anesthesia became less deep. We will reserve the discussion of these matters for a later paper.

ALFRED L. LOOMIS
E. NEWTON HARVEY
GARRET HOBART

LOOMIS LABORATORY
TUXEDO PARK, N. Y.

INTRANASAL OR GASTROINTESTINAL PORTAL OF ENTRY IN POLIOMYELITIS[1]

IN a recent issue of SCIENCE, Faber[2] reported data on 57 monkeys in which poliomyelitis virus had been introduced intranasally. His facts are admitted. He concluded that, since the virus passed through the brain stem and spinal cord from above downward, and because the virus was found present in all levels of the cord just before paralysis appeared, no explanation of the usually earlier and greater paralysis of the lumbar area was possible other than that offered by Fairbrother and Hurst,[3] *i.e.*, that the virus usually involves the anterior horn cells of the lumbar area because of greater susceptibility of these cells. Shall we deduce, then, that in cases with only bulbar poliomyelitis or only cervical horn cell involvement or only seventh nerve palsy the lumbar motor areas of these patients are not susceptible, or that in these particular patients the motor cells of those areas involved are more susceptible? How does one explain why the cervical enlargement is often hit later, *i.e.*, after the lumbar area has already become involved? With the theory of susceptibility, one would have to think that there are degrees of motor cell susceptibility depending upon location and involvement. If the cells of the lumbar area have such a high degree of susceptibility they should respond promptly to local injection of virus into the lumbar area of the experimental animal. But they do not thus respond, for even when the virus is injected directly into this enlargement, there is a delay before the disease is produced.[4]

I feel that in the monkey the disease results when two factors combine and the combination material destroys motor cells. One of these factors is monkey cord virus and the other is the toxic material produced in the animal's gut. In the human being the causative agent usually enters the digestive system "ready made," *i.e.*, it is already combined and capable of producing cell destruction immediately. All the vagaries of the disease both in the *M. rhesus* monkey and the human being, even the reason why the lumbar area seems usually to be first involved, are easily understood in the light of this theory. Much experimental and clinical work has been done that points to a relationship between the gastrointestinal tract, the sympathetic nervous system and the production of the experimental disease.[5] But ignoring this evidence, what else can be said? When virus is given either intracerebrally or intranasally, the experimental animal usually gets quadriplegia and dies. Poliomyelitis is thus produced, but even though this is poliomyelitis, *it is not the kind of poliomyelitis that is seen in the human being.* Our objective should be not only to produce the disease, but to produce it as it appears clinically. If we can produce poliomyelitis in the experimental animal in the same way as it is seen in the human being, it is plausible to suppose that the route taken to produce it in the monkey might be the same as that taken by the virus in the human being.[6,7]

Faber further states that the theory of gastrointestinal invasion has few remaining advocates since the very convincing study of Clark, Roberts and Preston.[8] The facts shown by these workers do not rule out the gastrointestinal tract as a probable portal of entry. Clark, *et al.*, put virus into the intestines of monkeys that are normally not susceptible to poliomyelitis, and they did not produce the disease. When one realizes that poliomyelitis virus acts almost like an enzymic catalyst with an obligate affinity for gray fibers and that the natural disease can be produced only when the axis cylinders of the gray fibers contact the virus and absorb it, it is easy to understand why these workers did not produce the disease. When I caused the virus to come in contact with these fibers, the disease was easily produced.[6]

The fact that intranasal inoculation is unsuccessful if the connection between the gray-fibered olfactory nerve and central nervous system is severed is interesting. However, transection of the olfactory nerve would be of importance only if such section made it impossible for us to produce the disease by the gastrointestinal tract.

If our theory as to the production of paralysis in the monkey is right then it is obvious that passive immune serum of great value can not be obtained by injecting monkeys with the virus alone. A high-titered antiserum was rapidly produced by injecting

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

[2] H. K. Faber, SCIENCE, 82: 42, 1935.

[3] R. W. Fairbrother and E. W. Hurst, *Jour. Path. and Bact.*, 33: 17, 1930.

[4] J. A. Toomey, *Proc. Soc. Exp. Biol. and Med.*, 32: 1185, 1935.

[5] *Idem, Annals Int. Med.*, 8: 854, 1935. *Jour. Prev. Med.*, 6: 379 and 397, 1932. *Proc. Soc. Exp. Biol. and Med.:* 30: 1082, 1933; 31: 502, 680, 702, 1015, 1934; 32: 423, 869, 1935. *Am. Jour. Dis. Child.:* 45: 1211, 1933; 46: 730, 1933; 47: 573, 1934; 48: 30, 1934. *Jour. Inf. Dis.*, 54: 74, 1934.

[6] J. A. Toomey, *Proc. Soc. Exp. Biol. and Med.*, 31: 680, 1934.

[7] *Idem, Proc. Soc. Exp. Biol. and Med.*, 32: 628, 1935.

[8] P. F. Clark, D. J. Roberts and W. S. Preston, Jr., *Jour. Prev. Med.*, 6: 47, 1932.

a sheep with these combined factors—virus and enteric toxin[9]—and recently we have produced paralysis in a horse by injecting these combined elements.

JOHN A. TOOMEY

HEMORRHAGIC NECROSIS AND REGRESSION OF SARCOMA 180[1]

BACTERIAL substances capable of eliciting the phenomenon of local skin reactivity to bacterial filtrates in rabbits[2] produce, upon intravenous injection, hemorrhagic necrosis and regression of transplantable malignant tumors of guinea pigs,[3] mice and rats.[4] There is, however, a high death rate in animals thus treated.

In experiments on the phenomenon of local skin reactivity to bacterial filtrates in rabbits it was observed that, in certain proportions, mixtures of *B. typhosus* culture filtrates with homologous antisera possess a high phenomenon-producing and low lethal potency. Studies were then made on the effect of single intravenous injections of these mixtures and of toxic filtrates alone upon 132 mice bearing twelve days old sarcoma 180. Best results were obtained with a mixture of 300 *B. typhosus* reacting units with 200 neutralizing units of antityphoid horse serum[5] tested in 27 mice. There was no early mortality (*i.e.*, 24 hours after the intravenous injection). Late mortality (*i.e.*, 2 to 20 days after the intravenous injection) occurred in 5 mice. Prompt hemorrhagic necrosis took place in 23 mice and complete regression of tumors with uneventful healing in 21 of these mice. According to Woglom,[6] untreated mice show only 1.33 per cent. of spontaneous regressions. As the amount of filtrate in mixture with 200 neutralizing units of the serum was increased, there occurred early mortality and a roughly proportionate rise in late mortality. The incidence of complete regressions of tumors of surviving mice was approximately the same. Doses of 125 and 250 reacting units of the filtrate alone (*i.e.*, without the serum) elicited early mortality as high as 70 and 95 per cent., respectively.

It becomes obvious from these experiments that in certain proportions mixtures of *B. typhosus* filtrates with homologous antisera possess a comparatively low lethal potency and yet elicit prompt and intense hemorrhagic necrosis with subsequent complete regression of sarcoma 180 in a high percentage of mice well above normal expectancy. Further work is under way in order to determine the effect of these and other combinations of bacterial filtrates with immune antisera upon animal and human spontaneous tumors.

GREGORY SHWARTZMAN

SCIENTIFIC APPARATUS AND LABORATORY METHODS

A THYRATRON CONTROL FOR INCUBATORS AND WATER BATHS

THE use of an electromagnetic relay for the control of heating elements in incubators and water baths has two fundamental disadvantages. (1) The current required to operate even highly sensitive relays is more than is desirable at the mercury platinum junction of the thermoregulator. This can be corrected by the use of an amplifying vacuum tube, but adds to the complexity of the set-up without avoiding the second disadvantage. (2) Any relay, no matter how well made, is apt to stick and possibly ruin an extensive experiment. This can be avoided by using a duplicate relay and thermoregulator, but again the system is complicated. These disadvantages are obviated by the use of a thyratron to replace the amplifying tube and relay. For this purpose we have used a General Electric Thyratron, FG154, which is a four-electrode, Argon-filled, low-grid current control tube. This tube is rated to carry a current of 2.5 amps. continuously, which is sufficient for the temperature control of most incubators and the average water bath. Under ordinary conditions, with currents not exceeding the maximum rated value, a tube may be expected to serve for at least one year. Another tube, FG98, capable of carrying .5 amps., is available for smaller incubators or temperatures near to that of the room.

The figure gives a wiring diagram of the set-up used. The tube has six terminals, four which fit into the base and are lettered F, F, P and G. F and F connect with the ends of the filament and P with its midpoint. G connects with the shield grid. The terminal of the control grid is at the side of the tube and the terminal of the anode at the top. The heating unit may be in any desired form. The filament transformer must be capable of delivering 35 watts at 5.0 volts A.C., and the filament current should be as nearly constant as possible to ensure a long life for the tube. The two batteries may be dry cells. The current drawn from them is so small that they may be expected to last approximately their "shelf life."

[9] *Idem, Proc. Soc. Exp. Biol. and Med.*, 32: 1346, 1935.

[1] From the laboratories of The Mount Sinai Hospital, New York City. Preliminary report. This investigation has been aided by a grant from the Josiah Macy, Jr., Foundation.

[2] G. Shwartzman, *Jour. Exp. Med.*, 48: 247, 1928.

[3] Gratia and Linz, *C. R. Soc. Biol.*, 108: 427, 1932.

[4] G. Shwartzman and N. Michailovsky, *Proc. Soc. Exp. Biol. and Med.*, 29: 737–741, 1932; D. Duran-Reynals, *Proc. Soc. Exp. Biol. and Med.*, 31[1]: 341, 1933–34; K. Apitz, *Ztsch. f. Krebsforst.*, 40[1]: 50, 1933.

[5] G. Shwartzman, *Jour. Exp. Med.*, 52: 781, 1930.

[6] William H. Woglom, personal communication.