia (twelfth), obstipation and respiratory and cardiac disturbances (tenth cranial nerve). The retention of the urine and the occasional paralyses of muscles of the limbs indicate that the spinal cord may be damaged at times. The deep reflexes are not disturbed. Romberg's and Babinski's signs both absent. No tremor and no spastic conditions have been described. We noted no angioneuroses of the skin. The sensations of the mucous membrane of the throat and mouth are dulled at times probably because of its dry condition.

CIRCULATORY AND RESPIRATORY DISTURBANCES

The temperature, pulse and respiration remain practically normal unless the vagus center is involved or a secondary infection takes place. The blood-pressure was found normal in our patients, and no abnormalities were noted in the blood itself. The feeling of compression and oppression in the chest complained of by some patients is probably nervous, not circulatory, in origin.

GENITO-URINARY SYSTEM

A lessening in the amount of practically normal urine is usually seen. At times this is due to retention. There may be paralysis of the bladder detrusors or sphincters. The small amount of urine later is perhaps due to the inability to swallow. Twenty-four hours or longer passes in some patients before urine is voided.

Throughout it must be constantly remembered that the symptoms may be extremely acute and followed by early death, or they may be gradually unfolded in their entirety, or only one or two characteristic evidences may appear.

The variations in the course of the disease may be due to the amount of toxin in the food eaten, to individual resistance or to the

amount of vascular thrombosis present. The prognosis for eventual complete recovery is good if the early part of the illness is survived. In the cases here reported only one of the twelve patients succumbed, although no early difference in the severity of the clinical picture could be seen between this patient and some of the others who recovered. Death usually occurs during the first or second week, seldom later. From 30 to 50 per cent. is a common death-rate. In the Ellezelles epidemic described by Van Ermengen only three of the thirty patients died.

DIFFERENTIAL DIAGNOSIS

The isolated case is the one that is most apt to lead to confusion in diagnosis, particularly with syphilis and poliomyelitis. When botulismus is severe enough to endanger life promptly, the disease picture is usually so distinct as to permit of ready recognition. The prominence of the paralysis of the eye muscles often brings the patient first to the ophthalmologist, who must bear in mind that conditions varying from a nystagmus to an absolute immovability of the eyeballs, always with a normal retina, may occur in botulismus. Poliomyelitis, the so-called asthenic bulbar paralysis, cerebral syphilis, the various toxic ophthalmoplegias, rabies, diphtheria, poisoning with plant alkaloids (atropin, gelsemium, hyoscyamin, etc.), methyl alcohol, and ptomains (methylguanidin, ethylendiamin, etc.) must all be ruled out before making a final diagnosis.

ANATOMICAL LESIONS, BY DR. OPHÜLS

As a result of van Ermengen's classical work the question of the pathology of botulismus appears to be well settled. The bacteriological findings have been confirmed by several later investigators and his animal experiments hardly leave any doubt as to the etiology of the disease. Although the symptoms produced in the experimental animals by means of administration of the toxin of the *Bacillus botulinus* are perhaps not absolutely identical with those observed in human beings, they are similar enough to recall the symptom-complex of the disease in man and moreover they coincide entirely with the result of intoxication of similar animals treated directly with the spoiled foodstuffs.

On the basis of the *clinical symptoms* largely one has assumed a specific action of the botulismus toxin on the ganglion cells of the central nervous system, although other effects of the poison have been observed, namely, a marked paralyzing effect on the gastro-intestinal canal and a tendency to the occurrence of multiple minute hemorrhages, more especially in pons and medulla. The former, the paralysis of stomach and bowel, might of course also be ascribed to

an affection of the motor ganglia of these organs, either centrally or peripherally.

This conception of a specific action of the toxin on the ganglion cells has been much strengthened by the histological findings in the central nervous system of animals subjected to the experimental intoxication. Van Ermengen in his original article⁴ describes peculiar degenerative lesions in the ganglion cells of such animals which involve largely the Nissl granules in them, although the nucleus also appears sometimes affected. Of these changes he says:

"There are almost none in the cerebrum or in the cranial nerves, but they are very pronounced in the spinal cord, less so in medulla, in pons and in the peduncles." He adds, however: "On the whole these lesions are very variable in intensity."⁵

He also finds small perivascular hemorrhages. Marinesco,⁶ who studied the same material, gives practically the same account of the alterations. He even speaks of a phagocytosis of the injured cells by neuroglial phagocytes. Kempner and Pollack⁷ confirm these observations of Marinesco and of van Ermengen, but believe that in their specimens, also obtained from animals treated with the botulismus toxin, they observed a still earlier lesion of the Nissl granules, which they speak of as *klumpige Schwellung*. They did not find any evidence of phagocytosis. The question was reexamined experimentally by Ossipoff⁸ in 1900. He experimented on monkeys, cats and pigs as the animals most susceptible and found lesions in the nerve-cells similar to those described by Marinesco and others. He also believes to have found evidences of phagocytosis of the damaged cells. He makes the following interesting statement:

"Within the hyperemic blood-vessels as well as on the outside of them there were found many white blood-corpuscles. In the vessels these corpuscles were sometimes bunched in masses."⁹

4. Van Ermengen: Contribution à l'étude des intoxications alimentaires, Arch. de Pharmacodyn., 1897, iii, 213, 499.

5. "Elles sont presque nulles dans le cerveau, absentes dans les nerfs craniens et très accusés dans la moelle épinière, moins prononcées dans le bulbe, la protuberance et les pedoncles." "Ces lésions, considérées dans leur ensemble, sont très variable comme intensité."

6. Marinesco: Pathologie générale de la cellule nerveuse. Lésions secondaires et primitives. IV. L'action du bacillus botulinus, La Presse Méd., 1897, v, 43.

7. Kempner and Pollack: Die Wirkung des Botulismustoxins (Fleischgiftes) und seines spezifischen Antitoxins auf die Nervenzellen, Deutsch. med. Wchnschr., 1897, xxiii, 505.

8. Ossipoff: Influence de l'intoxication botulinique sur le système nerveux central, Ann. de l'Inst. Pasteur, 1900, xiv, 769.

9. "Dans les vaisseaux hyperemiés ainsi qu'en dehors d'eux on rencontrait aussi beaucoup de globules blancs. Dans les vaisseaux il y avait parfois une agglomération de ces globules."

The importance of this statement will become more evident in the discussion of our own findings. On the basis of the findings in the ganglion cells, Römer and Stein¹⁰ attempted to localize more exactly the paresis of accommodation observed in some of the animals experimented on and came to the conclusion that the disturbance is localized in the nucleus of the oculomotor nerve, on account of the degenerative lesions found in certain parts of the nucleus.

It is surprising how few human brains have been the object of a careful histological investigation in this disease. Van Ermengen⁴ was unable to obtain any satisfactory material in his cases. Fischer,¹¹ who describes an outbreak of the disease due to spoiled beans, clinically came to the conclusion that the intoxication produced "central paralysis with successive elimination of certain motor nuclei in the brain stem and of the vital centers in the floor of the fourth ventricle," also that it eventually caused a descending paralysis of the motor neurons in the anterior gray columns of the spinal cord. Parts of the brains in several of his cases were sent to the Pathological Institute at Giessen for examination, but apparently no characteristic lesions were found. In the latest publication by Bürger several new post-mortem examinations on cases dead of botulism are mentioned but in *one* of the records only there is this short allusion to specific lesions in the central nervous system:

In the cerebrum the ganglion cells are well preserved, but in the region of the oculomotorius they show commonly dust-like disintegration of the Nissl's granules and eccentric position of the nuclei.¹²

It is well to bear in mind in this connection how equivocal these finer lesions in the bodies of the ganglion cells still are. So far as I can see they are given less significance at the present time by neurologists than they were shortly after their discovery by Nissl.

10. Römer and Stein: Experimenteller Beitrag zur Frage nach dem Sitz und Wesen der Accommodations-parese bei bakteriellen Intoxikations-Krankheiten, *Arch. für Ophth. (Graefe's)*, 1904, lviii, 291. "Die im Verlaufe der Botulismus-Vergiftung auftretende Accommodations-parese hat ihren Sitz im Oculomotorius-Kerngebiet und ist eine durch bestimmte Komponenten des Botulismus-Toxins hervorgerufene Degeneration von Ganglienzellen im Oculomotorius-Kern."

11. Fischer: Ueber eine Massenerkrankung an Botulismus infolge Genusses verdorbener Bohnenkonserven, *Ztschr. f. klin. Med.*, 1906, lix, 58. "Wir gewannen ferner aus den klinischen Beobachtungen den Eindruck dass es sich bei der Giftwirkung um das Auftreten zentraler Lähmungen handelt, um fortschreitende Ausschaltung der Kerne bestimmter motorischer Gehirnnerven im Gehirnstamme und der lebenswichtige Vorgänge auslösenden, automatischen Zentren im Boden der Rautengrube." "dass das Toxin vom Gehirnstamme und der Medulla allmählich absteigend die dem motorischen Apparate zugehörenden Neuronen der Vorderhörner des Rückenmarkes lähmt."

12. Bürger: "Im Grosshirn waren die Ganglienzellen gut erhalten, während sie im Oculomotoriusgebiete vielfach staubförmigen Zerfall der Nissl's Granula, excentrische Lage des Kernes usw. erkennen liessen," *Med. Klin.*, 1913, ix, 1846.

The brain in our case was obtained within twenty-four hours in a very good state of preservation. It has been remarked by others that in botulism the tissues remain intact for an unusually long period of time, which might suggest some interference with the normal autolytic ferments.

The gross findings at necropsy were entirely negative except for a moderate hyperemia of the cerebral vessels, which was especially pronounced at the base of the brain and in the region of the fourth ventricle, where there also was found some edema. No hemorrhages could be made out with the naked eye on several sections through the brain stem. The internal organs were markedly hyperemic, which was especially noticeable in liver, kidneys and intestines. This general hyperemia has been a constant finding in all cases of human botulism and is also found in the experimental disease in animals. The dilatation of all blood-vessels was also very evident in sections from all organs examined. Typical bronchopneumonic lesions were found in the lungs, which condition probably accelerated the death of the patient.

The following is a short description of the microscopical findings in the brain:

The brain stem was sectioned transversely at different levels at the time of the autopsy and carefully hardened in frequently changed absolute alcohol. Numerous sections were made from all levels and special attention paid to the regions of the more important nuclei. Sections were obtained from all motor and some of the sensory nuclei on both sides. The nuclei studied were those of the oculomotorius (third), trochlearis (fourth), trigeminus (fifth), abducens (sixth), facialis (seventh), acusticus (eighth), glossopharyngeus (ninth), vagus (tenth), and hypoglossus (twelfth) nerves. The following lesions were found:

Thrombosis of the right arteria vertebralis at lower end of the medulla and extending into the arteria basilaris some distance. The middle part of the arteria basilaris is free. The anterior portion of it again is filled with thrombus. There are thrombi in a few of the pial branches of the basilar artery. Many pial veins at the base of the medulla and pons are filled with thrombi more especially on the right side and there are several thrombi in the veins of the tela chorioidea above the corpora quadrigemina and the posterior part of the third ventricle. All blood-vessels in the brain-tissue are much distended and full of blood. Both in the ventral and in the dorsal parts of the brain-stem one finds quite a few small thrombosed blood-vessels, some of which are situated near important nuclei; for instance, one such was found near the right vagus nucleus, several in the nuclei of the olives, several in the substantia ferruginea, several in the right nucleus trochlearis, several near the right nucleus of the oculomotorius and similarly several near the left nucleus oculomotorius, but somewhat further away from it. Small perivascular hemorrhages were encountered quite commonly about thrombosed veins and others. The thrombi in all places were very rich in polymorphonuclear leukocytes, but no bacteria could be demonstrated in spite of the use of various staining methods, including Weigert's modification of Gram's method. All thrombi were very rich in fibrin and contained comparatively few masses of conglutinated blood platelets.

Fig. 1.—Thrombus in vertebral artery (from photomicrograph).

Fig. 2.—Thrombosis in small vein in brain tissue near oculomotor nucleus (from photomicrograph).

The Nissl granules stain unusually well in all sections especially in the large motor ganglion cells. They are quite normal in size and arrangement. Nothing unusual could be detected in spite of especially careful study of them. The nuclei of the ganglion cells are perfectly normal.

Sections were also taken from various parts of the cortex of the cerebellum. There was no difference in the appearance of the ganglion cells from these other regions. Few thrombi were seen in the pial veins. The blood-vessels in the cortex are dilated and full of blood, but none show thrombosis or perivascular hemorrhages.

No thrombi were found in any other organs in spite of the study of many sections except one in a vein in the submucosa of the intestine and the very beginning of the thrombotic process in few of the dilated vessels in the ovarian cortex.

Anaerobic cultures were made from the intestinal content both of the small and large intestines, from the cerebrospinal fluid, from the heart blood, and from the spleen. The cerebrospinal fluid and the heart blood were sterile and the *Bacillus botulinus* was not found in any of the other cultures.

I believe that on the basis of these findings it will be necessary to change considerably our ideas in regard to the action of the botulinus toxin. No evidence was found to substantiate the hypothesis of a specific action of the toxin on the nerve-cells. The negative findings in regard to any disturbance in the Nissl granules in our case are quite convincing in this regard in spite of the evidence to the contrary brought forward by other writers. The statement of Bürger¹² is so short and the lesions described in it are so slight that it hardly deserves much serious attention. But even so the fact remains that in our case the size and arrangement of the Nissl granules was quite perfect and if there should have been minor lesions they certainly were not sufficient to account for the severe clinical symptoms. So far as the positive findings in the experimental animals is concerned it may be pointed out that in them the localization of the lesions as described by Marinesco⁶ and van Ermengen⁴ and others does not coincide altogether with the clinical symptoms. They both emphasize the fact that the most marked involvement is found in the ganglion cells, both motor and sensory of the cord, whereas, in man at least, cord symptoms are late and rare and sensory symptoms have never been observed. The lack of histological findings in the ganglion cells does not of course prove that the poison may not have a specific action on the ganglion cells after all, but the matter remains a mere hypothesis which is greatly weakened by the positive finding of lesions which explain the clinical symptoms as well, if not more adequately.

There is present all evidence of a serious interference with the circulation in the meninges and in the brain which is most marked at the base of the brain, throughout the brain-stem where numerous hemorrhages testify to the seriousness of circulatory disturbance. Associated with this disturbance of the circulation one finds multiple

thromboses in the blood-vessels, in both the arteries and the veins. The upper part of the right vertebral artery, the posterior part of the basilar artery and again the anterior part of the same vessel are completely obstructed by thrombi. Several of the branches of these arteries in the pia are filled with thrombi. There are thrombi in many veins in the pia and in the substance of the brain, several within or in the immediate vicinity of important nuclei.

The disturbance in the blood-vessels evidently consists in an extreme vasodilatation with great slowing of the blood-current, and as such it is only part and parcel of a general paralysis of the vasculatory mechanism which has been observed and noted by all careful observers of cases of botulism. This has been usually referred to insufficient heart action. When we take into account, however, that the poison has a powerful paralyzing effect on the involuntary muscles of the gastro-intestinal tract, as is shown by the prompt paralysis of the stomach and the obstinate constipation, it would appear probable that the poison might have a similar effect on the muscular wall of the blood-vessels, either directly or indirectly through the vasomotor nerves, which would certainly have a tendency at least to contribute greatly to any interference with the circulation which, however, might be partly due to poor heart action.

Why the circulation in all cases should be especially poor at the base of the brain, more especially in pons and medulla, is not so evident. One might suggest, however, that the main blood supply to these parts through the vertebral arteries is not so abundant as the blood-supply to the cerebrum from the internal carotid arteries.

The origin of the thromboses is also somewhat puzzling. I believe the existence of them in both arteries and veins excludes the idea of embolism.

It is also somewhat difficult to explain why we should have in these cases a tendency to thrombosis so exclusively in the blood-vessels of the brain, because in other organs very little evidence of thrombosis could be detected, but even if we assumed a pretty general tendency to thrombosis those in the blood-vessels in the brain stem would provoke the most prominent symptoms on account of the crowding of so many important centers at that point.

At all events in our case the evidences of severe disturbance of circulation associated with hemorrhages and thrombosis in pons and medulla are clear and they are sufficient to explain the symptoms, whereas the assumption of specific action of the poison on certain ganglion cells, in our case, appears to be purely hypothetical.

TREATMENT

As soon as the possibility of botulism presents itself the most evident therapeutic procedure is to empty the stomach thoroughly

with a stomach tube, to wash out the large bowel and to leave in the stomach a brisk cathartic—castor oil or Epsom salts. Since the toxin is the cause of the symptoms and its absorption is slow because of the paralysis of the intestinal tract the foregoing measures should be carried out even after several days. The patient should be kept absolutely quiet, the body supplied with plenty of water, by rectum or under the skin if necessary, simple food given and great care used to prevent aspiration pneumonia. Strychnin seemed beneficial in the cases described in improving the action of the disturbed nervous centers. Other stimulants should be given as required.

The vascular conditions above described indicate the possibility of complete recovery from a condition that seems hopeless and should lend encouragement to keeping up a hard fight against the disease, even to prolonged artificial respiration in case of respiratory failure. The specific serum treatment has not been used in this country so far as I know. Leuchs¹³ and others have prepared a serum which is very effective in animals. Polyvalent serums have given the best results. In Berlin this serum is prepared by the government. It is quite evident from the animal experiments that it would have to be near at hand and used promptly to be successful. That such serums should be kept in the various centers of the country is evident, as extensive botulism poisoning is apt to occur at any time.

SOURCE OF POISON

In attempting to determine the foodstuff responsible for the poisoning of the described patients each one was carefully questioned as to foods partaken of at the meal in question. As noted, there were two kinds of string beans, one dark in color from a grocery and put up by a prominent canners' association, and another light green in color, domestically prepared during the previous summer. These latter beans were tender and were served as salad without preliminary heating by the Japanese cook. With mayonnaise dressing they tasted well and were eaten freely by those to whom they were served. Some of the guests were given only the dark-colored beans. None of these were taken ill. The symptoms of poisoning were so delayed that none of the bean salad was obtainable for examination but two extra cans of the same lot of home canned beans were placed at our disposal. The cans of tin were of quart size and the top was sealed with the hard red sealing wax often used for fruit jars, etc. One of these contained perfectly normal-appearing beans in a small amount of juice; the other was "blown" somewhat and its contents

13. Leuchs, J.: *Ztschr. f. Hyg.*, 1910, lxx, 55; Kolle and Wassermann: *Bacillus Botulinus (Immunität)*, *Handbuch der Pathogenen Mikroorganismen*, 1912, iv, 939 (full bibliography given).

fermented and slightly sour. Juice from both cans injected into animals had no evident toxic effects. In the fermented can Dr. R. H. Major found a long spore-bearing bacillus resembling somewhat the *Bacillus botulinus*. It was not that organism, but an unidentified one, apparently the so-called "bacillus Tourné," well known and dreaded by fruit- and catsup-canners because of the resistance of its spores to heat and its ability to spoil a pack when mixed with the raw product. Evidently the spores of the above-mentioned organism withstood the fractional sterilization of boiling of one hour on three successive days; so, while we did not find the *Bacillus botulinus* in the beans, we did find an organism which grows under similar conditions. The possibility then was present that had the beans been contaminated with *Bacillus botulinus*, that organism could have developed in one of the cans. Therefore the question of whether the string beans may provide a suitable medium is of the greatest interest in view of the present cases. The resistance of the spores of *Bacillus botulinus* to heat, (while less than that of many anaerobes), the favorable anaerobic conditions, the optimum growth at ordinary temperatures, the ability to grow either in faintly alkaline or acid mediums all favor the view that this is possible.

The famous Darmstadt epidemic was due to eating preserved bean salad served without heating. These were apparently ordinary beans (wax rather than string beans) prepared in a cooking school (Fischer¹⁴). Landmann¹⁵ suggests the possibility that small contaminated meat particles were mixed with the beans but brings out no evidence in support of this idea. The characteristic butyric acid (rancid) odor and slightly sour taste makes beans used for salad particularly dangerous, since with the usual dressing a slightly sour taste is agreeable to most individuals. The destruction of the toxin by heat was well illustrated in Darmstadt by the man who came late to the celebration and thinking the beans were being served as a vegetable and not as a salad, heated them along with other food and suffered no consequences. That canned green beans may also serve as a medium for the growth of other organisms is shown by the epidemic in Leipsic in 1906 described by Rolly,¹⁶ in which the *Bacillus coli* and *Bacillus paratyphosus* B. were later isolated from them. In California several instances of poisoning resembling botulismus have come to

14. Fischer, August: Ueber eine Massenerkrankung an Botulismus infolge Genusses "verdorbener" Bohnenkonserven (Nach Vorträgen, gehalten im ärztlichen—8/2/04—und im naturwissenschaftlichen Verein—8/3/04—in Darmstadt), Ztschr. f. klin. Med., 1906, lix, 58.

15. Landmann, G.: Ueber die Ursache der Darmstädter Bohnenvergiftung, Hyg. Rundschau, 1904, xiv, 449.

16. Rolly: Ueber Eine Massenvergiftungsepidemie mit Bohnengemüse (Bact. coli und Bact. paratyphi B), München. med. Wchnschr., 1906, liii, 1798.

our attention. Sheppard¹⁷ describes in a graphic manner the typical and fatal poisoning of two men and a woman while on a camping trip following the eating of canned pork and beans. Peck¹⁸ reported a similar and more extensive poisoning with eleven deaths at Sawtelle, Cal., in which he thought that canned pears were responsible.

In order to study the canned goods on which the *Bacillus botulinus* would grow, with the assistance of Drs. E. C. Dickson and E. G. Gary, a series of experiments were begun with a culture of *Bacillus botulinus* obtained from the New York Museum of Natural History by inoculating a number of cans of beans and keeping them under various conditions at various temperatures. Up to date one can tested had a slightly pungent smell and rabbits inoculated with the juice died with symptoms suggestive of botulism. The experiments will not be complete for some months, but they apparently point to string beans in sealed cans as a medium on which the *Bacillus botulinus* will grow. Further we cannot go at present. Van Ermengen¹⁹ has carefully worked out the details of the growth of this organism, its toxin and its destruction under varying conditions, and they need not be reviewed here. The only record found of this organism occurring in nature was that of Kempner and Pollack, who found it in pigs' feces. We have as yet been unable to find out whether pigs were kept near the beans in question or whether the beans were fertilized with pigs' feces. It is fortunate that an organism with such possibilities for harm is rare.

Nevertheless the greatest care should be used in the preparation of all canned foodstuffs, particularly those kept under anaerobic conditions and apt to be eaten uncooked, to see that sufficient steam pressure and heat is used to kill all organisms and their spores. The sterilization under high pressure in vogue with all large canning companies makes their pack safe, but with the variability in domestic preparation the least rancid odor should lead to rejection of canned food and all vegetables should be reheated before being served. A long series of experiments on the penetration of heat into the interior of cans in preserving meats, etc., have been made by Bischoff and Wintgen,²⁰ Pfuhl,²¹ Wolffhügel and Hueppe²² and others and the need

17. Sheppard: Report of Three Cases of Fatal Ptomain Poisoning, South. California Pract., 1907, xxii, 370.

18. Peck, G. W.: South. California Pract., 1910, xxv, 121.

19. Van Ermengen: Der Bacillus Botulinus und der Botulismus, Handbuch der Pathogenen Mikroorganismen (Kolle und Wassermann) 1912, iv, 909 (with full bibliography).

20. Bischoff, H., and Wintgen, M.: Beiträge zur Conservenfabrikation, Ztschr. f. Hyg., 1900, xxxiv, 496.

21. Pfuhl, E.: Beitrag zur bakteriologischen Untersuchung der Fleischconserven, Ztschr. f. Hyg., 1904, xlviii, 121.

22. Wolffhügel and Hueppe: Mitt. a. d. k. Gsndhsamte, 1881, i, 395.

of steam pressure as well as heat is emphasized. Bolduan²³ describes the work of Belser and others on "blown cans" and found that a number of different bacteria more or less resistant to heat were present.

The possible relationship of epidemics to *Kalbfieber* (milk sickness) because of its similarity to botulism must be borne in mind (Crawford,²⁴ Schneidemühl²⁵).

CONCLUSIONS

1. The twelve cases reported presented the typical clinical picture of botulism apparently due to eating of domestically prepared canned string beans served without preliminary heating. That string beans may act as a culture medium for the *Bacillus botulinus* is possible, and the possibility is being further investigated. The methods of sterilization under pressure in use by canning factories seems to preclude the possibility of the growth of *Bacillus botulinus* in their pack.

2. Vascular thromboses were found about the brain-stem in a patient dying with the symptoms of botulism. Such lesions explain better the clinical phenomena observed than does the more or less hypothetical assumption of a specific action of the botulin on certain ganglion cells.

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23. Bolduan: Food Poisoning, Treat & Co., 1909, p. 104.

24. Crawford, A. C.: The Supposed Relationship of White Snake Root to Milk Sickness or "Trembles," U. S. Dept. Agric., Bureau Plant Industry, Bull. 121, 1908, p. 5.

25. Schneidemühl: Ueber Botulismus beim Menschen und die sogenannte Geburtsparalyse bei Rindern, Centralbl. f. Bakteriologie, 1898, xxiv, 577.