Colonies which show color macroscopically also show it microscopically. The elements (*i. e.*, portions of the cells) of growth colored are similar to those colored in staining growths from ordinary media. Double staining was noted in a few instances in growths from methyl blue-eosin Y and Wright's stain suspension media. The microscopic picture of dye media growth was in several instances superior to that obtained when specimens were stained from growth on ordinary media. If dye could be prevented from diffusing out of dye media cultures without destroying structure it is probable that the microscopic picture would be much more desirable.

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## Experimental Production of Bulbar Poliomyelitis.

JOHN A. TOOMEY.

*From the Department of Pediatrics, Western Reserve University, and the Division of Contagious Diseases, City Hospital, Cleveland, Ohio.*

Poliomyelitis has been experimentally produced in *Macacus rhesus* monkeys by injecting the virus into the ileum between clamps or subserosally in the same area.[1] Levaditi, Kling and Hornus[2] introduced the virus into the gastrointestinal tract of a *Macacus cyanomolgus* monkey and the animal later became ill with the disease. In the former instance,[1] the clinical picture was similar to that seen in the human being ill with spinal poliomyelitis. The animals developed palsy of muscle groups, monoplegia and paraplegia of the legs, but not the condition of quadriplegia that usually follows intrasciatic and intracerebral inoculations and intranasal instillations.

It has been shown that the virus spreads along the axis cylinders of the sympathetic thoracolumbar outflow.[3] It has also been pointed out that such a spread from the gastrointestinal tract directly to the cord by way of the afferent and efferent grey fibers has a simple and logical anatomical explanation.[4] It is an explanation that would also apply to typhoid fever, another gastrointestinal disease.[5] Al-

[1] Toomey, John A., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 680.

[2] Levaditi, C., Kling, C., and Hornus, G., *Compt. rend. Soc. de biol.*, 1933, **112**, 43; *A. J. Dis. Child.*, 1934, **48**, 423.

[3] Toomey, John A., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 502, 702.

[4] Toomey, John A., *Jaahrb. für Kinderheilkinde*, in press; *Am. Coll. Physicians*, April 18, 1934; *Annals Int. Med.*, in press.

[5] Toomey, John A., *A. J. Dis. Child.*, 1934, **48**, 1296.

though the hypothesis as to the mechanism of spread of the virus holds true in the average case of the spinal type of poliomyelitis, it cannot be used to explain the mechanism of the production of bulbar paralysis.

Histopathological examination of the autopsied material revealed findings similar to those of Harbitz and Scheel[6] in that I found marked involvement of the nuclei of the brain stem and medulla, especially in grey fibered areas, as well as increased vascular markings. One was not always fortunate enough to see cases of so-called bulbar poliomyelitis from the onset, but the histories, symptomatology and objective findings of 45 of the 440 cases admitted to Cleveland City Hospital all presented such evidence that it could be stated that the initial involvement in practically every instance was vagal in character, *i. e.,* accompanied by vomiting, followed by dysphagia, dysarthria and aphonia with other symptoms developing later to indicate a spread to other cranial nerves. The fact that the vagus is the motor nerve to the small intestine made it logical to suppose that absorption of the virus could take place not only along the thoracolumbar outflow, but, in some cases, along the vagus nerve as well, and that the spread of the virus in cases manifesting bulbar symptoms was along the vagal nerves directly to the nucleus ambiguous on both sides and from there to other locations.

The object of these experiments was to produce the disease in *Macacus rhesus* monkeys by way of the vagus nerve, to note the symptoms and signs in these animals and to determine if the histopathological picture was like that found in the human being who died of bulbar involvement.

Several postmortem examinations showed that the right vagus nerve is slightly larger than the left and perhaps easier to approach from an operative standpoint. Operations were performed on 2 animals under general anesthesia. The vagus was exposed just lateral to the isthmus of the thyroid, the nerve separated from the carotid sheath and irritated by clamping it a few times with a Kelly hemostat. Electrocardiograph records showed only a tachycardia.

Eight animals were used for the next experiment. The right vagus nerve was exposed and irritated by clamping it a few times with a hemostat; 0.2 cc. of a 1% solution of virus was injected. The needle, 30 gauge, (made specially by Vim McGregor Instrument

[6] Harbitz, F., und Scheel, O., *Pathologisch-anatomische Untersuchungen über akute Poliomyelitis und verwandte Krankheiten von den Epidemien in Norwegen,* 1903-1906. *Videnskabs-Selskabets Skrifter, I. Math-naturv. Klasse.* 1907. No. 5. Christiania. In Kommission bei Jacob Dybwad. 1907.

Co.) was drawn back and forth inside the sheath to expose and further irritate the axis cylinders. The nerve was ballooned out after the injections. The vagus is very small, but if its epineurium is not cracked the dose mentioned can be injected if it is done slowly over a period of from 3 to 5 minutes.

Monkey No. 263 looked sick on the 4th day; he had anorexia; he could jump up and down but could not hold up his head. When the head was moved, it flopped back to the chest wall and the right arm hung flaccid. There was furring also. On the 5th day, the animal's cry was hoarse. When food or fluid was placed in the posterior pharynx he could not swallow and he was extremely restless. He died suddenly on the 6th day without having shown any evidence of paralysis of the legs. Grossly, the postmortem examination was negative.

Monkey No. 268 was active for 3 days before he became sick; the right arm and legs became weak and there was furring. The entire right side became paralyzed. On the 8th day he was found dead. His cry was always shrill and clear. At autopsy a massive bilateral pulmonary tuberculosis complicated the picture.

Monkey No. 269 became sick, his cry was hoarse and there was furring on the 3rd day. He also had tachycardia and cyanosis of the mucosa of the lips and mouth. On the 6th day, he could neither cry nor swallow, his head hung limp on his chest and both arms were flaccidly paralyzed. He could jerk himself up to a standing position, however. He died that night. Grossly, postmortem examination showed marked dilatation of the vessels of the small and large intestines, a dilatation of the small intestine, an almost gangrenous area in one part of the large intestine, a central engorgement of the adrenals, and a solitary tubercle in one lung.

Monkey No. 271 was active the 1st and 2nd days after the operation. His cry was hoarse on the 3rd day. On the 4th day, he was weak; when he cried his voice was hoarse and aphonic, he could not swallow and there was furring. The right arm and leg were weak and he died that night. Grossly, the postmortem examination was negative save for marked vascular hyperemia of the small intestines.

Monkey No. 286 was active and apparently normal until the 9th day when he was found hunched up in a corner of his cage. There was furring and he was obviously ill. On the 10th day, he could not cry out or eat, and the muscles of the neck and both arms were paralyzed. When he stood up, his arms hung by his side. When his head was pushed about, it flopped back on his chest. When food

or fluid was put in the posterior pharynx he could not swallow. On the 11th day, both legs were paralyzed. He died this day. Grossly, there was nothing remarkable at autopsy save some pleuritic adhesions of the right lung.

Three other animals that were injected did not develop paralysis.

Objectively, monkeys Nos. 263, 269, 271, and 286 acted in a manner similar to that of human beings in that they evinced dysphagia, dysarthria and the paralysis of the muscles of the arm that is so commonly seen in cases of bulbar paralysis. This is easily understood, however, when it is remembered that the connection with the thoracolumbar outflow by way of the cranial sympathetic nerve is rather free and that an involvement of the phrenic nuclei is a possibility. Monkey No. 268 did not develop any bulbar symptoms apparently; even the electrocardiograph taken 10 minutes before death was recorded as being negative.

Postmortem sections were made through the lumbar, thoracic and cervical areas of the cord, through the inferior medulla, pontine angle, middle of the pons, superior and inferior colliculus, vermis, dentate nucleus, the basal nuclei and the motor cortex. They were stained by hematoxylin and eosin and Nissl's stain.

The histological results will be described more in detail elsewhere. Briefly, they were similar to those found in cases of bulbar poliomyelitis in human beings.

As the virus has an obligate affinity for grey fibers, it would be illogical to expect typical central vagal involvement in all experiments since the virus may just as well pass down as up the vagus nerve. The important point is that it can pass up the vagus nerve in some animals and experimentally produce the typical objective picture and the histopathological findings of bulbar poliomyelitis, thus lending further credence to the belief that the disease primarily originates from the gastrointestinal tract. If the virus runs up inside the vagus nerve until it loses its myelin sheath, one would expect to find the virus spilling over into the local grey matter of the medulla, pons and the base of the brain. Such an absorption along the vagi to the medullary area with secondary involvement of other nerve nuclei by contiguous extension explains the entire clinical picture in these cases of bulbar poliomyelitis in the same manner as absorption along the thoracolumbar outflow to the cord explains the usual spinal type of poliomyelitis.