virus rather than its neutralization by antibody. The optimal time to collect cord tissue for both infection and immunization is at the height of paralysis.

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Active Immunization of Human Beings with Tetanus Toxoid.

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(Introduced by W. H. Park.)
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Apparently the first attempt at active immunization of man was made by Louis Bazy[1] working with Vallee. He gave iodized tetanus toxin obtained from Ramon at the Pasteur Institute to wounded soldiers. Three injections were given 5 days apart and 10 days after the last injection the men were bled and 1 cc. of the serum of each individual examined at the Pasteur Institute was found to contain from 10 to 100 "units" of tetanus antitoxin. In 1927 Ramon and Zoeller[2] used tetanus anatoxin, toxin treated with formaldehyde, and then incubated. They injected several hundred subjects. The greatest immunity was obtained by giving 0.5 cc. of anatoxin, 1 month later 1 cc. and 2 weeks later 1.5 cc. The immunity acquired was apparently so great that 1 cc. of the subject's serum neutralized 500 to 1,000 minimum lethal doses for a guinea pig. Twelve to 18 months later the immunity was still higher. After 1 to 2 years a single injection of anatoxin, the so-called "injection de rappel", resulted in a great increase in antitoxic power of the serum. 1 cc. of the serum neutralized 10,000 minimum lethal doses. The process of active immunization can not be hurried by shorter intervals between injections or large doses of anatoxin.

In May, 1930, we assembled 18 volunteers, 5 adults 18 years and over, and the rest children varying from 5 years up, who were bled and no trace of tetanus antitoxin found in their blood sera. At weekly intervals 3 doses of tetanus toxoid, made by treating the toxin with 0.4% formalin and incubating at 38° for 10 days, were injected intramuscularly. The injections were painful for about 5

[1] Bazy, L., *La Medecine*, 1926, **8**, 26.

[2] Ramon and Zoeller, *Comp. Rend. des Seances et Mem. de la Soc. de Biol.*, 1929, **100**, 92.

minutes, but no general reactions occurred and no local ones beyond moderately sore arms. Four to 8 months later the individuals were bled again and the sera of 4, all children, contained definite amounts of tetanus antitoxin, 1 cc. of serum neutralizing 1 to 2 minimum lethal doses for guinea pigs. The rest contained traces of antitoxin, appreciable because the test guinea pigs survived the control pigs by several days.*

Six months later 5 of the subjects with no measurable amount of antitoxin were reinjected; 2 with 4 doses of 1 cc. of toxoid at weekly intervals; 2 with 3 injections of 1 cc. at weekly intervals, and 1 adult with 4 doses of 1 cc. at monthly intervals. The sera of the first 2, tested 7 and 8 months after the injections, neutralized 50 and 75 minimum lethal doses per cc.; the sera of the 2 cases receiving 3 doses each, tested 6 months later, in 1 case neutralized 25 minimum lethal doses and in the other still showed only a trace of antitoxin. The serum of the adult neutralized 40 minimum lethal doses per cc. Of the 7 cases showing a trace of antitoxin after the first series of injections and were not reinjected, 6 were retested 12 to 18 months after the first test. Three adults and 1 child still showed only a trace but 2 children had sera neutralizing 5 minimum lethal doses to the cc. Of the 4 children who had definite amounts after the first series of injections and were not reinjected, 3 were retested after 18 to 19 months and in all there was an increase in the antitoxin content. Just recently we have retested the blood of 13 of those originally injected 3 years ago. Of the 4 individuals who acquired immunity after 1 series of injections, 2 were retested and both still showed marked amounts of antitoxin. In addition 2 subjects who had only a trace of antitoxin after the first injections and were not reinjected, now after an interval of 3 years have appreciably increased the antitoxic contents of their sera.

Of the 6 individuals reinjected 18 months ago, 4 were recently retested. The child who developed no immunity after the second series of injections still has none. The other 3 still have large amounts of antitoxin. One adult lost some of his immunity and 1 child more than doubled the antitoxic content of the serum.

This series is very small. Several facts, however, stand out. It is possible by injection of tetanus toxoid in small doses at weekly

* The method of testing used was to combine each cc. of serum or fraction thereof with varying amounts of toxin. This was allowed to stand one-half hour and was then injected subcutaneously into 350 gm. guinea pigs and the results compared with the control guinea pigs.

intervals to create in the blood tetanus antitoxin which remains without further injections for at least 3 years. It is interesting to note that 1 child of 5 years was not immunized after 2 series of injections, but who, nevertheless, had become immune to diphtheria as judged by the Schick test, from 3 injections of diphtheria toxin antitoxin. The Department of Health has had similar experience with horses whose ability to make different kinds of antitoxin may vary.

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Histopathology of Central Nervous System of Mice Inoculated with Poliomyelitis Virus.

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Harmon, Shaughnessy and Gordon[1] reviewed the contradictory results of former authors in inoculating rodents with the virus of poliomyelitis. They reported that after intraperitoneal or intracranial injection of the virus into mice the majority of them died sporadic deaths. The autopsy revealed gross lesions of lung consolidation, "but no microscopic sections were prepared from the tissues of mice".

The brain and spinal cords of 12 mice which had been injected with poliomyelitis virus by Dr. Nungester[2] together with those of 7 controls were cut serially and longitudinally and stained with cresylviolet. Four of the inoculated mice did not show any inflammation of the central nervous system. In 3 others mild inflammatory reactions in isolated segments of the dorsal and lumbar spinal cord were found in the form of perivascular leucocytic infiltration of one or 2 rows of cells and of a mild meningitis at the posterior surface in one case. In 3 other mice the leucocytic infiltration had spread into the posterior and anterior gray and was combined with hemorrhage into the anterior horns, mild increase in glia nuclei and meningitis along the spinal nerve roots. In 2 mice which had been injected with virus after passage through 3 gener-

[1] Harmon, Paul H., Shaughnessy, Howard J., and Gordon, Francis B., *J. Prev. Med.*, 1930, **4**, 98.

[2] Nungester, W. J., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1128.