sisted of two fine aluminum grids separated by a quartz disk 1 mm thick which had a 19 mm hole in the center. This was immersed in the liquid contained in a thin shallow glass dish which was in turn set into the wax surface. Fields up to 70,000 volts per cm showed that the "effective volume" was given by the geometric volume between the grids for separations from 0.5 to 2.5 mm. The radium, contained in a glass tube 8 mm long and .27 mm thick, was supported about 16 mm above the liquid surface and filtered with .75 mm brass plus 2 mm of bakelite. Applying approximate corrections for distance and filtration, the ionization produced by 1 mg of radium filtered with 1 mm of lead and at a distance of 1 cm from the wax surface was found to be 9400 e.s.u./cm³/hr. Assuming that the gamma ray absorption is proportional to the density of the liquid or gas and that the energy per ion pair is 24 electron volts as compared with 33 for air,[2] the above ionization would correspond to 6.9 roentgens per hour. Measurements made with the cell removed from the wax phantom showed the ionization to be almost entirely due to primary radiation. Similar measurements of the ionization produced in a mixture of CS_2 and ligroin (density = 1) by x-rays of equal doses generated at 120 kv and filtered with about .2 mm of copper gave an increase of about 30 per cent. due to back scattering as compared with 38 per cent. using a thimble ionization chamber calibrated in the usual manner. Since it is impossible to calibrate a thimble chamber for the radiation quality produced in the back scattering, the disagreement between the air and liquid measurements is not unexpected. Measurements made as here described in suitable liquids are independent of the radiation quality and hence the chambers need no calibration. While the above method seems well adapted to evaluating radium dosage in roentgens, the preliminary values given above are being investigated further in an endeavor to minimize the corrections.

LAURISTON S. TAYLOR
F. L. MOHLER
DEPARTMENT OF COMMERCE
NATIONAL BUREAU OF STANDARDS

TRANSMISSION OF THE VIRUS OF POLIOMYELITIS TO MICE

THE purpose of this paper is to report the successful propagation and serial transmission of the virus of poliomyelitis in mice. The mouse was chosen for this study for reasons described by one of us.[1]

Three series of mice were exposed to short repeated doses of x-ray and then inoculated, both intracerebrally and intraperitoneally, with suspensions of the spinal cords of monkeys, who had succumbed to poliomyelitis. In the first series, the animals were irradiated daily for 10 days prior to inoculation. On the second day after inoculation, x-ray treatments were begun again and were given daily for 8 days. On the eleventh day after injection, all the mice showed ruffled hair, sluggishness and dragged their hind legs, either on that day or the following one. Four of the animals died on the eleventh day, one on the twelfth, three on the sixteenth and three on the seventeenth day after inoculation. Two were autopsied on the eleventh and twelfth days. A suspension of their brains, when inoculated into mice and a monkey, failed to produce reaction.

In the second series, on the eleventh and twelfth day after inoculation they showed ruffled hair, ataxia, sluggishness and dragged their hind limbs. The animals in this group died or were killed. A suspension of their brains produced similar symptoms after an incubation period of from 14 to 24 days, in 5 out of 8 untreated mice, which were injected. A monkey inoculated with this suspension showed a rise in temperature. Serial passages were carried out, using mouse brains as the inoculum. Thus far, the virus has been maintained through 17 generations. With succeeding passages, the animal response became more definite and the incubation period became shorter; so that by the fifth passage, a 10 per cent. suspension brought down all the animals after an incubation period of 3 days. Using more concentrated brain suspensions, the incubation period may be shortened to 2 days, and with diluted suspensions it may be lengthened to 7 days. By successive transfer, the infectivity of the virus has been increased, so that by the twelfth passage it was infectious in a dilution of 1:1000.

In the third group, 4 out of 7 mice, inoculated with the brain material of irradiated mice that had succumbed, showed symptoms similar to those of the mice in the second series. Fifty control animals that were exposed to x-ray, but were not injected, developed no symptoms, although some of them received twice as many x-ray treatments as did the inoculated mice. When the filtrate of the suspension of the brains of 2 of the animals that came down with the aforementioned symptoms was injected into 8 untreated mice, 7 of them showed the usual hyperirritability, ataxia, sluggishness, ruffled hair and humped back. A monkey, inoculated with this filtrate, ran a typical course of poliomyelitis, with a characteristic histopathological picture in the cord. In the next passage, all twelve mice injected showed symptoms after an incubation period of 3 to 4 days. This series has undergone 14 transfers with changes of infectivity and incubation period, similar to those of the preceding series.

[1] M. Brodie, *Proc. Soc. Exp. Biol. and Med.*, March, 1935.

Now that the virus is fixed, the clinical picture in the mouse is quite acute. It begins with irritability, jumpiness, ruffled hair and goes on to ataxia, humped back, convulsions, circular movements, twisting of the head and sometimes ptosis of the eyelids. The animals usually die within a few hours after the onset of symptoms. The mice also can be infected by the intranasal route with an incubation period of 5 to 6 days.

In contradiction to the lesions in human and monkey poliomyelitis, those in the mice occur mainly in the brain and meninges, rather than in the spinal cord. In the pia-arachnoid and its projections there is an extensive mononuclear infiltration, mostly perivascular, which is most marked over the brain. In the spinal cord and brain stem, there is an occasional perivascular collar and some hemorrhagic foci; the cerebellum shows no changes; while the cerebrum shows perivascular collars, areas of hemorrhage, focal areas of necrosis and glia reaction with a rare polymorphonuclear leucocyte.

As in the monkey, the virus appears to be in the cerebro-spinal axis only. It is present in the cerebrum, brain stem, cord and cerebellum. The greatest concentration of the virus is in the cerebrum, which is in keeping with the distribution of the histopathological changes.

The following findings indicate that we are dealing with poliomyelitis and not a spontaneous virus infection of mice.

(1) The mouse virus was transferred to 13 monkeys and was infective in a dilution of 1:5000. A transfer of the virus from one of these monkeys to another monkey and back again to mice was successful. A complete histopathological study of the cords of four of these monkeys showed changes typical of acute anterior poliomyelitis.

(2) The serums of convalescent humans and monkeys, of actively immunized children and the serum of a so-called normal adult, containing anti-viral substance, neutralized this virus. Normal monkey serums failed to do so. Human convalescent serum protected a monkey against the virus and neutralized suspensions of cords removed from monkeys infected with the mouse virus. Upon diluting the serums, it was possible to obtain an end point in keeping with similar tests carried out in monkeys.

(3) Poliomyelitis in mice differs both clinically and histopathologically from the spontaneous mouse encephalomyelitis described by Theiler,[2] who kindly sent us some of his virus. The infectivity of the latter is irregular and its injection is followed by an incubation period of from 3 to 4 weeks. This spontaneous disease in mice runs a more protracted course with slowly progressing paralysis. The distribution of the virus in the cerebrospinal axis and the histopathological picture are also different from that of the mouse poliomyelitis.

One of us[3] has described the immunization of monkeys and children against poliomyelitis. However, the incidence of the disease is so low and the preparation of the vaccine so expensive that its application is limited. It has been found that not only convalescents, but also many normal children, even in the susceptible age group, have antiviral substances in their blood. Vaccination should be limited to those without any antibody. At present a test for antibody can be carried out only in monkeys. Results of preliminary experiments, in that they check with those of identical tests in the monkey, indicate that such a test can be carried out in the mouse. Thus it may be possible to use mice instead of monkeys to determine those who require vaccination and the results of the immunization.

In the mouse, the disease differs from that in the monkey, since in the smaller animal it is a meningo encephalomyelitis. The virus has lost its affinity for nerve cells, for it affects mainly the connective tissue elements of the central nervous system.

We believe that the outcome of the foregoing studies show that the virus of poliomyelitis has been transmitted successfully through mice by serial passage.

MAURICE BRODIE
SAMUEL A. GOLDBERG
PHYLLIS STANLEY

UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL SCHOOL, AND PRESBYTERIAN HOSPITAL, NEWARK, N. J.

[2] M. Theiler, SCIENCE, 80: 122, 1934.

[3] M. Brodie, *Jour. Immun.*, 28: 1, 1935; *Am. Jour. Pub. Health*, 25: 1, 1933.

BOOKS RECEIVED

BLACKWELL, C. P. *Applying Science to Agriculture.* Pp. 318. 42 figures. Agricultural Experiment Station of the Oklahoma A. and M. College.

CHAMBERLAIN, CHARLES J. *Gymnosperms: Structure and Evolution.* Pp. xi + 484. 396 figures. University of Chicago Press. $4.50.

DIRAC, P. A. M. *The Principles of Quantum Mechanics.* Second edition. Pp. xi + 300. Oxford University Press. $6.00.

LIEBEN, FRITZ. *Geschichte der Physiologischen Chemie.* Pp. x + 743. Franz Deuticke, Leipzig. M 23.

MARSH, J. S. *Principles of Phase Diagrams.* Pp. xv + 193. 180 figures. McGraw-Hill. $3.00.

MORROW, CLARENCE A. *Biochemical Laboratory Methods for Students of the Biological Sciences.* Revised and rewritten by WILLIAM M. SANDSTROM. Pp. xv + 319. 37 figures. Wiley. $3.75.

POMFRET, JOHN E. *The Geographic Pattern of Mankind.* Pp. xv + 428. 15 figures. 21 plates. Appleton-Century. $4.00.