

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

² M. Theiler, *SCIENCE*, 80: 122, 1934.

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 us³ 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 meningoencephalomyelitis. 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.

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

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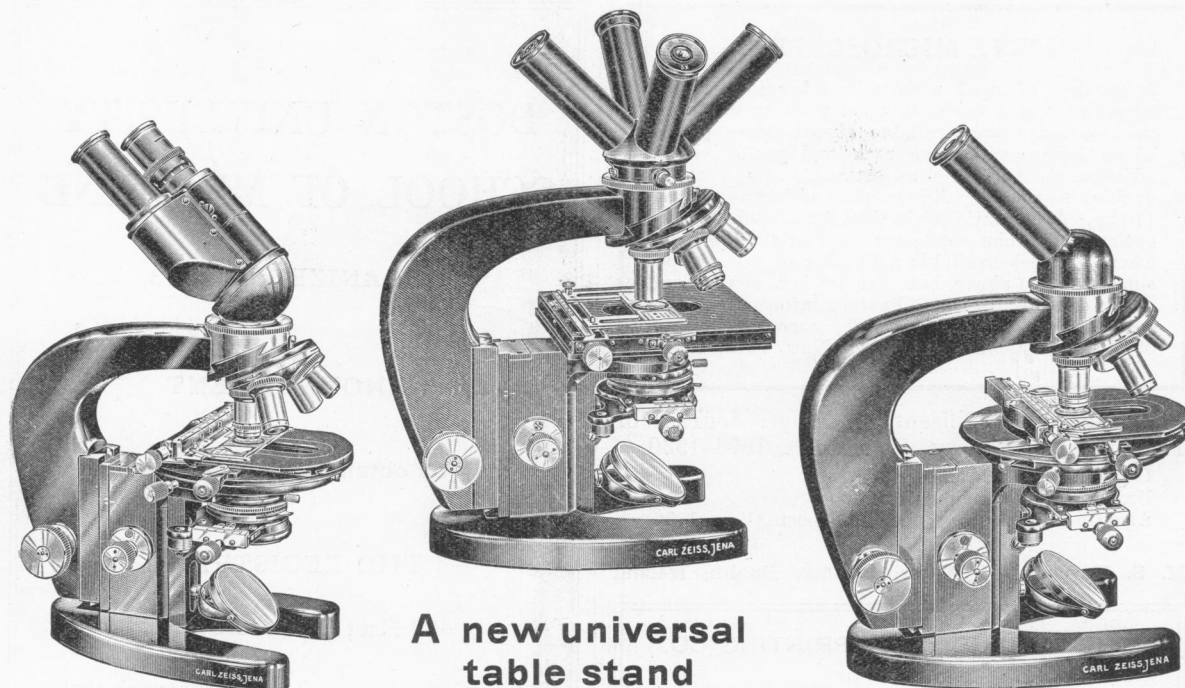
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